Optimizing anesthesia techniques in the ambulatory setting

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Cover design: a country road somewhere in Kerry, Ireland, representing the 'road home' for patients after ambulatory care

Optimizing Anesthesia Techniques in the Ambulatory Setting

Optimaliseren van anesthesietechnieken tijdens ambulante zorg

Proefschrift

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Chapter 1

Introduction

Ambulatory surgery refers to the process of admitting patients, administering anesthesia and surgical care, and discharging patients home following an appropriate level of recovery on the same day. The word ambulatory is derived from the latin word *ambulare,* which means ''to walk''. This means that patients treated on an ambulatory basis do not require hospitalisation and achieve a level of postoperative 'home readiness' that allows them to go home within hours of procedure completion.

The change in emphasis from inpatient to ambulatory surgical practise is one of the most significant developments in medicine during the last two decades (1). The advantages of ambulatory anesthesia and surgery are well documented. Patients benefit in terms of faster mobilization, which allows earlier return to daily activities. Shorter hospitalisation time reduces the risk of complications such as hospital acquired infections. Greater patient convenience and reduction in stress is achieved through dedicated elective procedure scheduling and absence of emmergency cases which may lead to surgery cancellation. Hospitals benefit because ambulatory procedures have been shown to be more efficient than inpatient care and thus more cost effective (1). Currently, ambulatory surgery and anesthesia is one of the most rapidly developing areas in the practise of medicine and this is reflected in the international trend towards a reduction in inpatient hospital beds (2). In the Netherlands, for the period 1998 to 2005, inpatient hospital beds have been reduced by approximately 1000 beds per year (figure 1). Procedures performed in the ambulatory setting represent the majority of elective surgery cases in many countries (3). It is estimated that in excess of 50% of all elective surgery in developed countries now takes place in the ambulatory setting and in some countries, this figure is as high as 75% (4).

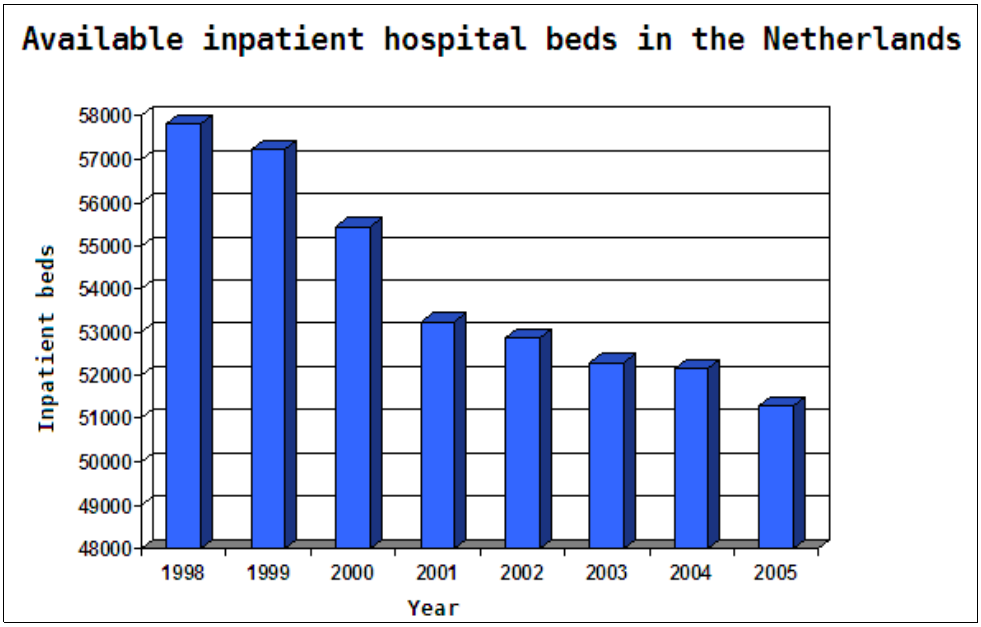

Figure 1.

History

The practise of ambulatory anesthesia and surgery is not in itself new, first literature reports of ambulatory anesthesia occurred in the late 19th century, when James Nicoll documented the successful administration of 8988 ambulatory anesthetics in Glasgow during the years 1899 to 1908 (5). Over the following half centuary, there was little organized effort to pursue outpatient surgery and anesthesia, and few papers devoted to ambulatory practise were published until 1959, when Webb and Graves published a paper describing 10 years of experience in providing anesthesia for outpatient surgical cases (6). Shortly afterwards, in 1962, an outpatient surgical clinic was opened within the hospital of the University of California, Los Angeles.

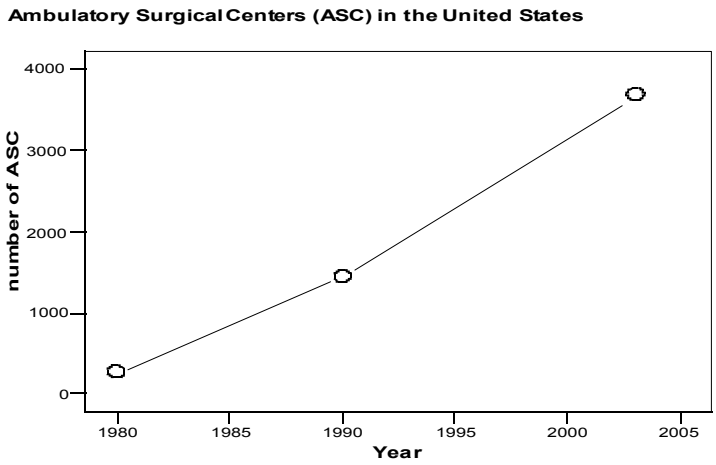

Figure 2. The rate of development of ambulatory practise in the United States.

In 1970, two anesthesiologists, Reed and Ford, opened the first ambulatory surgical centre in Phoenix, Arizona, which was not affiliated with an acute care hospital. In 1984, the society for ambulatory anesthesia (SAMBA) was organized as the first and only specialty within the American Society of Anesthesiologists dedicated to ambulatory anesthesia (7,8). Since that time, the creation of specialized ambulatory surgery centres, with or without a direct connection to academic medical centres has expanded dramatically within the United States, Figure 2.

However, it is only since the 1990´s that ambulatory practise has begun to truly develop on an international level. Up until then, ambulatory patients undergoing relatively short duration, low complexity procedures were generally 'sandwiched' on inpatient operating room schedules between longer duration, higher complexity, inpatient procedures. Such practise included little specific effort to address the needs of ambulatory patients and it is well recognised that mixed inpatient and outpatient programmes do not achieve the same high

standard of patient care as dedicated ambulatory programmes (9).

Outcome measures

The rate of expansion of ambulatory surgical centres, supports the notion that ambulatory anesthesia and surgery is acceptable to both patients and care providers. Ambulatory practise has a good safety record with low levels of morbidity and mortality (10) and low reported hospital readmission rates (11,12). However, on closer inspection, it is apparent that techniques used in ambulatory surgery and anesthesia are not as yet optimal. This is supported by published data, indicating a significant incidence of post discharge symptoms such as pain, post operative nausea and vomiting (PONV), dizziness, tiredness, hoarseness, throat morbidity etc... The occurrence of symptoms varies considerably, depending on the type of procedure performed and the patient population studied (13,14,15). While such symptoms are generally not severe enough to require readmission to hospital, they often lead to unplanned medical contacts by phone or in person, increased costs to the patient and delayed resumption of normal activities. They are thus, an indication that ambulatory techniques require further investigation and adjustment.

Contribution of anesthesia to ambulatory practise

While, it may be true to say that the expansion of ambulatory surgical practise in recent years has been driven to a large degree by rising hospital costs and the economic savings arising from same day patient home discharge after anesthesia and surgery, it is the recent advances in both surgical and anesthesia practise which allow such development to proceed safely. From a surgical aspect, there is a shift towards less invasive surgical procedures, with obvious benefits for patients. Likewise, anesthesia practise is continuously evolving

through better preoperative patient optimisation, integration of newer anesthetic agents with better recovery profiles into standard practise and expanding the use of locoregional anesthesia techniques. Indeed, the choice of anesthesia technique has been shown to be one of the most important determinants of same day home discharge in adult patients (16). The appropriate choice of anesthesia affects not only the duration of stay and unplanned hospital admissions, but also patient satisfaction and hospital cost savings (17).

Naturally, many of the challenges faced in the ambulatory and inpatient setting are similar. Indeed, developments in the ambulatory setting may be beneficially transferred to in-hospital anesthesia practise (18). One such example is that of anesthetist as perioperative physician, a role well developed in ambulatory anesthesia practise. Anesthetists are actively involved in confirming the suitability of patients for treatment on an ambulatory basis, ensuring that the possibility of patient cancellation on the scheduled day of surgery are minimised (19). Similarly, following anesthesia and surgery, confirmation of patient suitability for same day home discharge is established by both anesthetic and surgical discharge criteria.

New technique development

In order to ensure continued safe and efficient expansion of ambulatory care, investigation and development of techniques is essential. New techniques, devices, and pharmacological agents are being continuously developed and may offer benefits to patients treated on an ambulatory basis. A prerequisite of any new technique is that it contributes to the safe delivery of good intraoperative anesthetic and surgical conditions, coupled with a rapid and pain controlled recovery with a minimal of adverse side effects. Anesthesia is multifaceted, and no one technique has evolved as the gold standard for all

patients. The increasingly varied patient population presenting to ambulatory centres requires the development of techniques offering benefit to individual patients in specific circumstances. Optimisation of anesthesia practise in terms of offering a greater range of safe and effective techniques, better recovery profiles, better pain control and less post operative morbidity is essential.

To maintain high levels of safety, efficiency and patient satisfaction, fine tunning of many aspects of the anesthesia process is required. The purpose of new techniques should be, to ultimately allow a broader range and greater number of patients access to the benefits of having surgery performed safely in the ambulatory setting. As stated in the reccommendations for ambulatory anesthesia practise, ´each anesthetist should develop techniques that permit the patient to undergo the surgical procedure with minimum stress, maximum comfort and optimise their chance of early discharge´ (3).

This thesis is based on clinical studies which focus on optimisation of both technical and pharmacological aspects of anesthesia practise in the ambulatory surgical setting.

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Outline of the thesis

This thesis focuses on a number of aspects of anesthesia practise of particular concern in the ambulatory anesthesia setting. Chapters 1, 2 and 3 focus on technical aspects of ambulatory anesthesia. The first 2 chapters deal with methods which allow accurate and objective identification of locoregional block outcomes. Measurement of temperature using infrared thermography and peripheral flow index using a pulse oximetry probe are compared to traditional methods of patient response to pinprick and cold sensation as a means of identifying successful and failed blocks. Study results and the advantages of such objective techniques are discussed.

Chapter 3 decribes a randomised controlled study, comparing 2 different types of supraglottic airway device in terms of insertion characteristics, adequacy of ventilation and postoperative morbidity.

Chapters 4 and 5 focus on pharmacological aspects of ambulatory anesthesia practise. Chapter 4, is concerned with determining the optimal dose of remifentanil for use in patients undergoing extra corporeal shock wave lithotripsy. Closer attention to delivering optimal levels of analgesia offer definite benefits to patients in terms of limiting adverse side effects which may contribute to delayed patient discharge, increased costs and lower patient satisfaction scores.

Chapter 5, describes a double blind randomised placebo controlled trial. The study investigated the potential benefits in terms of recovery characteristics, of modafinil, a drug traditionally used in the treatment of narcolepsy, to patients receiving sedation and analgesia.

Chapter 2

Thermographic temperature measurement compared to pinprick and cold sensation in predicting the effectiveness of regional blockades

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Abstract

We designed this study to evaluate the usefulness of thermographic temperature measurement with an infrared camera, compared with patient response to cold and pinprick, as a means of assessing the success or failure of axillary blockades. Axillary blocks were performed on 25 patients undergoing surgery on the hand or forearm using a nerve stimulator technique with mepivicaine 1.5%. Pinprick and cold sensation were assessed on the operative site at 5-min intervals for 30 minutes. A thermographic image of the operative limb was recorded at similar time intervals. Thermographic images of the unblocked limb were taken before block placement and at 30 min. Temperature values at the operative site and unblocked limb were calculated from the thermographic images. Results revealed that thermography had higher combined values for sensitivity, specificity, and positive and negative predictive values that both cold and pinprick at all time intervals, with statistically significant differences at 15 min (thermography versus cold, P = 0.006; thermography versus pinprick, P = 0.026) and 30 min (thermography versus cold, P = 0.038; thermography versus pinprick, P = 0.040). For thermography as a method of block assessment, an optimal time of 15 min after mepivicaine local anesthetic injection gives the highest combined values for predicting a successful block (P = 0.004). We conclude that thermography provides an early and objective assessment of the success and failure of axillary regional blocks.

Introduction

Various assessment methods are used to determine the adequacy of perineural block techniques, such as the patient's response to the sensations of cold and pinprick (1,2). A review of regional techniques by Curatolo et al.(3) stated that no standard method of applying these assessment techniques appears to exist. Moreover, sensitivity, specificity, and predictive values of such sensory tests in relation to surgical stimuli have not been investigated and may provide useful information for daily clinical practice (3).

A successful block occurs when a local anesthetic agent blocks both sensory and sympathetic nerve fibers (4). Sensory A (δ) fibers are assessed using tests such as response to cold (4,5) and pinprick sensation (6). Blockade of small unmyelinated sympathetic nerve fibers with local anesthetics causes vasodilatation, an increase in blood flow and a rise in local temperature. It is not yet known whether the extent of the temperature change can be used to predict successful and failed regional blocks. Thermography is a technique whereby temperature can be accurately measured over a large area of skin surface at a specific time (7). The goal of this study was to determine whether thermography can be used as an early and reliable method of assessing the success or failure of axillary regional anesthesia blocks and to compare it with currently used techniques of patient response to cold and pinprick.

Methods

We performed an observational study on 25 ASA physical status I to II adult patients, aged from 22- to 75-yr -old, who were scheduled for elective hand surgery under axillary plexus anaesthesia. Informed consent was obtained from each patient before axilary block placement. Exclusion criteria included patient refusal, sensitivity to local anaesthetic agents, anticoagulation, and skin infection at the site of needle insertion. Patients who were using analgesic medications including opioids and nonsteroidal antiinflammatory drugs or had

evidence of peripheral neuropathy were not included. Any patient who requested sedation during block insertion was excluded.

Before insertion of the axillary block, all patients had IV access secured. Routine monitoring i.e., non-invasive arterial blood pressure, electrocardiogram and oxygen saturation was applied. Patients were placed in a supine position with the arm to be anaesthetised abducted to 90° and rested on a pillow. Blocks were performed by various anaesthetists, all using the same technique of nerve stimulation with a 50-mm insulated needle and stimulator (Stimuplex® B.Braun, Melsungen, Germany). Once an appropriate motor response was localised to a nerve that supplied the area on which surgery was planned with a current of 0.2-0.5mA, 40mL of mepivicaine 1.5% local anaesthetic solution (AstraZeneca, Zoetermeer, Netherlands) was administered over a period of 2 min. A single injection technique was used on all patients.

Time zero (t = 0) was defined as the time corresponding to the end of the regional anaesthesia procedure; i.e., the time of removal of the insulated needle from the skin. A thermographic image was taken of the operative limb at t = 0, immediately followed by an assessment of patient response to pinprick and cold sensation. Both a thermographic photo and pinprick/cold sensory tests were repeated at 5-min intervals (t = 5, t = 10, t = 15, t = 20, t = 25, t = 30) on the operative dermatome(s) until 30 min after completion of the axillary blockade. At each time point, a thermographic image was made before pinprick and cold sensation assessment. Pinprick sensation was assessed using a 22-gauge needle and compared with the patient's response to similar stimulation on the same dermatome of the control limb. Pinprick sensation was recorded on a 2-point scale (sensation or no sensation/numb). Cold sensation was assessed by applying a gel pack cooled to 4°C to the operative dermatome and was recorded on a 2-point scale (cold/not cold) as compared with the sensation felt on the opposite limb. A thermographic photo was taken of the unblocked limb, before block insertion and at t = 30 to calculate limb

temperature changes arising from factors other than the block, such as limb immobility and environmental temperature.

The investigator who recorded the thermographic photos was not present during the nerve localisation with the nerve stimulator. Cold and pinprick sensation were assessed by the same anesthesiologist for each patient. Thermography was performed using a computer-assisted infrared thermography camera (ThermaCAM SC2000, Flir Systems, Sweden). The spectral range is 7.5 to 13 mm and the built-in digital video has 320 x 240 pixels (total 76800 pixels). Data were obtained through a high-speed (50Hz) analysis and recording system (Thermacam Researcher 2001® HS, Berchem, Belgium) coupled with a desktop PC. Thermograms were stored on a hard disk (14-bit resolution) until the images were processed and evaluated with analytical software (Thermacam Researcher 2001 HS).

The thermographic camera produces a matrix of temperature values. These temperature values are each represented by a pixel in the thermographic image. For further analysis a frequency table is calculated. Temperature classes are created consisting of temperatures with an interval of 0.1°C. The emissive factor of the skin is 0.98, which means that the heat radiated by the skin is almost entirely dependent on the temperature of the skin itself and not on the heat reflected onto the skin from the surroundings. The analytical software uses the mean of the pixels composing the targeted area within the image in order to calculate the temperature. The target area was marked by applying a 1cm circular piece of silver paper to the operative dermatome(s) which ensured that temperature measurements were made at the same site on each consecutive image. The calculations were done as follows; 1. Dermatome(s) supplying the operative site were selected. 2. Average temperature for the dermatome(s) was calculated at 5-min time intervals from time zero (t = 0) to 30 min later (t = 30). This resulted in 7 individual temperatures. 3. Temperature difference between each time interval was then calculated; e.g., the temperature change from t = 0

to t = 5 was calculated by t = 5 minus t = 0. 4. Results were plotted in a graph, as temperature difference in the successful group against time and temperature difference in the failed group against time.

A minimum of 30 min after block placement, patients were transferred to the operating room. The operating surgeon assessed the operative site for pain sensation using a surgical forceps. If patients reported the sensation of pain at this time, the block was described as unsuccessful and either a supplemental regional block or general anaesthesia was administered by the anaesthesiologist responsible for each individual patient's care. If the block was successful surgery proceeded as usual.

The aim of this study was to obtain a significant sensitivity and specificity for thermography as an axillary block assessment method. As no useful data could be found in the literature to perform a power analysis, we therefore conducted a pilot study. Seven patients were included in the pilot study and underwent the protocol as described in Methods. The results obtained from the pilot study were used to perform a power analysis. The failure rate for axillary blocks is reported in the literature to be from 10%-15%. The average mean temperature increase in the successful blocks at 15 min was $4.5^{o}C \pm 2.0^{o}C$. For the failed blocks the average increase in temperature at 15 minutes was $1.5^{o}C \pm 0.87^{o}C$. These numbers were used to perform a power analysis, using average temperature increase of dermatomes involved as the primary outcome. To obtain a power of 95% at 15 min, with $\alpha = 0.05$, 20 patients are required. A total of 25 patients are included in this current study.

Patient characteristics on age, height, weight and body mass index between the successful and failed groups were compared using a Student's *t*-test. Between-group comparisons for ASA distribution, male-female distribution, nerve involved, operation site involved, and operation type were analyzed with χ^2 test for independence.

To calculate the sensitivity and specificity of the three methods tested

(cold pack, pinprick and thermography), a receiver operating characteristic curve (ROC) analysis was used. For patient response to cold pack, the sensation of cold was assigned a value of 1 and the absence of cold sensation was assigned a value of 0. For patient response to pinprick the same method was applied, 1 = sensation and 0 = absence of sensation. Temperature was calculated according the method described in the Methods. The coordinates of the graph are defined by calculating the sensitivity and specificity at different values of the diagnostic test, so called "cutoff points". Sensitivity is the ratio of the number of patients in whom a block assessment method predicted a successful block over the total number of patients with a surgically successful block. Specificity is the ratio of the number of patients in whom a block assessment method predicted a failed block over the number of patients with a surgically failed block. This results in a graph of the true positive rate against the false positive rate for the different possible 'cutoff points' in a given diagnostic test. The accuracy is described using a 5-point system based on the area under the curve: excellent (area of 1-0.9), good (area of 0.9-0.8), fair (area 0.8-0.7) poor (area of 0.7-0.6), and fail (area of 0.6-0.5) (8,9).

Table 1. Equations for the Calculation of Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of All Assessment Methods Used.

		Clinically successful block			
		Positive	Negative	Total	Calculations
Assessment method used	Positive	A	B	A+B	$Positive\ predictive\ value = \frac{A}{A+B}$
	Negative	C	D	C+D	$Negative\ predictive\ value = \frac{D}{C+D}$
Total		A+C	B+D	N	
Calculations		$Sensitivity = \frac{A}{A+C}$	$Specificity = \frac{D}{B+D}$		

More insight into the diagnostic value of thermography is gained when the positive and negative predictive values are calculated. The positive predictive value is the proportion of patients with positive test results who are correctly diagnosed. The negative predictive value is the proportion of patients with negative test results who are correctly diagnosed. A summary is given in Table 1, explaining the mathematical equations used in the calculation of the diagnostic values.

Table 2. Patient Characteristics (n=25)

Variable	*Overall*	*Successful*	*Unsuccessful*
Age (yr)	46.8±14.9	46.5±14.9	48.4±16.4
Gender (M:F)	11:14	8:12	3:2
Nerve (ulnar:medial:ulnar / medial :all)	5:12:6:2	4:10:4:2	1:2:2:0
ASA Classification (I:II)	19:6	15:5	4:1
Height (m)	1.75±0.12	1.74±0.12	1.81±0.13
Weight (kg)	79.5±15.3	76.5±13.3*	91.8±18.0
BMI ($kg*m^{-2}$)	25.7±3.5	25.2±3.4	27.8±3.6
Operative nerve dermatome(s):			
Ulnar nerve (n)	5	4	1
Median nerve (n)	12	10	2
Ulnar & median nerves (n)	6	4	2
Ulnar & median & radial nerves (n)	2	2	0
Operation type:			
Dupytrens (n)	5	4	1
Trigger finger release (n)	4	3	1
Arthroplasty (n)	3	2	1
Tenolysis (n)	2	2	0
Miscellaneous (n)	11	9	2

Values are expressed as mean ± SD unless otherwise indicated.

*Statistical significance between group successful and unsuccessful.

Results

Twenty-five patients, whose demographics are shown in Table 2, scheduled to undergo hand or wrist surgery under axillary plexus blockade were included. There were no significant between group differences for successful and failed groups, apart from weight, which was heavier in the failed block group (P = 0.0423). The overall block success rate was 80%.

At time zero (t = 0) there was no significant difference in baseline limb temperature values in the sucessful and failed groups (Figure. 1). After 5 min the temperature change in the successful group started to increase rapidly, achieving a maximum temperature change from baseline of + 4.5°C after 20 min. In the failed group a slight temperature increase began after 10 min, but the maximum temperature increase was only 0.8°C at 20 min.

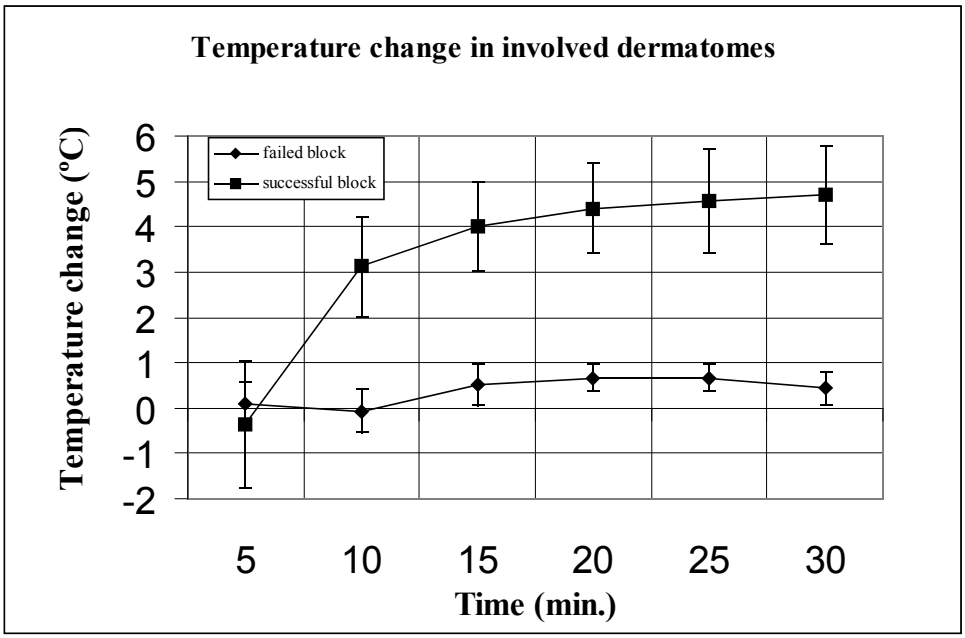

Figure 1. Average temperature change in the involved dermatomes at 5-min intervals in successful and failed blocks.

Data on sensitivity and specificity over time for the 3 different types of block assessment methods (cold, pinprick and thermography) are shown in Figure 2 and Table 3. Up to time 5 min, cold and thermography demonstrate similar sensitivity as a block assessment technique. However, at 10 min the sensitivity of cold sensation decreases compared with that of thermography which achieves a sensitivity of 95% at time 15 min and maintains a sensitivity in excess of 90% until time 30 min. The sensitivity of pinprick as an assessment method is initially low at 20%, but by time 15 min reaches a maximum of 80%.

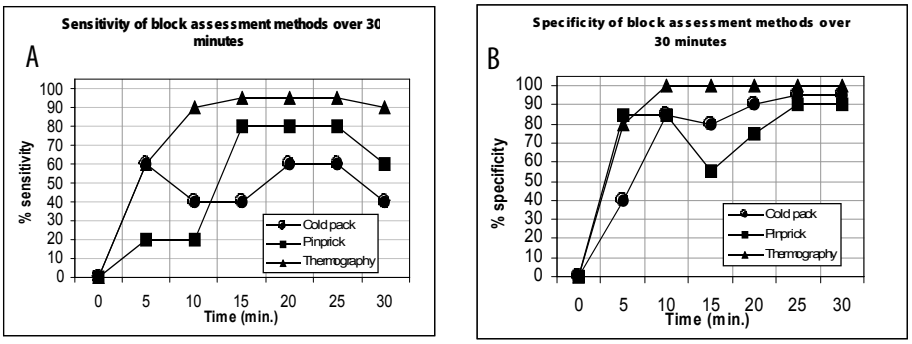

Figure 2. A, Sensitivity of cold, pinprick and thermography methods for the assessment of successful and failed axillary plexus blocks. B, Specificity of cold, pinprick and thermography methods for the assessment of successful and failed axillary plexus blockades.

The specificity of cold and thermography block assessment methods is initially comparable, but at 10 min, thermography achieves a specificity of 100% maintaining this level until time 30 min. The specificity calculated for pinprick is inconsistent ranging from a high level of 85% at time 5 min and falling to 55% at time 15 min.

Positive predictive values are higher for thermography at all time intervals compared with cold and pinprick, achieving a value of 100% at 10 min, which is maintained until the end of the study period. Negative predictive values are similar for all 3 assessment methods; thermography achieved a

negative predictive value of 98% at 10 min, increased to 99% at 15 min, and maintained these values to the end of the study period. Cold has a maximal predictive value 93% at 20 min, which was less at 30 min. Similarly, pinprick, which achieved a maximal value of 99% at 2 min, decreased to 93% at 30 min ($P < 0.05$) (Table 3).

Table 3. Sensitivity, Specificity, Positive Predictive Value, Negative Predictive Value and Cut-Off Points for Cold Pack, Pinprick and Thermography in the Assessment of Successful and Failed Blocks.

	Sensitivity			Positive predictive value (prevalence (%) =15)				Specificity			Negative predictive value (prevalence (%) =15)		
Time	Cold pack	Pin-prick	Thermo graphy	Cold pack	Pin-prick	Thermo graphy	Cut-off points	Cold pack	Pin-prick	Thermo graphy	Cold pack	Pin-prick	Thermo graphy
0	0	0	0	0	0	0		0	0	0	0	0	0
5	60	20	60	15	19	35	>0.2	40	85	80	85	86	92
10	40	20	90	32	19	100	>1.1	85	85	100	88	86	98
15	40	80	95	26	24	100	>1.3	80	55	100	88	94	99
20	60	80	95	51	36	100	>1.5	90	75	100	93	86	99
25	60	80	95	68	63	100	>1.5	95	90	100	93	99	99
30	40	60	90	59	51	100	>1.6	95	90	100	90	93	98

Values for sensitivity, specificity, positive predictive value and negative predictive value are expressed as a percentage (%). Temperature is expressed as degrees Celsius (°C). Time is expressed in minutes (min).

Statistically comparing the area under the ROC curve for each assessment method (Table 4) revealed a significant difference in the accuracy values between 'thermography and cold' at 10 min ($P = 0.035$), 15 min ($P = 0.006$) and 30 min ($P = 0.038$). Difference in accuracy values between thermography and pinprick were statistically significant at 15 ($P = 0.026$) and 30 ($P = 0.040$) min.

Comparison between cold and pinprick was not significant at the different time intervals.

For thermography as a method of block assessment, the ROC curve at time 15 minutes (t =15) gives the highest combined values of sensitivity and specificity to predict a successful block (P = 0.004). Highest combined values for cold pack and pinprick were calculated to be at 25 min; P = 0.019 and P = 0.023, respectively.

Table 4. Statistical Comparison of Cold, Pinprick and Thermography ROC Curves.

	ROC Area			Statistical comparison of ROC area		
Time	Cold	Pinprick	Thermography	Cold vs. Pinprick	Cold vs. Thermography	Pinprick vs. Thermography
5	0.50±0.15	0.53±0.15	0.59±0.15	0.03±0.03	0.09±0.17	0.07±0.14
10	0.63±0.15	0.68±0.15	0.94±0.05	0.05±0.20	0.32±0.15*	0.27±0.15
15	0.60±0.15	0.68±0.15	0.98±0.02	0.08±0.18	0.39±0.14*	0.31±0.14*
20	0.75±0.14	0.78±0.13	0.99±0.02	0.03±0.14	0.24±0.14	0.22±0.13
25	0.78±0.13	0.85±0.14	0.99±0.02	0.08±0.13	0.22±0.13	0.14±0.20
30	0.75±0.15	0.75±0.14	0.98±0.03	0.08±0.16	0.30±0.04*	0.23±0.13*

All values are expressed as area under the curve ± SD. Time is expressed in minutes.

* $p < 0.05$. ROC = receiver operator characteristic curve.

Discussion

In the current study we observed that thermography is an early and accurate predictor of axillary block success or failure. The occurrence of a temperature increase secondary to regional anesthesia blockade is a well recognized phenomenon and has been previously reported (10). However, the sensitivity

and specificity of temperature measurement as a predictor of successful and failed blocks has not been studied.

Our findings demonstrate that a successful axillary block is associated with an increase in skin temperature in the anesthetized dermatomes. A failed block is not associated with a temperature increase and this was confirmed by patients reporting pain on application of a forceps to skin, a test used routinely in clinical practice as the final check of a block before surgical incision. Statistical analysis using ROC provides a means of combining calculations of specificity, sensitivity, and positive and negative predictive values, allowing more complete analysis of a block assessment method. The highest combined values for the use of thermography as a predictor of regional block outcome were achieved 15 minutes after the local anesthetic was injected. A period of 15 minutes correlates well with the known onset time of mepivicaine, which is up to 20 minutes for peripheral nerve blockades (11).

An important advantage of thermography in the assessment of regional blockades is that it is completely objective. No patient input is required, unlike currently used methods such as pinprick and cold sensation which are highly subjective and depend on the patient's ability to interpret the stimulus applied. Also, both techniques may be influenced by patient anxiety levels and prior administration of sedating and analgesic agents. As thermography is an objective method, sedating agents may be used without affecting the usefulness of the technique. Thermography is likely to be a useful option in younger patients or patients with communication difficulties.

This objectivity of thermography may represent a significant advantage over the "swelling illusion" technique, recently described by Paqueron et al. (12), whereby patients report a sensation of swelling in a successfully anesthetized limb. The subjective nature of the assessment and the fact that the anesthetized limb is not always perceived as uniformly swollen, with swelling being more vivid in the distal parts of the limb limits its application (12). In

contrast, thermography which may be used on any part of the body as a measure of temperature change and, based on the results of this study, is an accurate predictor of block outcome.

According to our results, thermographic temperature measurement predicts a successful axillary block with a sensitivity of 95% and a positive predictive value of 100%. For unsuccessful blocks, thermography predicts with a specificity of 100% and a negative predictive value of 99%. In this current group of patients, predictive values for cold and pinprick concerning both successful and failed blocks are lower than previously reported (12). The higher values reported in that study may have been influenced by the fact that 53 patients were used to calculate results on 201 nerves. This means that for the same patient both successful and failed nerve blocks were registered, which may have biased results. Also, not all dermatomes from which results were calculated were eventually operated on, as an absolute confirmation of a successful nerve blockade.

For purposes of this study, patients with neuropathies in the limb to be anesthetized were excluded. Such neuropathies may interfere with a patient's ability to perceive pinprick and cold sensation. Such patient's may also have altered sympathetic function, the extent to which this might alter vasodilatation and subsequent increase in temperature observed after successful blockade is not known. Thermography has, however, been shown to be a reliable tool in the diagnosis and assessment of patients with chronic pain, many of whom have documented neuropathies (13). Other factors which may potentially influence the temperature in a limb after blockade include the patient's use of caffeine and tobacco products.

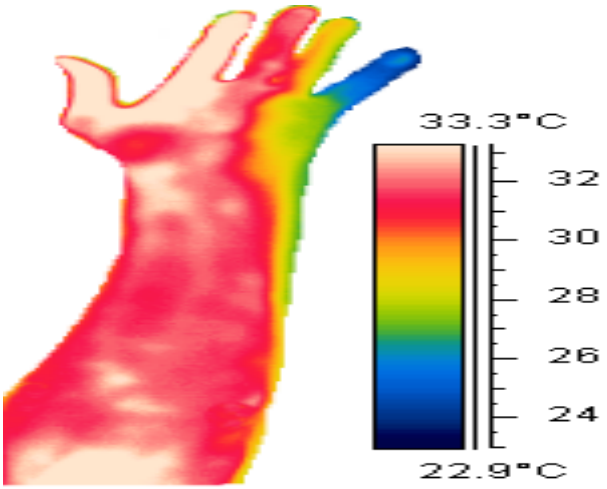

Figure 3. A thermographic photo taken at 15 min after an axillary block was performed. The area supplied by the ulnar nerve is dark in colour, representing a lower temperature than the remainder of the hand, indicating that the ulnar nerve is not anaesthetised, while medial and radial nerves are successfully anaesthetised. The failed ulnar nerve block was confirmed when the patient reported pain on application of a surgical forceps to the fifth digit.

A system of color coding of the thermographic photos according to temperature, allows photos to be quickly and easily interpreted (14). The higher the temperature of a dermatome, the brighter the color it displays on the thermographic photo; conversely, darker areas represent lower temperatures (Fig. 3). A color to temperature scale allows accurate interpretation of the increase in temperature. No complex mathematical calculations or formulas are necessary. In clinical practice, the camera may be used in isolation without the aid of a computer. The anesthesiologist may directly visualize the anesthetized limb through the camera as required and observe the temperature changes

immediately. The computer software is only required for purposes of photo storage and detailed interpretation and comparison, as in a research situation.

Thermography may also be useful in clinical anesthetic practice, where limited financial resources require maximal use of operating room time. Precise temperature measurement using thermography may allow anesthesiologists to quickly and accurately identify failed blocks. Thus, appropriate action such as supplemental block administration may be taken at an earlier stage, avoiding unnecessary operating room time delays. Indeed, thermography may represent a means of limiting such additional blocks to clinically appropriate situations because the administration of additional injections carries a small, but definite, risk of morbidity (15). As regards cost issues, the previously expensive purchase infrared thermographic cameras is no longer a restrictive issue. Growing demand for such devices in both health and non health care settings has led to large reductions in purchasing costs and portable, hand-held, user-friendly models may now be purchased for a fraction of previously quoted prices.

Further studies are necessary to establish the specificity, sensitivity, and predictive values of thermography in assessing other types of regional blocks and other local anesthetics. Future research on the reliability of performing local temperature measurements with a simple laser point thermometer is also warranted. Importantly, the costs associated with implementing the routine use of thermography in regional blockade assessment need to be evaluated in the contexts of operating room time and patient satisfaction.

We conclude that thermography is an early, objective, noninvasive technique with high specificity, sensitivity, positive and negative predictive values, for assessing the success or failure of axillary blockades.

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Chapter 3

Peripheral flow index compared to pinprick and cold sensation in the early assessment of regional blockades

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Abstract

We investigated the usefulness of peripheral flow index (PFI) measurement using a standard pulse oximetry digit probe, for early prediction of successful and failed regional blocks. Sixty-six patients scheduled for limb surgery underwent either axillary or sciatic block using a nerve stimulator technique with mepivicaine 1.5%. PFI, which is the ratio of the pulsatile versus the non-pulsatile component of the pulse oximetry signal, was recorded from 10 min before block insertion until 30 min afterwards. PFI recordings of the unblocked limb were similarly recorded. Pinprick and cold sensation were assessed at 5 min intervals, until 30 min after blockade. An increase in PFI by a factor of 1.55 at 10 min after axillary block placement ($P = 0.006$), and 12 min after sciatic block placement ($P = 0.001$) was required to predict a successful block. The sensitivity and specificity of PFI was 100% for predicting axillary block outcomes at this time. For sciatic blocks, sensitivity and specificity were 90% and 100%, respectively. The calculated positive predictive value at time 12 min for sciatic blocks was 94% and negative predictive value was 92%. At 15 min after block placement, cold sensation had a sensitivity of 77% and a specificity of 100%, whereas pinprick had a sensitivity of just 20% with a specificity of 100%. We conclude that PFI provides a simple, early, and objective assessment of the success and failure of nerve blocks.

Introduction

The availability of a block assessment technique with a high sensitivity and specificity may increase confidence among both staff and patients in the use of regional blocks, as well as aid operating room logistics, particularly in rapid patient turnover ambulatory units.

Traditional methods of block assessment include patient response to the sensations of cold and pinprick (1). In a previous publication, we (2) highlighted both the subjective nature and variable results obtained using such block assessment methods and demonstrated that temperature measurement using infra red thermography may be an appropriate alternative.

After successful peripheral and neuroaxial blockade, local vasodilatation and increased local blood flow occur as a result of blockade of sympathetic nerve fibers. Laser Doppler has been used to demonstrate the effect of epidural and sympathetic blocks on local blood flow (3, 4). However, the usefulness of such blood flow changes has not been specifically investigated in relation to regional block outcome. With its current widespread availability, the potential for pulse oximetry to provide clinical measurements other than simply oxygen saturation is now being exploited. One such application is that of peripheral flow index (PFI), the ratio of the pulsatile to nonpulsatile component of the pulse oximetry plethysmograph, and a simple and accurate indication of changes in digital blood flow (5). To measure PFI values, a standard pulse oximeter probe with relevant monitoring software, already incorporated into some monitoring systems, is required.

The goal of the current study was to determine whether PFI is a reliable and objective method for assessing the success or failure of regional anesthetic blockades at an early stage and to compare it with currently used techniques of patient response to cold and pinprick.

Methods

We conducted an observational study on 63 ASA physical status I-III adult patients, aged 18-73 years old, who were scheduled for elective upper or lower limb surgery under regional anaesthesia. The study was approved according to local ethics committee guidelines and informed consent was obtained from each patient before block placement. Exclusion criteria included patients using antihypertensive medications such as α- and β-blocking drugs, diabetes mellitus, peripheral vascular disease, neuropathy, and any contraindication to the use of regional anesthesia techniques including patient refusal, known sensitvity to local anesthetics or skin infection at the site of needle insertion.

Before block placement, all patients had IV access established. Routine monitoring (non-invasive arterial blood pressure, electrocardiogram, and peripheral oxygen saturation) was applied. Patients were placed in a position appropriate for the insertion of the relevant block as follows: axillary blocks, supine position with the arm to be anaesthetised abducted to 90^{o} and rested on a pillow; proximal sciatic nerve blocks, patient lying in a lateral position with the leg to be blocked upper most and flexed at the knee; distal sciatic nerve blocks, patient lying in a prone position with feet resting off the end of the bed allowing the distal sciatic nerve to be blocked a 7cm proximal to the popliteal fossa crease. The same technique was used for each block, i.e., nerve stimulation using either 50mm or 150mm insulated needle and stimulator (Stimuplex® B.Braun, Melsungen, Germany). Once an appropriate motor response was localised to the nerve to be blocked, with a current of 0.2-0.5mA, either 20mL (sciatic nerve block) or 40mL (axillary block) of mepivicaine 1.5% local anaesthetic solution (AstraZeneca, Zoetermeer, Netherlands) was administered. In the case of axillary blocks, only a motor response in a nerve supplying the planned surgical site was accepted. All blocks were performed using a single injection technique.

Time zero (t = 0) was defined as the time corresponding to the end of the regional anaesthesia procedure, i.e., time of removal of the insulated needle. Immediately, an assessment of patient response to pinprick and cold sensation was performed. Pinprick /cold sensory tests were repeated at 5-min intervals (t = 5, t = 10, t = 15, t = 20, t = 25, t = 30) on a dermatome, supplied by the blocked nerve, until 30 min had elapsed. Pinprick sensation was assessed using a 22 gauge needle and compared with the patient's response to similar stimulation on the same dermatome of the unblocked limb. Response was recorded on a 2-point scale (sensation or no sensation [numb]). Cold sensation was assessed by applying a gel pack cooled to 4^{o}C to the same area of skin and recorded on a 2-point scale (cold / not cold) as compared with the sensation felt on the opposite limb. A pulse oximetry probe connected to a monitor (Phillips, Eindhoven, The Netherlands) capable of measuring PFI was placed on both the blocked and control limb for a minimum of 10 min before local anaesthetic injection. For axillary blocks, the probe was placed on a digit supplied by the same nerve as supplies the planned surgical site dermatome, which was the nerve stimulated prior to local anesthetic injection. The probe remained *in situ* for a period of 30 min. An identical probe was placed on the same number digit of the unblocked limb. The average PFI change was recorded at 1-min intervals from 10 min before block insertion (t = 0 minus 10) to 30 min later (t = 30) resulting in 40 individual PFI recordings.

After a minimum of 30 min, patients were transferred to the operating room. The operating surgeon assessed the operative site for pain sensation using a surgical forceps. If patients reported pain at this time, the block was described as "failed" and a supplemental block or general anesthesia was administered according to the decision of the anesthesiologist responsible for each individual patient's care. For successful blocks, surgery proceeded as usual.

Patient characteristics of age, height, weight and body mass index

between the successful and failed groups where compared using a Student's *t*-test. Between group comparisons for age, ASA distribution, male-female distribution, nerve involved, and operation site involved and were analyzed using χ^2 test for independence.

To calculate the sensitivity and specificity of the three methods tested (cold sensation, pinprick sensation and PFI), a receiver operating characteristic curve (ROC) analysis is used. The ROC is a very good indicator of the discriminating power of a diagnostic method. PFI values were taken directly from the monitoring screen. For patient response to cold, the sensation of cold was assigned a value of 1, and the absence of cold sensation was assigned a value of 0. For patient response to pinprick, the same method was applied: 1 for sensation and o for absence of sensation. For PFI values, calculations for sensitivity and specificity were made at 1-min time points. We choose "cut off" values that resulted in the highest combined sensitivity and specificity. Sensitivity is the ratio of the number of patients in whom a block assessment method predicted a successful block over the total number of patients with an actual successful block. Specificity is the ratio of the number of patients in whom a block assessment method predicted a failed block over the number of patients with a surgically failed block. This results in a graph of the true positive rate against the false positive rate for the different possible "cut off" points in a given diagnostic test. The area under the ROC is a measure of the accuracy of the diagnostic test. The accuracy is described using a 5-point system: excellent (area of 1-0.9), good (area of 0.9-0.8), fair (area 0.8-0.7) poor (area of 0.7-0.6), fail (area of 0.6-0.5) (6, 7). More insight into the diagnostic value of assessment tests is gained when the positive and negative predictive values are calculated. The positive predictive value is the proportion of patients with positive test results who are correctly diagnosed. The negative predictive value is the proportion of patients with negative test results who are correctly diagnosed.

Results

Sixty-three patients, whose demographics are shown in Table 1, scheduled to undergo upper or lower limb surgery under regional anesthetic block were included. There were no significant between-group demographic differences for sciatic and axillary groups apart from age, which was younger in the sciatic nerve block group. Arterial blood pressure, heart rate and oxygen saturations did not differ between groups. The main types of surgery performed included tenolysis, lesion excision, plate removal, arthroscopy, and hallux valgus correction.

Table 1. Patient characteristics (n = 63)

Variable	*Sciatic (n = 37)*	*Axillary (n = 26)*
Age (Years)	39 ± 15*	49 ± 19*
Gender (M:F)	16:21	14:15
ASA Classification (I:II:III)	21:15:1	16:6:4
Height (cm)	172 ± 9	173 ± 12
Weight (kg)	77 ± 13	78 ± 16
Block success rate (%)	81	90

Values are expressed as mean ± SD unless otherwise indicated. *P < 0.05 sciatic block versus axillary block. n = both successful and failed blocks.

PFI values recorded before block placement were averaged to give a baseline PFI value for each patient. There was no significant difference between baseline PFI values in the successful and failed block groups for both sciatic and axillary nerve blocks (Figs. 1,2).

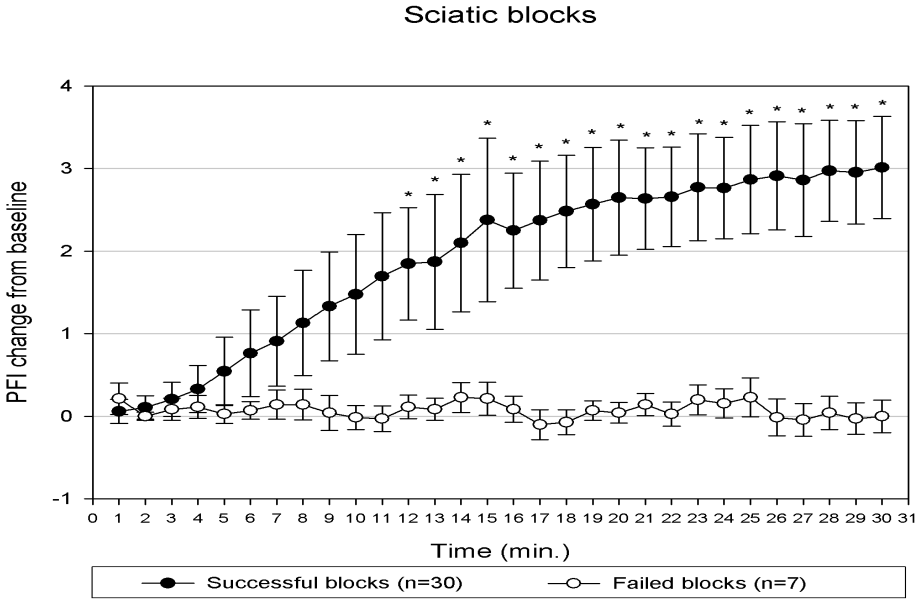

Figure 1. Sciatic blocks. Average change in peripheral flow index values from baseline in blocked limb at 1-min intervals in successful and faled sciatic blocks. Values are expressed as mean ± SD unless otherwise indicated. *Statistically significant change in PFI value compared with baseline ($P \leq 0.001$), area ≥0.9, sensitivity ≥90%, and specificity ≥90%. n = 37.

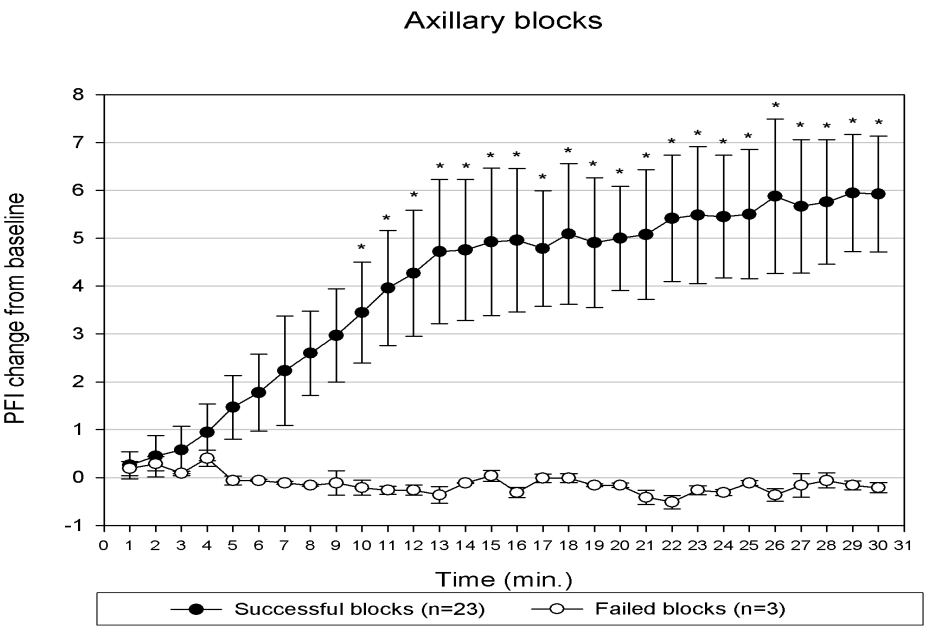

Figure 2. Axillary blocks. Average change in peripheral flow index values from baseline in blocked limb at 1-min intervals in successful and failed axillary blocks. Values are expressed as mean ± SD unless otherwise indicated. *Statistically significant change in PFI value compared wit baseline ($P \leq 0.05$), area ≥ 0.9, sensitivity ≥ 90%, and specificity ≥ 90%. n = 26.

In all patients with a successful block, PFI values increased in the blocked limb, whereas no change in PFI values occurred in the unblocked limb, indicating that external factors such as room temperature did not contribute to the increase in PFI values recorded in the blocked limb. There was no recorded statistically relevant increase in PFI values compared to baseline after a 30 min-period in the failed block patients.

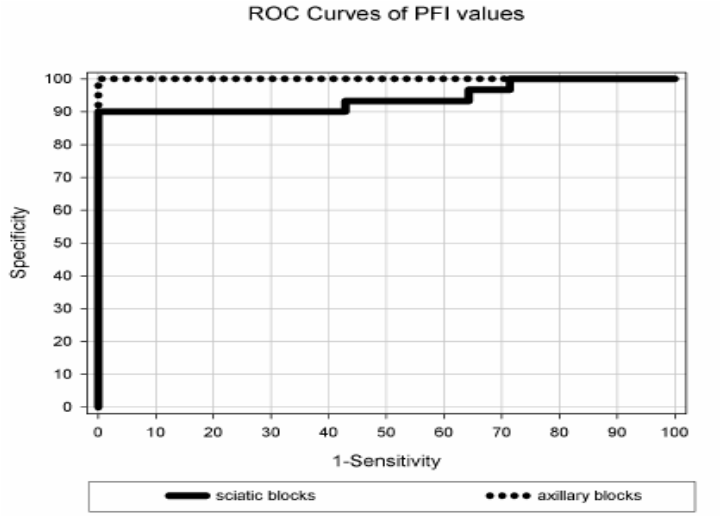

Figure 3. ROC curves of PFI values. ROC curve for sciatic blocks at 12 min. Cutpoint = 1.55, area = 0.94, sensitivity = 90% and specificity = 100%. n = 37. ROC curve for axillary blocks at 10 min. Cut point = 1.55, area = 1, sensitivity = 100% and specificity = 100%. n = 26.

For both block types, the earliest time at which the ROC area was ≥ 0.9 in combination with sensitivities and specificities of ≥ 90% was choosen (Fig. 3).

In the successful sciatic block group, PFI values started to increase as early as 4 min after the mepivacaine was injected and achieved a statistically significant increase compared to baseline at 12 min (t = 12) (P = 0.001). At this point, PFI had increased by a factor of 1.55 and the sensitivity and specificity of PFI as a predictor of block outcome were 90% and 100% respectively. The calculated positive predictive value at time 12 min was 94% and negative predictive value was 92%. In the axillary block group, PFI values began to increase 3 min after the mepivacaine was injected and increased by a factor of 1.55 times baseline values at 10 min (p = 0.006). At this time, both sensitivity and specificity were calculated to be 100%. Positive predictive value was 95% and negative predictive value was 93%.

For comparative purposes, calculations for cold and pinprick were made at a time of 15 min (t = 15), which was the closest time after the statistically significant findings for PFI at 12 min and 10 min for sciatic and axillary blocks, respectively. For sciatic blocks, cold sensation revealed a sensitivity of 77% and a specificity of 100%; pinprick revealed a sensitivity of 20% and a specificity of 100%. For axillary blocks, cold and pinprick sensations had the same calculated values for sensitivity and specificity at 71% and 100% respectively.

No patient in this study who was deemed to have a successful block, assessed using a preincision forceps, subsequently reported pain during the surgical procedure.

Discussion

In the current study we observed that PFI is an early and accurate predictor of regional blockade success or failure. The occurrence of changes in local blood flow secondary to regional anesthesia is a well recognized phenomenon and has been reported (8). However, the relative increase in blood flow that occurs

after a successful block and its potential use as a predictor of the success or failure of regional techiques has not been investigated.

The results of this study show that successful blocks are associated with an increase in PFI values compared with baseline, beginning as early as 3 minutes after local anesthetic injection and reaching statistical significance at a time of 12 minutes and 10 minutes for sciatic and axillary blocks, respectively. At these times, PFI values had increased by a factor of 1.55 compared with baseline pre-block values, and in this group of patients, such an increase in PFI values indicates a successful block with high sensitivity and specificity. Significantly, patients with failed blocks demonstrated minimal or no change in PFI values, suggesting that the increase in PFI values is directly related to nerve blockade rather than serum levels of local anesthetic.

PFI measurement using a standard digital pulse oximetry probe is relatively new to clinical practice. To implement PFI as a means of block assessment, a single pulse oximetry probe placed on the limb to be blocked and a monitoring system with relevant software are required. Values are presented numerically and are easy to interpret without a requirement for specifically trained personnel. Based on this study and previously reported data (5), there is large individual variation in baseline PFI values, varying from 0.1 to 10.0. With regard to early and reliable prediction of block outcome, the important factor is not the actual PFI value itself, but the relative change in PFI value over time, after local anesthetic injection.

PFI offers several advantages over currently used block assessment techniques. First, PFI is an objective means of assessing block outcome unlike both pinprick and cold sensation techniques, which require patients to report the precise sensation felt on application of a given stimulus. Also, patients are not subjected to the potential discomfort of pinprick and ice pack testing.

A disadvantage of regional anesthesia is the incidence of failed blocks estimated to be from 10%-20% for single injection techniques (1). This study

suggests that PFI may be a simple method for identifying such failed blocks early, allowing time for alternative action such as block supplementation or conversion to general anesthesia, thus avoiding potentially costly operating room time delays and low patient and/or administration satisfaction levels. PFI may also have a useful role to play in the area of regional anesthesia research, as a reliable and objective tool in comparative studies assessing the effectiveness of various block injection techniques and local anesthetics.

Important comments on this study include the fact that additives such as epinephrine and clonidine were not added to the local anesthetic solution, and therefore we have not investigated the potential effect that such drugs might have on relative increase in PFI values. Also, patients with diabetes or neuropathic injuries were specifically excluded. Such diseases may alter the degree of vasodilation that occurs after a successful peripheral block and thus the relative increase in PFI values. It is important to note, however that in a previous study recording baseline PFI values in volunteers, no significant difference was found between those with or without vascular disease (diabetes, hypertension) or between those who were smokers and non smokers (5). Finally, as the value measured is recorded using a pulse oximetry probe, the use of this technique is currently limited to blocks that supply a digit.

In conclusion, PFI is a simple, early, objective, noninvasive technique with high specificity and sensitivity for assessing the success or failure of regional blocks as compared with conventional assessment of changes in sensation.

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Chapter 4

Randomized prospective study comparing the CobraPLA and LMA-Classic during controlled ventilation for gynaeocological laparoscopy

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Abstract

Background: An increasing number of noninvasive, supraglottic airway devices are currently available. In this randomized single blind study, we compared the Cobra Perilaryngeal Airway (CobraPLA) to the Laryngeal Mask Airway (LMA-Classic) during gynecological laparoscopy.

Methods: Forty patients received either an LMA-Classic or a CobraPLA. Insertion, ventilation and removal characteristics were noted, as well as any throat morbidity.

Results: Devices were similar for insertion characteristics, adverse events and throat morbidity. Before pneumoperitoneum, peak airway pressures were 20.3 ± 4.9 cm H_2O in the LMA-Classic group versus 25.5 ± 7.9 cm H_2O in the CobraPLA group, P = 0.01. This difference was maintained during pneumoperitoneum; LMA-Classic (22.8 ± 6.1 cm H_2O) and CobraPLA (28.1 ± 8.5 cm H_2O), P = 0.04. Macroscopic blood occurred only on the CobraPLA, seen on 40% of the devices after removal, P = 0.001.

Conclusion: During gynecological laparoscopy, the CobraPLA provides similar insertion characteristics, but higher airway sealing pressures than the LMA-Classic. The usefulness of this finding requires further investigation.

Introduction

An increasing number of non-invasive, supraglottic airway devices are currently available. The first such device, the LMA-Classic (The Laryngeal Mask Company Limited, Henley-on-Thames, U.K.) is now widely used, while the Cobra Perilaryngeal airway (CobraPLA) (Engineered Medical Systems Inc, Indianapolis, IN, USA) is relatively new to the market.

Both the LMA-Classic and CobraPLA consist of a tube with a distal cuff, inflated when positioned in the patient's hypopharynx, to achieve a seal, thus allowing ventilation of the lungs. However, the CobraPLA has a larger internal tube diameter and a larger more proximally situated circumferential cuff. The CobraPLA has been evaluated and found to be an adequate alternative to the LMA-Classic in terms of insertion and recovery characteristics (1,2). Higher sealing pressures have been reported with the CobraPLA compared to the LMA-Classic during controlled ventilation (1).

In this current randomised, controlled, single-blind study, the primary aim was to evaluate the use of the CobraPLA as an alternative to the LMA-Classic in patients undergoing laparoscopic gynaecological surgery. In particular, we compared the devices in terms of insertion and removal characteristics and ability to ventilate at higher airway pressures.

Methods

Following institutional ethics committee approval, 40 ASA I and II, female patients gave written informed consent to be included in this study. Inclusion criteria were, fasting patients, Mallampati score I or II, no history of gastric reflux disease, body mass index < 30 and absence of throat morbidity. Exclusion criteria included known difficult intubation and pregnancy.

Patients received either an LMA-Classic or CobraPLA. IV access was established and patients had routine monitors attached. After administration of

100% oxygen, anesthesia was induced using sufentanil and propofol.

Insertion time was measured from the moment the device was placed in the patient's mouth to time of connection of the breathing circuit. Additional manipulations, performed to achieve an adequate airway were recorded. A failed insertion could be followed by two further attempts. Using a cuff inflator pressure gauge (Portex Ltd, Kent, England) air was injected until the cuff pressure measured 60cm H2O. Successful placement was confirmed by the presence of bilateral chest wall movement and occurrence of a square wave trace on the capnograph during manual ventilation. Anesthesia was maintained with propofol at 10 to 15 $mg \cdot kg^{-1} \cdot h^{-1}$ with a fresh gas flow rate of 3 L/min with 33% oxygen in air. Volume- controlled ventilation was used; tidal volume of 8 mL/kg and respiratory rate of 10 bpm with rate adjustment to ensure an end-tidal carbon dioxide of 4-6 KPa. Inspiratory to expiratory ratio was set at 1:2.

The peak pressure at which a leak occurred for each airway device was then assessed before and during pneumoperitoneum. To measure the pressure at which a leak was audible, pressure controlled ventilation was used, commencing at a pressure of 10cm H_2O and increased in intervals of 5cm H_2O to a maximum of 40cm H_2O. A pressure difference of at least 15 cm H_2O was maintained between peak airway pressures and positive end-expiratory pressure, throughout the testing period by adjustment of positive end-expiratory pressure. Once an audible leak occurred, peak airway pressure was recorded and testing stopped. Before induction of a pneumoperitoneum, a muscle relaxant, mivacurium was given at a dose of 0.01 $mg \cdot kg^{-1}$ to facilitate the surgical technique. Maximal allowed head- down Trendelenberg position was approximately 15º and maximal intra-abdominal pressure was 15 mm Hg. The testing process was repeated during pneumoperitoneum, until a leak was heard and peak pressures were recorded. Adverse events were also recorded.

Airway devices were removed when patients were breathing

spontaneously and able to respond to simple commands. The presence or absence of macroscopic blood on each device as well as throat pain or difficulty swallowing was noted.

Power analysis

To estimate the group size, a pilot study was conducted measuring the leak pressures for the LMA-Classic in patients during laparoscopic gynecological surgery in 30 patients. The standard deviation of the leak pressure in this group was 4.5 cm H_20. For our power calculation, we assumed equal standard deviation for leak pressure in the CobraPLA group. We wanted to be able to show a difference of 4cm H_2O in leak pressure between the two groups in this study. With an alpha = 0.05, two tailed and a power of 80%, we needed 20 patients per group, hence a total of 40 patients were included in this study.

Statistical analysis

Data are expressed as mean ± SD or as categorical distributions. Between-group comparisons for numerical data were analysed with an unpaired *t*-test. Between-group comparisons for distributions were analysed using a Fisher's exact test for data with two categories and a χ^2 test for data with more than two categories.

Results

Forty patients were enrolled. The two groups were demographicically similar as shown in Table 1.

Table 1. Demographics of the Study Groups (n = 40)

	LMA-Classic	CobraPLA
Age (yr)	31.3 ± 6.9	37.0 ± 1.63
Height (cm)	1.69 ± 0.06	1.70 ± 0.09
Weight (kg)	67.1 ± 5.0	65.0 ± 8.3
ASA I / Π	17/3	17/3
MP I / Π	18/2	16/4

A supra laryngeal device was successfully inserted in all patients. Results are summarized in Table 2. There was no statistically significant between-group differences for the total dose of anesthetic drugs used or duration of anesthesia..

The LMA-Classic insertion time was 10.3 ± 3.5s, successful on first attempt in 19 of 20 patients. The CobraPLA insertion time was 11.6 ± 5.9s, successful on first attempt in 17 of 20 patients. There were no adverse events. Adequate ventilation was achieved in both groups with just one patient in the LMA-Classic group experiencing a brief oxygen desaturation to < 94%.

The mean volume of air inserted in the cuffs to achieve a cuff pressure of 60 cm H_2O was 16.6 ± 6.8 mL for the LMA-Classic group and 34.5 ± 9.2mL for the CobraPLA group. There were more additional device movements required in the CobraPLA group compared with the LMA-Classic group. Airway ventilation pressures required to hear a leak were 20.3 ± 4.9cm H_2O in the LMA-Classic group and 25.5 ± 7.9cm H_2O in the CobraPLA group before pneumoperitoneum. These differences were statistically significant, P = 0.01 (Fig. 1). During pneumoperitoneum, peak airway pressure at which a leak was audible around the classic LMA was 22.8 ± 6.1cm H_2O and for the CobraPLA 28.1 ± 8.5cm H_2O. This was also statistically significant, P = 0.04 (Fig. 1). On removal of the device, no macroscopic blood was seen in any patient in the LMA-Classic group. Blood

was seen on the device after removal in eight patients in the CobraPLA group which was statistically significant, P = 0.001. No patient had sore throat and /or dysphagia before discharge.

Table 2. Comparison of CobraPLA and LMA-Classic in Patients Undergoing Gynaecological Laparoscopy (n = 40)

	LMA-Classic	**CobraPLA**
Duration of anesthesia (min)	36.1 ± 17.1	38.7 ± 10.0
Laparoscopy diagnosis/sterilisation	11/9	15/5
Sufentanil at induction (•g)	9.88 ± 0.86	10.32 ± 1.89
Propofol at induction (mg)	208.5 ± 28.2	217.6 ± 51.9
Mivacurium (mg)	7.26 ± 1.18	7.28 ± 1.64
TIVA with Propofol (mg)	413.7 ± 215.3	402.5 ± 145
Insertion time (s)	10.3 ± 3.5	11.6 ± 5.9
Insertion attempts 1/2/3	19/1/0	17/1/2
Additional movements 0/1/2/•3	19/1/0/0	14/4/1/1
Volume in cuff (mL)	16.8 ± 6.8	34.5 ± 9.2*
Blood (yes/no)	0/20	8/12*
Throat (yes/no)	0/20	0/20
Dysphagia (yes/no)	0/20	0/20
Desataturation (yes/no)	1/19	0/20
Laryngeal Spasm (yes/no)	0/20	0/20
Bronchospasm (yes/no0	0/20	0/20
Device size 3/4/5	0/15/5	14/6/0

* Statistically significant versus LMA-Classic, $p < 0.05$. TIVA = Total intravenous anesthesia; additional movements = head tilt, chin lift, jaw thrust, extension or flexion of the neck and pushing the airway device in or out.

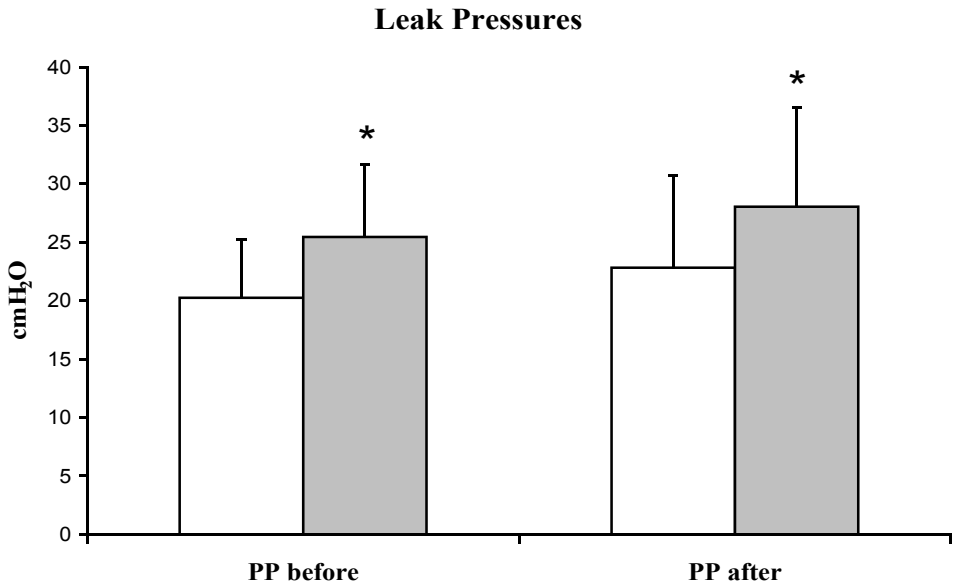

Figure 1. Peak airway pressures (PP) before and during pneumoperitoneum with CobraPLA and LMA-Classic devices. *Peak airway pressure at which audible leak occurred was significantly greater for CobraPLA than for LMA-Classic before pneumoperitoneum (P = 0.01) and after pneumoperitoneum (P = 0.04). LMA-Classic is represented by white bars and CobraPLA is represented by gray bars.

Discussion.

This is the first study to compare the CobraPLA with the LMA-Classic in patients undergoing controlled ventilation during laparoscopic surgery. The devices had similar insertion times, and both provided an adequate airway and ventilation throughout the surgical procedures without adverse clinical effect. However, the CobraPLA achieved statistically significant higher airway sealing pressures, both before and during pneumoperitoneum.

Previous studies have shown that the LMA-Classic may be successfully used to ventilate patients' lungs during laparoscopic surgical procedures (3,4). Our findings confirm the results of a previously published study (1), which

demonstrated a higher airway sealing pressure using a CobraPLA compared to a LMA-Classic during positive-pressure ventilation, in the absence of pneumo-peritoneum (1). Our study is the first to confirm that there is also a statistically significant difference in sealing pressures between the CobraPLA and LMA-Classic, during positive-pressure ventilation in the presence of a pneumo-peritoneum.

More additional airway and device maneuvres were required in the CobraPLA versus LMA-Classic group. We noted an absence of a definitive resistance when placing CobraPLA devices, unlike the easily felt resistance observed when placing LMA-Classic devices. Interestingly, the amount of air inserted in the cuff of both devices to achieve a cuff pressure of 60 cm H_2O was far less than the values recommended by the manufacturers, highlighting the importance of cuff pressure measurement when using supra-laryngeal devices, since excessive cuff pressure may have potentially damaging effects on local structures (5,6).

There are several publications reporting successful and safe use of supralaryngeal airway devices in patients undergoing laparoscopic surgery (3,4,7). In our series of selected patients, there was no evidence of gastric regurgitation or pulmonary aspiration, with airway pressures in some cases briefly as high as 40 cm H_2O. As stated in an editorial (8), estimating the risk for pulmonary aspiration can be extremely difficult and requires consideration of patient, operative and anesthetic factors. The use of supra-laryngeal devices in patients undergoing laparoscopic surgery requires careful attention to patient selection and adherence to strict guidelines for maximum intraabdominal pressures and degree of head down (Trendelenberg) positioning.

It is important to note that while this and earlier studies demonstrate that higher airway sealing pressures may be achieved using the CobraPLA when compared to the LMA-Classic, the manufacturers of both devices recommend peak airway pressures to be maintaine <20 cm H_2O for routine use (9,10). The

use of higher airway pressures in conjuction with supra-laryngeal airway devices may result in greater flow of gases into the gastrointestinal tract with resultant gastric distension and a posibly increased risk of regurgitation and aspiration. Because of the more proximal positioning of the CobraPLA cuff in the patient's hypopharynx and it's circumferential design which contributes to its ability to achieve a higher sealing pressure, should regurgitation of gastric contents occur, the chances that any regurgitated gastric secretions might flow toward the trachea may, in theory, be greater than with the more distally, situated, noncircumferential cuff of the LMA-Classic.

Other supra-laryngeal devices such as the Proseal LMA, have been studied and successfully used during laparoscopic surgery (11,12). An advantage of this device is the presence of a conduit extending from the distal end of the cuff to the exterior, which is designed to drain gastric contents. In this study we choose to compare the newer CobraPLA with the LMA-Classic, as the latter device is widely available and has been successfully used during laparoscopic surgery. However, a future study comparing the Proseal-LMA with the CobraPLA might offer further useful information.

We noted a more frequent occurence of macroscopic blood on the CobraPLA (40%) as compared to the LMA-Classic (0%) after device removal. We postulate that this may have been a consequence of the relatively stiff nature of the device tip. However, none of the patients in this study group reported throat morbidity, in contrast to earlier studies which reported an incidence of throat pain of 10%-50% after CobraPLA use (1,2,13).

In conclusion, it would appear from this study, that both the both LMA-Classic and CobraPLA provide an adequate airway for positive pressure ventilation in selected patients with and without pneumoperitoneum. Higher airway pressures were tolerated using the CobraPLA, the usefulness of which requires further investigation. CobraPLA use was associated with a higher incidence of macroscopic blood on the device after removal.

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Chapter 5

Remifentanil as a single agent for extracorporeal shock wave lithotripsy; comparison of infusion doses in terms of analgesic potency and side effects

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Abstract

This randomised, double-blind study was designed to evaluate analgesic effectiveness and side effects of two remifentanil infusion rates in patients undergoing extracorporeal shock wave lithotripsy (ESWL) for renal stones. We included 200 patients who were administered either remifentanil 0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (n = 100) or 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (n = 100) plus demand bolus of 10 µg of remifentanil via a patient controlled analgesia (PCA) device. No other sedating drugs were given. The frequencies of PCA demands and deliveries were recorded. Arterial blood pressure, oxygen saturation, and respiratory rate were recorded throughout the procedure; postoperative nausea and vomiting (PONV), dizziness, itching, agitation, and respiratory depression were measured post treatment. Visual analog scale (VAS) scores were taken preoperatively, directly postoperative and 30 min after finishing the procedure. There were no statistically significant differences in the frequency of PCA demands and delivered boluses or among perioperative VAS scores. The extent of PONV and frequency of dizziness and itching immediately after and dizziness 30 min after the end of treatment were significantly reduced in the lower dose group. We conclude that a remifentanil regimen of 0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$ plus 10 µg demands is superior to 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ plus demand, as it has equal analgesic potency and a lower incidence of side effects in patients receiving ESWL.

Introduction

Extracorporeal shock wave lithotripsy (ESWL) is a noninvasive procedure used for the treatment of kidney stones. Acoustic shock waves break stones down to sand-like fragments that may then be excreted. The treatment may be associated with significant pain, depending on the strength of the shock waves delivered. In general, the treatment is an outpatient procedure and the choice of sedatives and analgesics is limited to those that provide rapid recovery. The ideal drug which provides effective analgesia for the duration of the procedure in combination with a low level of sedation and minimal side effects. Numerous studies have been performed to determine the most suitable drug for this procedure and several drugs including midazolam, sufentanil, fentanyl, ketamine, desflurane and propofol have been studied (1-4).

Remifentanil, an opioid agonist appears to be a suitable option; administered IV, it has a fast onset time, may be delivered by a continuous infusion and is rapidly metabolized by esterases (5). This means that both its analgesic effect and potential side effects are quickly reversed, which is of importance in ESWL treatment, as pain is experienced mainly during the procedure itself, with minimal post operative pain. Intermittent boluses of remifentanil with propofol sedation have been shown to be a useful alternative to fentanyl, alfentanil and sufentanil to provide analgesia during ESWL (2). One study suggested that an infusion rate of remifentanil of 0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$ plus a remifentanil bolus of 12.5 µg in combination with a propofol infusion provided adequate analgesia and sedation for ESWL (6). Remifentanil use as a sole drug for ESWL treatment has not been investigated. The purpose of the current single-blind study was to determine whether the administration of remifentanil as a single drug provided adequate analgesia for ESWL treatment and to determine which dose is associated with the fewest side effects. Remifentanil infusion doses of 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and 0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$ plus demands of 10 µg of remifentanil via a patient controlled analgesia (PCA) pump were compared.

Methods

We studied 200 ASA physical status I-II adult patients, ages 18-80 yr old who were scheduled for elective ESWL treatment of kidney stones using a Dornier Lithotripter S (MedTech, Wessling, Germany). Written informed consent was obtained from each patient before the ESWL treatment commenced. The study protocol was approved by the institutional ethics committee. Patients with any conditions precluding the ability to use a PCA device or known allergy to remifentanil and those receiving preoperative opioids were excluded from the study. After the insertion of a peripheral 18-gauge or 20-gauge IV canula on the forearm or hand, normal saline 0.9% was infused slowly. Patients received diclofenac 75 mg IV before commencement of the ESWL treatment unless contraindicated, in which case paracetamol 1 g was administered in suppository form to provide post treatment analgesia. No preoperative sedatives were administered. Prophylactic antiemetics were not administered. Patients with a history of nausea and vomiting (PONV) after previous ESWL treatment were excluded, as it is the policy of our department to administer prophylactic antiemetics routinely to such patients. The number of previous ESWL treatments was noted for each patient, as well as data on age (years), sex (male/female), ASA classification, and kidney being treated (left or right).

Before commencement of the ESWL treatment, patients were asked to score their level of pain from the presence of kidney stones using an 11-point visual analog scale (VAS) 0 - 10, with 0 being no pain and 10 being the worst pain imaginable. Routine monitors were applied before the commencement of treatment to measure arterial blood pressure , electrocardiogram, and oxygen saturation (SpO2). All patients received 6 L/min oxygen administered via a facemask. Patients were randomly allocated remifentanil (Ultiva®, Glaxo-SmithKline, Zeist, The Netherlands) either 0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (n =100) or remifentanil 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ (n=100). Remifentanil solutions were prepared by an anaesthetic nurse and were randomly allocated to patients by drawing

numbers from a bag. The investigator who recorded all study data was unaware of the remifentanil concentration administered to the patient. The patients were also blinded as to which remifentanil concentration was being administered. All patients were given a PCA device (IVAC Medical systems, Hampshire, England) capable of delivering a bolus dose of 10 μg of remifentanil on demand, with a lock out period of 1 minute. We included a PCA demand feature as we felt it would be unethical to test a smaller infusion dose of analgesic without offering patients an additional source of analgesia. Patients were instructed to press the PCA button when they experienced pain during the ESWL treatment. Each patient received 3000 shocks over exactly 30 min. During the procedure routine monitoring was maintained and the occurrence of hypertension or hypotension (20% change from the baseline value), oxygen desaturation (oxygen saturation < 94%), and respiratory depression (respiratory frequency of less than 8 breaths per minute) was recorded. Three minutes before the treatment procedure was completed the remifentanil infusion was discontinued. Both the frequency of demands by the patient during the 30-min period and the actual number of deliveries via the PCA were recorded for each patient.

Immediately after ESWL treatment a VAS from 0 -10 was used to record the pain experienced during he entire treatment session. The occurrence of PONV was recorded on a scale of 0 - 3 (0 = no nausea-vomiting; 1= mild, no pharmcological treatment required; 2= moderate, pharmacological treatment administered with good effect; 3=severe, pharmacological treatment administered with no relief of PONV). Pharmacological treatment of PONV consisted of granisetron 1 mg IV. The presence of dizziness, itching, and agitation were also noted directly postoperatively.

Thereafter, patients were transferred to the recovery room. Half an hour after the end of treatment, a third VAS was recorded, as was the presence of dizziness, nausea and respiratory depression. At the same time, patient

satisfaction was noted (satisfied, not satisfied or neutral). Patients were discharged to the ward when all discharge criteria were met; i.e., stable vital signs and absence of pain and nausea.

The VAS score was our primary outcome variable. To evaluate the standard deviation of the VAS score in our practice, we conducted a pilot study on 100 patients receiving ESWL treatment with 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ during a 2 month period. The patients reported a mean ± SD VAS score of 1.7 ± 2.0 on a 0 –10 scale. Therefore, we assumed an expected standard deviation of 2.0 in both study groups. With 100 patients in both groups, our study was able to demonstrate a difference of 0.8 in VAS score between groups ($\alpha = 0.05$, 2-sided unpaired Student's *t*-test, $\beta = 0.80$). We felt this was an acceptable level.

Between-group comparisons for numerical data were performed with Student's *t*-test. Within-group comparison for VAS scores over time were performed with repeated-measures analysis of variance with Bonferroni post-testing. Data distribution and frequency differences were analyzed with either a Fisher's exact test or a χ^2 test for independence. Statistical significance was accepted at $P < 0.05$.

Results

Table 1. Patient demographics

	0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$	0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$
Age (years, Mean±SD)	53.1±11.5*	46.9±13.0
Sex (Male/Female, n)	53/45	65/36
ASA classification 1 (n)	56	61
ASA classification 2 (n)	43	40
Prior ESWL treatments (Mean±SD)	2.6±2.4	2.5±2.8
Side (Left/Right)	54/42	59/42

Values are mean ± SD or *n*. ESWL = extracorporeal shock wave lithotripsy. *Statistically significant difference between groups.

Patient demographics are shown in table 1, with statistically significant differences indicated.

Perioperative measurements are shown in Table 2. In both study groups the VAS score recorded immediately after treatment was significantly higher than the preoperative VAS score and the VAS score 30 min after the procedure. The average extra dose received from the PCA was 0.017 ± 0.024 $\mu g \cdot kg^{-1} \cdot min^{-1}$ in group 0.05 and 0.024 ± 0.031 $\mu g \cdot kg^{-1} \cdot min^{-1}$ in group 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$, which was not statistically significant.

Table 2. Perioperative measurements.

	0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$	0.1 $\mu g \cdot kg^{1} \cdot min^{-1}$
Tension depression during procedure(Yes/No, n)	0/100	1/99
Decreased saturation during procedure (Yes/No, n)	0/100	1/99
Respiratory depression during procedure(Yes/No, n)	0/100	1/99
Agitation during procedure(Yes/No, n)	4/96	5/95
Recovery bypass (Yes/No, n)	1/92	7/87
Nausea 30 min after procedure (Yes/No, n)	9/90	13/86
Respiratory depression 30 min after procedure (Yes/No, n)	1/99	2/98
Patient satisfaction (n) (Yes)	78	80
Patient satisfaction (n) (Neutral)	18	16
Patient satisfaction (n) (No)	2	4
Anesthetist satisfaction (n) (Yes)	79	80
Anesthetist satisfaction (n) (Neutral)	2	1
Anesthetist satisfaction (n) (No)	1	1
Urologist satisfaction (n) (Yes)	78	80
Urologist satisfaction (n) (Neutral)	2	3
Urologist satisfaction (n) (No)	2	1
PCA demands (Median and range)	2 (0-104)	3 (0-108)
PCA deliveries (Median and range)	1 (0-19)	3 (0-22)
VAS score pre-operative (Mean ± SD)	0.9 ± 1.7*	1.2 ± 2.0*
VAS score directly postoperative (Mean ± SD)	3.2 ± 2.3	3.5 ± 2.6
VAS score 30 min after procedure (Mean ± SD)	1.1 ± 1.8*	1.0 ± 1.9*

Values are *n,* median (range), or mean ± SD. PCA = patient-controlled analgesia; VAS = visual analog scale. * Statistically significant differences versus VAS score immediately after surgery.

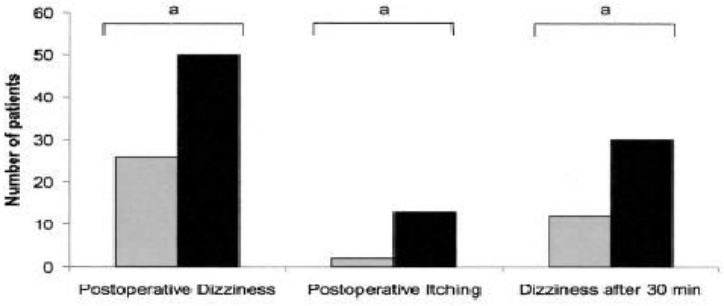

Figure 1. Postoperative side effects. Data on postoperative dizziness and itching and dizziness after 30 min. Gray bars represent the group receiving 0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of remifentanil; black bars represent the group receiving 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of remifentanil. Statistical significance: a, between both study groups.

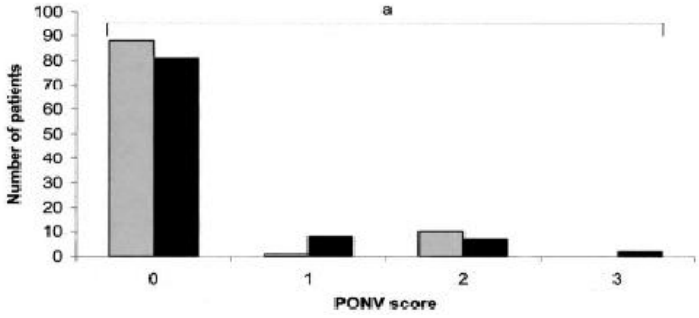

Figure 2. Data on postoperative nausea and vomiting (PONV). Gray bars represent the group receiving 0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of remifentanil; black bars represent group receiving 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of remifentanil. Statistical significance: a, between both study groups.

In Figure 1, the frequencies of dizziness and itching directly postoperatively and of dizziness 30 min after the procedure are shown. In the group that received 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of remifentanil, there was significantly more itching and dizziness.

Data on PONV are shown in Figure 2. In the group receiving 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ of remifentanil, there was significantly more PONV.

Discussion

ESWL is performed in several hundred centers throughout the world on a daily basis, but, although there are relatively fixed guide lines for the urological management of renal stones, there is a great deal of variation in methods used to manage the pain associated with ESWL. Many different options have been used, including regional, general, local and sedation techniques, with varying degrees of success (7-9). In general, ESWL is done as an ambulatory procedure, with patient discharged home occurring within hours of its completion. This has implications in terms of cost effectiveness and efficiency and improving patient acceptance of the treatment. Remifentanil, because of its unique profile, appears to be emerging as the drug of choice for the management of such patients. However, the ideal dose regimen has yet to be identified accurately when remifentanil is used as the sole drug. The remifentanil continuous infusion rates used in our study were based on our observations during a 6-month period before commencing the study. We initially adopted the recommendations of a previously published study (10) and infused remifentanil at a rate of 0.025 $\mu g \cdot kg^{-1} \cdot min^{-1,}$ reducing shock wave intensity when patients experienced pain. However, we noted that this had the effect of prolonging the total treatment time and, therefore, the period of time during which patients had to maintain a relatively fixed position, a factor which potentially increases patient anxiety and may not be appropriate for patients

with co-morbidities such as arthritis and muscular complaints. We therefore opted to use larger doses of analgesia to maintain the intensity of the shock waves, allowing more accurate prediction of total treatment time. This also allows for better scheduling of patient treatments and more efficient use of the ESWL equipment and trained personnel.

The method of remifentanil administration used in this study (i.e., continuous infusion in combination with PCA boluses) allowed us to assess remifentanil requirements. The amount of remifentanil required as a single drug may be larger than when used in combination with other sedative or analgesics. Remifentanil administration as a bolus dose is a controversial topic in the literature (11). Clinically significant hypoventilation after bolus administration of remifentanil in spontaneously breathing patients has been shown to occur (12). However, Egan et al, (13) recently demonstrated that boluses of 25 μg of remifentanil or less had algometry responses not significantly different from placebo ($P < 0.05$). In the current study, in addition to a continuous infusion, a demand dose of 10 μg of remifentanil was used with a lockout period of 1 minute. As an additional precaution, all patients received supplemental oxygen during the treatment.

We also noted the experience of a previous study by Sa Rego et al,.(6) who suggested that using intermittent bolus injections of remifentanil 25 μg or a continuous infusion of 0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$ supplemented with intermittent bolus of 12.5 μg injections may be more effective than a variable-rate infusion of remifentanil during propofol sedation. They did not demonstrate any increased risk of hypoventilation associated with the use of remifentanil boluses, even though all patients studied received a propofol infusion of 50 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and midazolam 2 mg orally before commencement of treatment. In the current study, we choose to administer remifentanil as a single drug rather than in combination with another sedating agent. Additionally, we did not administer sedating premedication. Such use of remifentanil as a sole drug

is likely to lessen the potential for respiratory depression; however, this study was not designed to compare remifentanil use as a sole drug to the use of remifentanil in combination with sedating drugs.

A study by Babenco et al. (14) showed that peak respiratory depression occured 2.5 minutes after administering a remifentanil bolus. In the current study, rather than administer an initial bolus, we opted to start the remifentanil infusion 1 to 3 minutes before the commencement of shock therapy, thus ensuring that the time of potential remifentanil-induced respiratory depression coincided with the time of initial pain stimulation, thus limiting the potential for reduced respiratory function.

Our results show that remifentanil infusions of both 0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$, plus an additional PCA boli of 10 µg, provide adequate analgesia for ESWL treatment of renal stones. Interestingly, we noted that although one group received twice the basal remifentanil infusion rate of the other, there was no significant difference between the total doses of additional remifentanil administered via the PCA. This suggests that, despite instruction on PCA use, patients may tend to press such self-controlled devices in excess of requirements for pain. Such an occurence may be related to anxiety levels, which were not specifically assessed during the treatment, but would appear to be similar in the two groups based on the results for the number of PCA bolus demands and deliveries administered. Indeed, it has been shown that psychological factors can significantly influence postoperative pain and PCA use (15). We noted that there was no difference in the degree of agitation observed in the immediate posttreatment phase in the recovery room.

This is the first study in which remifentanil as a single drug was studied during ESWL therapy. We found no significant difference in the VAS scores obtained directly after treatment between the two groups, suggesting that the lower infusion rate of 0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$, plus demands of 10 µg, provides adequate analgesia for ESWL treatment. The post treatment VAS score referred

to the overall pain experienced hroughout the entire tatment session. Such posttreatment pain scores have been shown to be an accurate measure of analgesic effect during the actual procedure (16). The degree of respiratory depression, hypertension or hypotension, and oxygen desaturation did not differ significantly between the groups, which were similar in terms of gender and number of previous ESWL treatments. Although the groups did differ in age (53.1±11.5 years versus 46.9±13.0 years in the 0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$ and 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ groups respectively), we believe that it is unlikely that this contributed to any differences observed between groups. The absence of significant respiratory depression provides useful information in terms of the potential for respiratory problems associated with remifentanil usage in the group of patients studied (i.e., ASA I-II patients). Of course, higher risk patients may be more prone to haemodynamic and respiratory abnormalities.

The potential emetic effect of remifentanil has been documented previously (17,18). Our study supports the belief that nausea and vomiting associated with remifentanil use is dose-related. Although only reported once in the literature (19), in our study a common side effect of remifentanil use was dizziness. The occurence of dizziness appears to be dose-related, with an almost two-fold increased incidence in the larger infusion rate group in the immediate post operative period, increasing to an almost threefold difference at 30 minutes after cessation of the remifentanil infusion. There is no pharmacological treatment available for postoperative dizziness. Because the incidence is likely to be dose related, it is therefore important that patients receive the minimal effective analgesic dose of remifentanil.

Itching or pruritis is a side effect associated with the use of opioids (20, 21). Our study confirmed this finding with 15 of 200 patients studied reporting itching. As with dizziness, the occurence of pruritis appears to be dose-related, with a sixfold more frequent incidence reported in the 0.1 $\mu g \cdot kg^{-1} \cdot min^{-1}$ versus the 0.05 $\mu g \cdot kg^{-1} \cdot min^{-1}$ remifentanil group immediately posttreatment. Our

results suggest that using a smaller dose of remifentanil would significantly reduce the occurrence of pruritis.

In this study, VAS scores for pain were taken after the actual ESWL session had been completed; i.e., in the recovery room, where patients were asked to score overall pain experienced during the treatment. Although, this method has been validated elsewhere (16), it could be seen as a potential deficiency the study design.

In conclusion, this study suggests that the single use of an IV remifentanil infusion of 0.05 $\mu g \cdot kg^{-1} \cdot min^{-1,}$ plus intermittent demands of 10 µg, is as effective as an infusion of 0.1$\mu g \cdot kg^{-1} \cdot min^{-1}$ plus intermittent demands of 10 µg in the providing analgesia for ESWL treatment. The smaller dose is associated with statistically significantly fewer side effects, such as PONV, dizziness and pruritis.

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Chapter 6

Modafinil reduces tiredness after sedation/analgesia

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Abstract

Background: Early recovery of patients following both sedation/analgesia and anesthesia is an important goal in ambulatory practise. The aim of this study was to assess whether modafinil, an 'awakening' drug widely used for the treatment of narcolepsy and obstructive sleep apnoea/hyperapnea syndrome improves recovery following sedation/analgesia.

Methods: Patients scheduled for extracorporeal shock wave lithotripsy were randomly assigned to one of four groups after giving informed consent. Two groups received a combination of fentanyl/midazolam with either modafinil or placebo. The remaining groups received remifentanil/propofol with either modafinil or placebo. A dose of modafinil 200 mg was adminsitered per os to treatment group patients, at a time of approximately 1 hour prior to commencing sedation /analgesia. Groups were compared using the digital symbol substitution test (DSST), trail making test (TMT), observer scale of sedation and analgesia (OAA/S) and Aldrete score. Verbal rating scale scores for energy, appetite, nausea, restlessness, tiredness, relaxation, dizziness, pain, sleepiness, agitation, nervousness, excitement, appetite, headache and itch were also recorded prior to treatment, and at 15 minutes and 1 hour after treatment.

Results: 67 patients succesfully completed ESWL therapy. Modafinil and placebo treated groups received similar doses of sedation and analgesic agents. No statistically significant difference was found for the DSST between modafinil and placebo treated groups. Mean VRS score for tiredness was less in the modafinil treated midazolam/fentanyl group compared to the placebo treated group, $P < 0.05$. Such a difference was not found between the remifentanil/propofol groups. Dizziness was greater in the modafinil treated remifentanil/propofol group versus placebo, $P < 0.05$. No other significant adverse effects occurred after modafinil use. No statistically significant difference between modafinil and placebo treated groups was identified for the TMT, OAA/S and Aldrete scores.

Conclusions: Modafinil improves recovery following longer acting forms of sedation/analgesia in terms of subjective patient reporting of tiredness, however does not improve psychomotor function as measured by objective tests. Further research is required to establish whether specific subgroups of patients, such as those with obstructive sleep apoea/hypopnea sydrome would benefit in terms of recovery from sedation and anesthesia.

Introduction

An increasing number of patients are having anesthesia and surgery performed in an ambulatory setting, where focus is on rapid recovery. Developments in surgery and anesthesia have conributed to the groth of ambulatory care. Anesthesia techniques have been adjusted to help ensure patients satisfy requirements for same day home discharge.

Modafenil (2-[(diphenylmethyl) sulphinyl]acetamide) is a wake promoting agent, that is attracting increasing attention for its potential benefits in a wide array of illness, including narcolepsy, obstructive sleep apoea/hypopnea sydrome (OSA/H), shift work sleep disorder, attention deficit/hypersensitivity disorder (ADHD), cocaine-dependancy and depression (1,2,3,4,5). Modafinil has been shown to counter the adverse effects of overnight sleep deprivation on working memory during the performance of moderately difficult tasks (6). However, despite increasing clinical application of the drug, no broad consensus exists on the underlying mechanisims of modafinil pharmacology (7). Evidence suggests that modafinil may exert it's effects through interaction with cathecholamine neurotransmitters in the brain (7). There is also some evidence to suggest that modafinil increases wakefulness by promoting glutamate release and and inhibiting GABA release (8). Modafinil does not appear to act via histamine H(3)-receptors unlike other drugs with similar effects (9). Its 'wakefulness' promoting effect has been compared to that of amphetamines and caffeine, but importantly, modafinil appears to lack potential for tolerance and withdrawal symptoms on cessation of use (10).

An earlier study on modafinil use in patients following various forms of general anesthesia (11) reported a beneficial effect in terms of reducing the incidence of ´subjective moderate to severe fatigue´ in modafinil treated patients versus placebo. In this current study, we hypothesized that the administration of modafinil by improving psychomotor function would improve patient recovery following standardized forms of sedation/analgesia.

Our primary objective was to evaluate the effect of modafinil on the ability of patients to complete the digital symbol substitution test (DSST) (12), a test of psychomotor function, following sedation/analgesia. Secondary objectives included evaluation of the effect of modafinil on patient's ability to complete the trail making test (TMT) (13) and it's effect on various subjective aspects of recovery such as tiredness and energy levels. An additional goal was to identify the occurrence of specific side effects related to the administration of modafinil in patients receiving sedation/analgesia.

Methods

Following local ethics committee approval, 67 patients scheduled for elective extracorporal shock wave lithotripsy (ESWL) treatment of kidney or ureter stones, were enrolled in this study. ESWL was choosen as it is an homogenous procedure in terms of duration and intensity of the treatment according to established guidelines. Inclusion criteria were ASA physical status I-II adult patients, aged 18-80 years old. Exclusion criteria included patients of ASA class 3, 4 or 5, visual or motor impairement, known liver or renal impairement, psychiatric illness, known allergy to any of the medications used in the study, epilepsy, breastfeeding or use of oral contraceptive pill. Inadequate renal stone visualization also resulted in patients being excluded from the study. The study was approved by the local medical ethics committee. All patients gave written informed consent.

Before the start of sedation-analgesia, baseline tests of psychomotor function were performed, these were the Trail Making Test (TMT) and Digital Substitution Test (DSST). Additionally, an Observer's Assessment of Alertness and Sedation (OAA/S) (14) score was made prior to treatment by one of two investigators, blinded to group allocation. Additionally, all patients were asked to give a score on an eleven point 0 to10 verbal rating scale (VRS) for their

feeling of energy, appetite, nausea, restlessness, tiredness, relaxation, dizziness, pain and sleepiness. All questions were asked by one of two investigators, and phrased as follows e.g. for energy, patients were asked to score their feeling of energy, where 0 meant a feeling of having no energy and 10 meant a feeling of having the maximum amount of energy the patient could imagine having.

Patients were randomised to one of 4 possible groups by removing numbers from a bag. Two of the groups received a combination of midazolam and fentanyl, with either placebo (group MFP) or modafinil (group MFM) and the other two groups received a combination of remifentanil and propofol, with either placebo (group RPP) or modafinil (group RPM). The placebo was prepared by our institution's pharmacy department and was identical in apperance to the modafinil tablet. Both modafinil and the placebo were administered one hour before the ESWL therapy to ensure that the time of peak plasma concentration of modafinil, which is 2 to 4 hours after oral adminstation, coincided with the recovery period following ESWL treatment. Adminstration times of modafinil/placebo and sedation/analgesia administration were recorded. The drug regimen for groups MFP and MFM was midazolam 0.03 $mg \cdot kg^{-1}$ and fentanyl 1 $mg \cdot kg^{-1}$, plus extra boluses of fentanyl 0.5 $\mu g \cdot kg^{-1}$ plus midazolam 0.15 mg according to patient response in terms of reported pain or observed level of sedation. A standard target level of sedation, whereby patients were calm, co-operative and responded to verbal instruction was used. For groups RPP and RPM, the dosing regimem was propofol 1-3 $mg \cdot kg^{-1} \cdot hr^{-1}$ and remifentanil 3-6 $\mu g \cdot kg^{-1} \cdot min^{-1}$ starting at the lowest dose and increasing according to patient levels of pain and sedation.

During the ESWL therapy and in the recovery room after treatment, all patients had electrocardiogram, non-invasive arterial blood pressure and peripheral pulseoximetry monitoring. Supplemental oxygen was administered via a face mask at a rate of 6 L per min. Before commencing sedation/analgesia, all patients received granisetron 1 mg and dexamethasone 8 mg IV as anti-

emetic prophylaxis and diclofenac 75 mg IV for post treatment pain. Where there was a contraindication to diclofenac, paracetamol 1 g was given IV. The occurrence of any adverse events such as bradycardia, oxygen desaturation and hypotension or hypertension.

Once ESWL treatment was completed, sedation/analgesia drugs were discontinued and patients were transferred to the recovery room (phase 1 recovery). Total doses of all drugs administered were noted. Approximately 15 minutes after ending the ESWL therapy, the TMT and DSST were repeated. A second OAA/S and VRS (0 to 10) were also performed in the recovery room. A post anesthesia recovery score (Aldrete Score) was recorded for the first time. Exact time from completion of ESWL shocks to performance of these tests was recorded.

Patients were discharged from the recovery room to the ward (phase 2 recovery) when vital signs were normal, pain scores satisfactory (VRS $\leq$ 4) and without nausea or vomiting. 1 hour after the last ESWL shock, patients completed a third and final TMT, DSST and VRS, and a second OAA/S and Aldrete score were recorded. The exact time of these tests was recorded for each patient.

On the day after the ESWL treatment, patients were contacted by telephone and asked to score on a VRS (0-10), their feeling of sleepiness, agitation, nervousness, excitement, appetite, headache and itch.

Power analysis

To calculate the number of patients per group to be enrolled in the study we used the results from a previous study. We took the outcome of the DSST as our primary outcome variable. With our study we wanted to be able to show a difference of 7 symbols in the DSST between groups. Within group data from a study by Lichtor et al, (15) showed a standard deviation of 6 symbols in the

DSST. We accepted an α-value of 0.05 (and thus 0.025 for 4 group comparison) and a power of 80%. This results in a minimum study size of 15 per group and 60 for the total study.

Statistical analysis

Intergroup comparisons for age, weight, operative time and VRS scores, were conducted using a repeated-measures analysis of variance with Bonferroni post testing or a nonparametric Kruskal–Wallis test. Intergroup comparisons for ASA class distribution and male/female ratios were analyzed with the Fisher test for independence. Intragroup comparisons of VRS scores over time were made using a repeated-measures analysis of variance with Bonferroni post testing or a Friedman nonparametric test where appropriate. A Student's *t*-test was used to demonstrate a significant difference between the maximal anticipated VRS score and the maximal real post operative VRS score. Intergroup comparisons of VRS intensity scores were analyzed using a repeated-measures analysis of variance with Bonferroni post testing, a nonparametric Kruskal–Wallis test, or a Student's *t*-test, as appropriate. Statistical significance was accepted at a probability value less than 0.05.

Results

In total 67 patients were enrolled in the study, randomly distributed over 4 groups. Demographic details of patients who completed the study showed no statistically significant differences for age, weight, height, ASA classification, oxygen desaturation, bradycardia, hypoventilation, duration of ESWL treatment, total number of shocks and shock level. There was a statistically significant difference in the percentage of male patients in group RPM compared to RRP, P = 0.05, Table 1. Total doses of sedating and analgesic agents administered did

not differ between placebo and modafinil treated groups.

For VRS pre ESWL, in the recovery room and 1 hour after ESWL, the following statistically significant differences between groups were found; pre ESWL pain scores were statistically significantly greater in group RPM versus groups MFM and RPP. The VRS for tiredness 1 hour post ESWL was statistically significantly greater in group MFP versus group MFM (Fig. 1a). Dizziness scores post ESWL were statistically significantly greater in group RPM versus group RPP (Fig. 1b).

Table 1. Demographics and details of ESWL therapy.

Groups	*MFP (n=17)*	*MFM (n=16)*	*RPP (n=16)*	*RPM (n=18)*
Age (years)	47.7 ±12.1	51.1±14.9	50.1±14.4	53.0±12.6
Weight (Kg)	80.5±11.6	92.8±17.5	82.1±15.8	84.6±13.3
Male%	70	75	63*	94*
Height (cms)	175.9±10.5	175.3±10.1	172.8±9.5	177.3±7.9
ASA 1/11	13 / 4	9 / 7	10 / 6	12 /6
ESWL duration	36.6±5.9	32.9±4.2	33.4±5.83	32.4±5.7
Number of shocks	2000±0	2000±0	1900±219	1967±141
Shock level.	7.3±1.06	7.4±1.03	7.0±0	7.5±2.0

Values are mean ± SD. * Statistically significant difference in percentage males between groups RPM and RPP. ESWL duration measured in minutes.

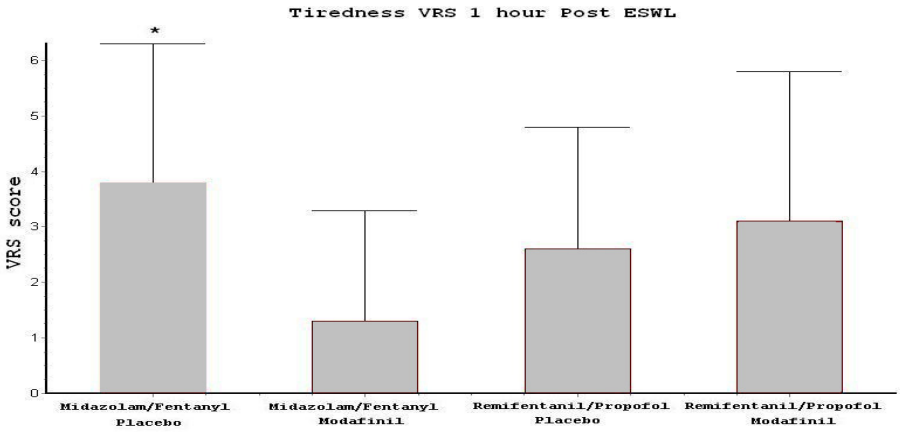

Figure 1a. Values are mean ± SD. *Statistically significant difference for VRS score for tiredness 1 hour post ESWL in group modafinil/fentanyl/placebo versus group modafinil/fentanyl/modafinil, $P < 0.05$.

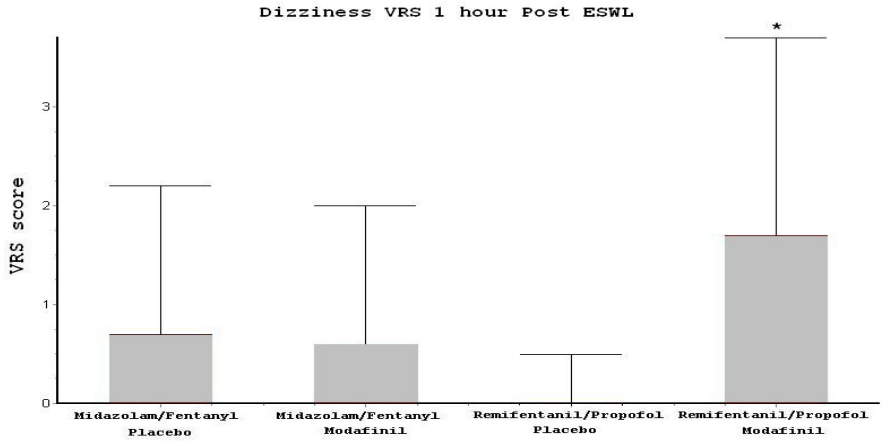

Figure 1b. Values are mean ± SD. *Statistical significant within group difference in group modafinil/fentanyl/placebo for VRS score for dizziness VRS 1 hour post ESWL in group remifentanil/propofol/modafinil versus group remifentanil/propofol/placebo, $P < 0.05$.

Statistical analysis within each group over time, demonstrated statistically significantly lower VRS scores for energy in the recovery room compared with pre ESWL in group MFP (Fig. 2a). In the RPP group, there was also a statistically lower energy level reported in the recovery room compared with pre ESWL (Fig. 2b). In the modafinil treated groups, such significant differences in energy levels were not observed. Within group MFP, a statistically higher mean VRS for both sleepiness and tiredness was found in the recovery room compared with pre ESWL (Figs. 2c and 2d).

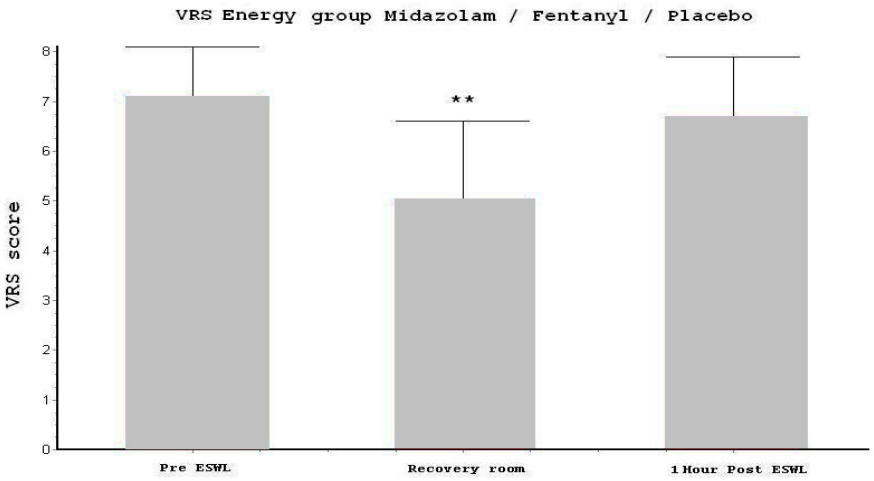

Figure 2a. Values are mean ± SD. *Statistically significant within group difference for VRS score for tiredness in group modafinil/fentanyl/placebo in the recovery room comapared with pre ESWL, $P < 0.05$.

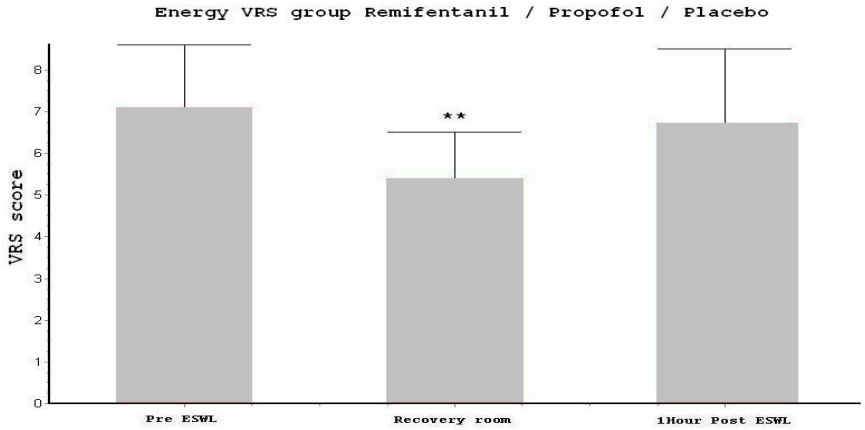

Figure 2b. Values are mean ± SD. **Statistically significant within group difference for VRS score for energy in group remifentanil/propofol/placebo group in the recovery room compared with pre ESWL, $P < 0.001$.

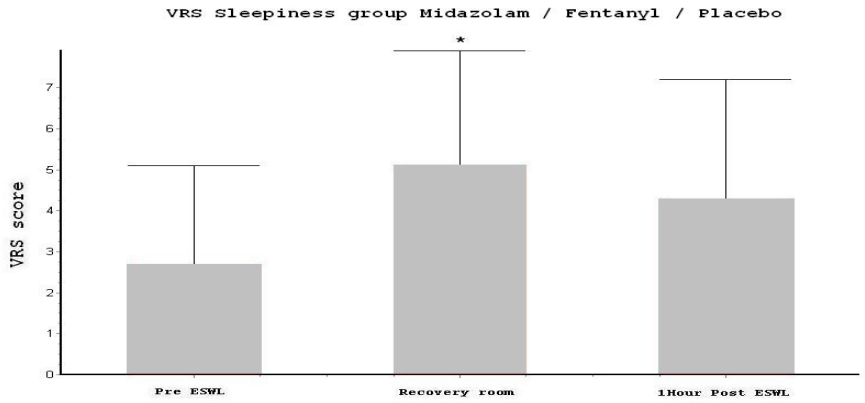

Figure 2c. Values are mean ± SD. *Statistically significant within group difference for VRS score for sleepiness in group modafinil/fentanyl/placebo in the recovery room compared with pre ESWL, $P < 0.05$.

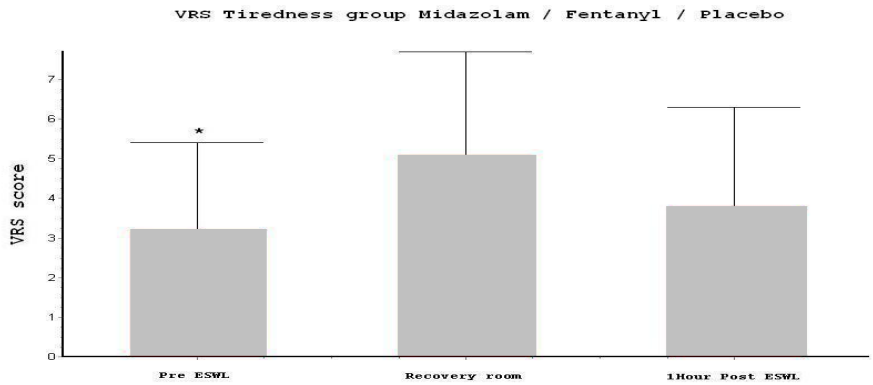

Figure 2d. Values are mean ± standard deviation. *Statistically significant within group difference for VRS score for tiredness in group modafinil/fentanyl/placebo in the recovery room compared with pre ESWL, $P < 0.05$.

VRS recorded the day after ESWL therapy demonstrated a statistically significantly higher score for appetite in group RPP than in group MFP. No other statistically significant differences were found between groups.

For DSST, TFT, OAA/S and Aldrete scores, no statistically significant between or within group differences were demonstrated at all three time points measured.

Discussion

This is the first randomised, double blind, placebo controlled study, examining the influence of modafinil on the recovery of patients following sedation/ analgesia. The main finding of this study, is that modafinil decreases the reported feeling of tiredness experienced by patients following sedation with midazolam and fentanyl compared to a control group treated with placebo.

This result is in keeping with earlier studies, which reported less postoperative ´moderate to severe fatigue´, in a modafinil versus placebo treated group following non standardized general anesthesia (11) and an improvement in opioid-induced sedation in modafinil treated patients with non-malignant pain (16). In this current study, there was no difference in reported tiredness between placebo and modafinil treated groups who received the remifentanil/propofol combination, suggesting that the ´awakening´ effect of modafinil is greatest following longer acting sedation/analgesia drugs.

Importantly, there were no significant side effects associated with modafinil use. Dizziness was statistically significantly greater in the modafinil versus placebo treated remifentanil/propofol group 1 hour after the ESWL treatment. Although dizziness is a recognised side effect of remifentanil use (17), the doses received by both study groups were similar, indicating that the higher incidence of dizziness is likely to be related to modafinil. Earlier clinical trials have reported dizziness as a side effect of modafinil use (18).

An important feature of modafinil is its reported lack of interference with recovery sleep (19). In this current study, recovery sleep was not specifically assessed but there was no difference in the level of sleepiness reported by modafinil and placebo treated groups on the day after treatment.

The other tests used in this study i.e., DSST and TMT are designed to objectively measure visual/motor co-ordination and speed, while OAA/S and Aldrete scores are objective assessments of a patient´s clinical status. Our primary end point, DSST did not reveal a statistically significant difference between modafinil and placebo treated groups, nor did any of the other objectively scored tests used. This suggests that although modafinil treated patients had a better recovery profile, in terms of subjective tiredness, such an improvement did not translate into an improvement in psychomotor function.

Clearly, more research is required to definitively establish the role of modafinil in the recovery of patients following both general anesthesia and

sedation. An improvement in the subjective feeling of tiredness is significant in that it may contribute to a patient's overall satisfaction level. Levels of patient tiredness may also influence the physician's decision to discharge patients home following ambulatory treatment. However, eventhough scales to measure tiredness have been used in research for some time now (20,21), unlike pain scales, there appears to be no standardized cut-off point to describe a level of tiredness at which intervention is indicated.

Investigation of both the most effective dose and most effective timing of modafinil administration are neccessary. Whether or not, pre-operative administration of modafinil increases subsequent anesthesia or sedation requirements, should administration of such drugs coincide with peak plasma concentrations of modafinil, at 2 to 4 hours after oral intake is not known.

In conclusion, administration of modafinil before sedation/analgesia does not improve objective measures of psychomotor function in treated patients. However, reported levels of subjective patient tiredness were lower in modafinil treated patients. Whether this reduction in subjective tiredness allows an earlier return to the activities of daily life needs to be established. Further investigation of modafinil use in specific subgroups of patients, including those with narcolepsy or obstructive sleep apnoea/hypopnea syndrome may have important implications for allowing the treatment of such patients in the ambulatory setting.

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Chapter 7

General discussion

General discussion.

Ambulatory anesthesia and surgery have undergone dramatic expansion over the last 2 decades to its current position of treating in excess of 50% of elective surgical cases (1). The growth of ambulatory practise has arisen due to a number of factors, including organisational, anesthetic, surgical, financial and patient issues. However, important questions are now being considered. How far has ambulatory care advanced thus far and what further steps can be taken to ensure continued delivery of quality patient care ?

While morbidity and mortality rates in relation to ambulatory care are recognised to be low (2), as are unscheduled patient admission rates immediately following surgery and post discharge readmission rates (3,4), it is clear on closer inspection of outcome measures that there are some areas in need of further improvement. Post discharge syptoms such as pain, nausea and tiredness are frequently reported (5,6,7). Obviously, such adverse effects are not limted to the outpatient setting but are also a major challenge in the care of inhospital patients. However, the important difference for hospitalised patients is that trained medical and nursing staff are readily available to assess patient status and implement any neccessary treatment. Such an option does not exist for ambulatory patients and it is therefore essential that every effort is made to minimise the occurence of such problems after discharge.

During ambulatory treatment, both anesthetic and surgical techniques must be tailored to achieve rapid recovery and minimal adverse effects in patients who are scheduled to be discharged home within hours of the procedure. Increasingly diverse surgical procedures performed on older and sicker patients require a variety of anesthesia techniques to be utilised in order to achieve the best care for individual patients both during admission and after discharge. Surgical techniques strive to be minimally invasive and not of excessive duration. Anesthetic techniques aim to combine good operating conditions with a rapid recovery, adequate analgesia and minimal side effects while

maintaining high patient turnover rates.

Important developements in the delivery of ambulatory anesthesia include better preoperative patient evaluation, optimisation of patient health status, incorporation of drugs with better recovery profiles, use of less invasive airway devices and expansion of the role of locoregional anesthesia techniques. A faster and better quality patient recovery has been demonstrated using newer anaesthetic agents such as sevoflurane and desflurane (8). The development and widespread use of supralaryngeal/supraglottic airway devices has had important consequences. Avoidance of endotracheal intubation has reduced the potential for trauma to the vocal cords and teeth, as well as reducing the use of muscle relaxants and reversal agents, with their associated side effects (9). Multi-modal approaches to both pain management and post operative nausea and vomiting (PONV) have demonstrated benficial effects. However, it is clear that despite such advances, there exists a need for even greater optimisation of available techniques.

Use of techniques long established in inpatient practise do not neccessarily produce adequate outcome measures in ambulatory patients. More precise techniques are indicated to ensure that patients achieve an optimal level of recovery prior to discharge home. Achieving such standards of care in a busy ambulatory setting requires the development of techniques which facilitate such a process. This thesis has concentrated on a number of areas within the practise of ambulatory anesthesia whereby, either through adjusting pre-existing techniques or incorporating new techniques, patients benefit in terms of the accuracy of care provided and the associated reduction in adverse effects.

The first area of focus is that of locoregional anesthesia. There has been a renewed interest in locoregional anesthesia techniques over the last decade or so, as evidenced by the enormous growth in the number of publications on the subject. Benefits to patients in terms of post operative pain control, red-

uction of opioid related side effects and mobilisation have been extensively reported (10). New techniques such as continuous nerve block catheters, stimulating catheters, ultrasound guided nerve block placement are being continuously evaluated (11,12,13). There remains however the difficulty of accurately identifying the success or failure of nerve blockade. Relying on traditional methods of patient response to cold or pinprick sensation is not ideal, for several reasons not least of which is the lack of objectivity. As demonstrated in two of the studys reported in this thesis (14,15), such traditional approaches to locoregional block assessment can lead to late discovery of failed blocks. Failed bocks require the administration of a supplemental locoregional anesthesia block, infiltration with local anesthetic or in certain circumstances conversion to general anesthesia. In addition to the stress which such practise causes to both patients and practioners, it may also lead to delays in operating room schedules. In this thesis, two non-invasive, objective techniques of locoregional block assessment are studied and shown to be more reliable than both pinprick and cold sensation in the identification of block outcomes, allowing alternative methods of anesthesia to be put in place prior to surgical incision (14,15).

The first technique, infrared thermography measures temperature change in the blocked limb and has the advantage of creating a colour coded visual image of the area. Any regions failing to show a temperature increase secondary to local anesthetic blockade are easily identifiable by the absence of a temperature increase (14). A limitation of this method is cost, although the financial aspect is becoming less of a deterrant as cheaper, hand held devices are now available. Peripheral flow index (PFI) is the second technique investigated (15). This technique is simple to use and available through application of additional software to pre-existing pulse oximetry probes, allowing alterations in blood flow through a digit to be easily measured and presented as a numerical value. This study has shown that failed blocks do not cause an increase in the value for PFI. Both of the aforementioned techniques offer a means

of more accurately identifying block outcomes and offer a means of improving both the quality and effiency of patient care, when using locoregional techniques.

In the area of airway management there has also been a change in the ambulatory setting. During recent years, there has been a dramatic move away from tracheal intubation towards the use of less invasive supraglottic or supralaryngeal airway devices. In the majority of ambulatory treated patients, such devices represent the airway device of first choice, with tracheal intubation being reserved for situations in which specific contra-indications to supraglottic airways exist. New airway devices are increasingly marketed, but do the newer devices offer any specific benefits for patients over the original classic laryngeal mask airway (LMA-Classic) ? In a study comparing the Cobra perilaryngeal airway (CobraPLA) to the original LMA-Classic, the CobraPLA has been shown to have higher sealing pressures in patients both with and without pneumoperitoneum, which may be of benefit to specific patients (16). The finding of an increased incidence of macroscopic blood on the CobraPLA compared to the LMA-Classic did not translate into an increased incidence of throat morbidity and thus, in terms of post operative side effects, devices were similar.

Concerning anesthetic pharmacological developments, agents such as sevoflurane, desflurane, propofol, alfentanil, fentanyl, sufentanil and remifentanil have certainly contributed to the advancement of anesthesia practise both in the inpatient and outpatient setting. The faster metabolism and more rapid recovery profiles associated with such drugs allow quicker recovery of patients following procedures. The analgesic drug, remifentanil, in particular has gained popularity in ambulatory practise due to its' rapid onset and offset. The side effect profile of remifentanil (17), which includes nausea, vomiting and dizziness (18) has however limited use. The question arises as to whether, remifentanil is being used in an optimised manner. The findings of the next

study in this thesis (19) highlight the need for careful attention to setting a remifentanil dosing regimen, so that the benefits of this unique drug are not negated by any dose related side effects. The study om remifentanil use during extracorpoeal shock wave therapy demonstrates that careful attention to achieving an optimal level of analgesia, while avoiding excessive administration, minimises the occurence of side effects and achieves good patient satisfaction levels.

Finally, it may be time to look beyond the limits of traditional anesthesia drugs to ensure good outcomes in ambulatory practise. Modafinil, a traditionally non anesthetic drug, widely used as an 'awakening' agent in the treatment of narcoplepsy, appears to offer a beneficial role in recovery of patients following combination sedation/analgesia. In patients recovering from a combination of midazolam and fentanyl, modafinil did not improve objective tests of psychomotor function, however, patient self reported tiredness, was reduced in modafinil versus placebo treated patients. Further evaluation is required to determine whether modafinil has a positive impact on time to resumption of normal activities and paid employment, post anesthesia and surgery, an issue with obvious financial implications for the community in general. Additionally, use of modafinil in specific patient groups such as those with narcolepsy or obstructive sleep apnoea/hypopnea syndrome may have important implications for the treating such patients in the ambulatory setting.

The conclusion of this thesis is that greater focus on detail and optimisation of anesthesia technique provides improved patient care. Patients benefit when locoregional anesthesia blocks are objectively and reliably assessed prior to surgical incision. Selection of the most appropriate airway device for specific patients offers benefit in terms of allowing optimal ventilation of the lungs. Careful adjustment of analgesic drug dosing regimem to achieve optimal levels of pain control while avoiding dose related side effects improves patient satisfaction. Finally, looking beyond the boundaries of trad-

itional anesthesia practise toward the use of drugs such as modafinil may be an important key to ensuring the continued expansion and development of ambulatory anesthesia care.

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Chapter 8

Summary/ Samenvatting

Chapter 1. Introduction.

Ambulatory anesthesia and surgery is the delivery of high quality and efficient care to patients on a same day basis. The aim is that patients should achieve a rapid recovery with minimal post operative complications allowing same day home discharge and avoidance of a need for hospitalisation. It is a rapidly expanding area of medicine and currently in excess of 50% of elective surgical patients are treated on an ambulatory basis in many developed countries. Ambulatory treatment offers patients advantages in terms of faster resumption of normal activities, decreased risk of hospital accquired infections and hospitals benefit by cost savings. A large part of the success of ambulatory surgery is due to the role of anesthesia in adapting techniques to ensure rapid recovery and minimal post operative side effects. Treatment of patients in the ambulatory setting has been shown to have low levels of morbidity and mortality and scores well in terms of patient satisfaction. Problems however remain, such as complaints of pain, nausea and tiredness after discharge home, suggesting that optimal modes of practise need to be developed. Anesthesia care is multifaceted and various factors including appropriate patient, technique, drugs and equipment selection contribute to the final result. For continued safe and efficient expansion of ambulatory care, development of techniques for an increasingly diverse group of patients undergoing more complex surgical procedures is required.

Chapter 2. Thermographic temperature measurement compared with pinprick and cold sensation in predicting the effectiveness of regional blocks.

There is no standardized means of assessing the sucess or failure of loco-regional blocks, with the inevitable result that failed blocks are frequently identified at a late stage, requiring alternative or additional techniques of anesthesia to be put in place, leading to operating room schedule delays and increased stress for both patients and staff. This study was designed to evaluate the usefulness of thermographic temperature measurement with an infrared camera, compared with patient response to cold and pinprick, as a means of assessing the success or failure of axillary blockades. Axillary blocks were performed on 25 patients undergoing surgery on the hand or forearm using a nerve stimulator technique with mepivacaine 1.5%. Pinprick and cold sensation were assessed on the operative site at 5-min intervals for 30 min. A thermographic image of the operative limb was recorded at similar time intervals. Thermographic images of the unblocked limb were taken before block placement and at 30 min. Temperature values at the operative site and unblocked limb were calculated from the thermographic images. Results revealed that thermography had higher combined values for sensitivity, specificity, and positive and negative predictive values than both cold and pinprick at all time intervals, with statistically significant differences at 15 min (thermography versus cold, P = 0.006; thermography versus pinprick, P = 0.026) and 30 min (thermography versus cold, P = 0.038; thermography versus pinprick, P = 0.040). For thermography as a method of block assessment, an optimal time of 15 min after mepivacaine local anesthetic injection gives the highest combined values for predicting a successful block (P = 0.004). We conclude that thermography provides an early and objective assessment of the success and failure of axillary regional blocks.

Chapter 3. Peripheral flow index is a reliable and early indicator of regional block success.

Pulse oximetry probes are now part of standard monitoring for the measurement of oxygen saturation levels during during all forms of anesthesia. A secondary measurement, peripheral flow index (PFI), which is the ratio of the pulsatile versus the nonpulsatile component of the pulse oximetry signal may also be measured using these probes. The purpose of this study was to investigate the usefulness of peripheral flow index (PFI) measurement using a standard pulse oximetry digit probe for early prediction of successful regional blocks. Sixty-six patients scheduled for limb surgery underwent either axillary or sciatic block using a nerve stimulator technique with mepivacaine 1.5%. PFI, was recorded from 10 minutes before block insertion until 30 minutes afterwards. PFI recordings of the unblocked limb were similarly recorded. Pinprick and cold sensation were assessed at 5-min intervals until 30 min after blockade. An increase in PFI by a factor of 1.55 at 10 min after axillary block placement ($P = 0.006$), and 12 min after sciatic block placement ($P = 0.001$) was required to predict a successful block. The sensitivity and specificity of PFI was 100% for predicting axillary block outcomes at this time. Positive predictive value was 95% and negative predictive value was 93%. For sciatic blocks, sensitivity and specificity were 90% and 100%, respectively. The calculated positive predictive value at time 12 min for sciatic blocks was 94% and negative predictive value was 92%. At 15 min after block placement, cold and pinprick sensations had the same calculated values for sensitivity and specificity at 71% and 100%, respectively, for axillary blocks. For sciatic blocks, cold sensation had a sensitivity of 77% and a specificity of 100%, whereas pinprick had a sensitivity of just 20% with a specificity of 100%. We conclude that PFI provides a simple, early, and objective assessment of the success and failure of nerve blocks.

Chapter 4. A randomized prospective study comparing the cobra perilaryngeal airway and laryngeal mask airway-classic during controlled ventilation for gynecological laparoscopy.

An increasing number of noninvasive, supraglottic airway devices are currently available. In this randomized single-blind study, the Cobra Perilaryngeal Airway (CobraPLA) was compared to the Classic Laryngeal Mask Airway (LMA-Classic) during gynecological laparoscopy. Forty patients received either an LMA-Classic or a CobraPLA. Insertion, ventilation and removal characteristics were noted, as well as any throat morbidity. Devices were similar for insertion characteristics, adverse events, and throat morbidity. Before pneumo-peritoneum, peak airway pressures were 20.3 ± 4.9 cm H2O in the LMA-Classic group versus 25.5 ± 7.9 cm H2O in the CobraPLA group, $P = 0.01$. This difference was maintained during pneumoperitoneum; LMA-Classic (22.8 ± 6.1 cm H2O) and CobraPLA (28.1 ± 8.5 cm H2O), $P = 0.04$. Macroscopic blood occurred only on the CobraPLA, seen on 40% of the devices after removal, $P = 0.001$. We conclude that during gynecological laparoscopy, the CobraPLA provides similar insertion characteristics, but higher airway sealing pressures than the LMA-Classic.

Chapter 5. Remifentanil as a single drug for extracorporeal shock wave lithotripsy: a comparison of infusion doses in terms of analgesic potency and side effects.

This randomized, double-blind study was designed to evaluate analgesic effectiveness and side effects of two remifentanil infusion rates in patients undergoing extracorporeal shock wave lithotripsy (ESWL) for renal stones. We included 200 patients who were administered remifentanil either 0.05µg .kg-1. min-1(n = 100) or 0.1µg .kg-1. min-1(n = 100) plus demand bolus of 10µg of remifentanil via a patient-controlled analgesia (PCA) device. No other sedating drugs were given. The frequencies of PCA demands and deliveries were recorded. Arterial blood pressure, oxygen saturation and respiratory rate were recorded throughout the procedure; postoperative nausea and vomiting (PONV), dizziness, itching, agitation, and respiratory depression were measured post treatment. Visual analog scale (VAS) scores were taken preoperatively, directly postoperatively, and 30 minutes after finishing the procedure. There were no statistically significant differences in the frequency of PCA demands and delivered boluses or among perioperative VAS scores. The extent of PONV and frequency of dizziness and itching immediately after and dizziness 30 min after the end of treatment were significantly reduced in the smaller dose group. We conclude that a remifentanil regimen of 0.05µg.kg-1.min-1 plus 10µg demands is superior to 0.1µg.kg-1.min-1 plus demands, as there was no difference in the VAS scores recorded between groups and it has a less frequent incidence of side effects in patients receiving ESWL.

Chapter 6. Modafinil reduces tiredness after combination sedation/analgesia.

The aim of this study was to assess whether modafinil, an 'awakening' drug widely used for the treatment of narcolepsy and obstructive sleep apnoea/hyperapnea syndrome improves recovery following sedation/analgesia. 67 patients scheduled for extracorporeal shock wave lithotripsy were randomly assigned to one of four groups. Two groups received a combination of fentanyl/midazolam with either modafinil or placebo. Remaining groups received remifentanil/propofol with either modafinil or placebo. Groups were compared using the digital symbol substitution test (DSST), trail making test (TMT), observer scale of sedation and analgesia (OAA/S) and Aldrete score. Verbal rating scale (VRS) scores for energy, appetite, nausea, restlessness, tiredness, relaxation, dizziness, pain, sleepiness, agitation, nervousness, excitement, appetite, headache and itch were recorded. Modafinil and placebo treated groups received similar doses of sedation and analgesic agents. No statistically significant difference was found for the DSST between modafinil and placebo treated groups. Mean VRS score for tiredness was less in the modafinil treated midazolam/fentanyl group compared to the placebo treated group, $p<0.05$. Such a difference was not found between the remifentanil/propofol modafinil versus placebo groups. Dizziness was greater in the modafinil treated remifentanil/propofol group versus placebo, $p < 0.05$. No significant adverse effects occurred in relation to modafinil use. No statistically significant difference between modafinil and placebo treated groups was identified for the TMT, OAA/S and Aldrete scores. In conclusion, this study has shown that modafinil improves recovery following longer acting forms of sedation/analgesia in terms of subjective patient reporting of tiredness, however does not improve psychomotor function as measured objectively. Further research is required to establish whether specific subgroups of patients, would benefit in terms of recovery from sedation and anesthesia.

Samenvatting

Hoofdstuk 1. Introductie.

Bij ambulante anesthesie en chirurgie draait het om het leveren van hoge kwaliteit en efficiënte zorg aan patiënten in dagbehandeling. Het doel is dat patiënten een snelle postoperatieve hersteltijd hebben met zo min mogelijk complicaties, zodat zij dezelfde dag nog het ziekenhuis kunnen verlaten zonder opgenomen te hoeven worden. Het is een snel groeiende tak van de geneeskunde en momenteel wordt in vele landen 50% van de electieve chirurgische patiënten in dagbehandeling behandeld. Ambulante behandeling biedt patiënten vele voordelen waaronder het sneller kunnen hervatten van normale activiteiten en een afgenomen risico op in het ziekenhuis opgelopen infecties. Voor ziekenhuizen levert het een kostenbesparing op. Een groot aandeel in het succes van ambulante chirurgie valt ten deel aan de anesthesie, door het aanpassen van de technieken om zo een snelle hersteltijd te bevorderen met minimale postoperatieve bijwerkingen. Behandeling van patiënten in dagbehandeling heeft laten zien dat er een lage morbiditeit en mortaliteit is en dat er goed gescoord wordt als gekeken wordt naar patiëntentevredenheid.

Problemen als pijnklachten, misselijkheid en vermoeidheid na ontslag wekken de suggestie dat een meer optimale manier van behandelen ontwikkeld moet worden. Anesthesiologische zorg omvat vele facetten en variabele factoren, waaronder een juiste patiëntenselectie, gebruikte technieken en uitrusting, en de toegediende medicatie, die allemaal bijdragen aan het uiteindelijke resultaat. Voor een veilige en efficiënte groei van de ambulante zorg zal een verdere ontwikkeling van technieken, voor een toegenomen diversiteit aan patiënten, die steeds meer complexe chirurgische ingrepen ondergaan, noodzakelijk zijn.

Hoofdstuk 2. Thermografische temperatuurmeting in vergelijking met speldenprik en koude sensaties om de effectiviteit van regionale blokken te voorspellen.

Er bestaat geen gestandaardiseerde manier om het succes of falen van regionale blokken vast te stellen, wat onvermijdelijk resulteert in falende regionale blokken die in een te laat stadium worden geïdentificeerd, waardoor alsnog alternatieve of additionele technieken toegepast dienen te worden. Dit leidt er onvermijdelijk toe dat er een vertraging optreedt in het operatiekamerschema, als ook toegenomen stress voor zowel patiënten als personeel. Dit onderzoek is ontworpen om de bruikbaarheid van thermografische metingen met een infrarood camera te evalueren in vergelijking met de patiëntenreactie op een speldenprik en koude sensaties, om het succes of falen van axillair blokken vast te stellen.

De axillair blokken werden bij 25 patiënten, die chirurgie aan de hand of onderarm ondergingen, uitgevoerd met behulp van een zenuwstimulator en mepivacaine 1,5%. De speldenprik en koude sensaties werden aan de te opereren extremiteit toegepast gedurende 30 minuten met een interval van 5 minuten. Thermografische beelden van de te opereren extremiteit werden op dezelfde momenten vastgelegd. Thermografische beelden van de contralaterale arm werden vastgelegd voordat het axillair blok geplaatst werd en 30 minuten na het plaatsen van het blok. Het aantal graden werd berekend aan de hand van de thermografische beelden van de te opereren en de contralaterale arm. De resultaten lieten zien dat de thermografische metingen hogere sensitiviteit, specificiteit, en positief en negatief voorspellende waarden hadden dan wat werd waargenomen voor zowel de speldenprik als de koude sensaties. Dit gold op alle tijdsintervallen, met statistisch significante verschillen op 15 minuten (thermografie versus koude, $P = 0.006$; thermografie versus speldenprik, $P = 0.026$) en op 30 minuten (thermografie versus koude, $P = 0.038$; thermografie versus speldenprik, $P = 0.040$). Als thermografie wordt gebruikt

om het succes of falen van een blok vast te stellen, dan blijkt de optimale tijd 15 minuten na de locaal geïnjecteerde mepivacaine te zijn om een succesvol blok te voorspellen (P = 0.004). Wij concluderen dat thermografie vroegtijdig en objectief het succes of falen van een axillair regionaal blok vaststelt.

Hoofdstuk 3. Perifere flow index is een betrouwbare en vroege indicator voor het succes van een regionaal blok.

Puls-oxymetrie meters zijn inmiddels een onderdeel van de standaard monitoring geworden voor het meten van de zuurstofsaturatie tijdens elke vorm van anesthesie. Een tweede toepassing, de perifere flow index (PFI), welke de ratio is van de pulstatiële versus de non-pulstatiële component van het puls-oxymetrie signaal, kunnen ook gemeten worden met deze systemen. Het doel van deze studie was om te onderzoeken of de perifere flow index (PFI) meting, middels het gebruik van een standaard puls-oxymetrie meter, bruikbaar is als vroege voorspeller van het succes van een regionaal blok. Zesenzestig patiënten die gepland stonden voor een operatie aan een extremiteit ontvingen òf een axillair òf een ischiadicus blok aan de te opereren zijde met behulp van een zenuwstimulator techniek met mepivacaïne 1,5%. De PFI werd gemeten en genoteerd vanaf 10 minuten voor de blokplaatsing tot 30 minuten na de blokplaatsing. De PFI metingen aan de contralaterale extremiteit werden gelijktijdig genoteerd. Een speldenprik en koude sensaties werden met een interval van 5 minuten toegepast tot een half uur na het zetten van de blokkade. Een toename van de PFI met een factor 1.55, gemeten 10 minuten na het plaatsen van het axillaire blok (P = 0.006) en 12 minuten na het plaatsen van het ischiadicus blok (P = 0.001), was vereist om een succesvol blok te voorspellen. De sensitiviteit en specificiteit van de PFI was 100% voor het voorspellen van de uitkomst van het succes van het axillaire blok na 10 minuten. De positief voorspellende waarde was 95% en de negatief

voorspellende waarde was 93%. Voor ischiadicus blokken waren de sensitiviteit en specificiteit respectievelijk 90% en 100%. De berekende positief voorspellende waarde na 12 minuten was 94% en de negatief voorspellende waarde was 92% voor dit blok. Bij het axillaire blok hadden, 15 minuten na het plaatsen van het blok, de koude en speldenprik sensaties dezelfde berekende waarden voor sensitiviteit en bij de specificiteit waren de waarden respectievelijk voor koude en speldenprik sensaties 71% en 100%. Voor de ischiadicus blokken hadden de koude sensaties een sensitiviteit van 77% en een specificiteit van 100%. Daarentegen hadden de speldenprik sensaties maar een sensitiviteit van 20% met een specificiteit van 100%. Wij concluderen dat PFI een simpel, vroeg en objectief onderzoek is om het succes en falen van een zenuwblokkade vast te stellen.

Hoofdstuk 4. Een gerandomiseerde prospectieve studie die vergelijkt tussen de peri-laryngeale airway en het klassieke larynxmasker gedurende een gecontroleerde ventilatie tijdens gynaecologische laparoscopieën.

Een toegenomen aantal non-invasieve, supraglottische beademingshulpstukken zijn momenteel verkrijgbaar. In deze gerandomiseerde enkelblinde studie werd de Cobra Perilaryngeal Airway (CobraPLA) vergeleken met het klassieke larynxmasker (LMA-Classic) tijdens gynaecologische laparoscopieën. Veertig patiënten kregen òf het klassieke larynxmasker òf de CobraPLA. Bijzonderheden bij zowel de insertie als de ventilatie en de verwijdering werden genoteerd, evenals elke vorm van keel morbiditeit. Beide beademingshulpstukken waren gelijk voor wat betreft de karakteristieken voor het inbrengen, bijwerkingen en keel morbiditeit. Voor aanvang van het pneumoperitoneum waren de piek beademingsdrukken 20.3 ± 4.9 cm H2O in de LMA-Classic groep versus 25.5 ± 7.9 cm H2O in de CobraPLA groep ($p = 0.01$). Dit verschil bleef gehandhaafd gedurende het pneumoperitoneum, waarbij de piek

beademingsdrukken voor de LMA-Classic 22.8 ± 6.1 cm H2O en voor de Cobra-PLA 28.1 ± 8.5 cm H2O waren (P = 0.04).
Na het verwijderen van het beademingshulpstuk werd alleen bij 40% van de CobraPLA- groep macroscopisch aantoonbaar bloed gevonden (P = 0.001). Wij concluderen dat tijdens gynaecologische laparoscopie de CobraPLA dezelfde insertiekarakteristieken laat zien, maar hogere beademingsdrukken, na volledig afsluiten middels een cuff, dan de LMA-Classic.

Hoofdstuk 5. Remifentanil als monotherapie bij niersteenvergruizing: een vergelijking van analgetische potentie en bijwerkingen bij verschillende infusie doseringen.

Deze gerandomiseerde dubbelblinde studie is ontworpen om de analgetische effectiviteit en de bijwerkingen van remifentanil te evalueren, bij 2 verschillende infusie standen, in patiënten die een extracorporele shock wave lithotripsie (ESWL = niersteenvergruizing) ondergingen. Wij includeerden 200 patiënten die remifentanil ontvingen in een dosis van of 0.05 µg .kg-1. min-1 (n = 100) of 0.1µg.kg-1. min-1 (n = 100) met daarbij de mogelijkheid tot het krijgen van een bolusinjectie remifentanil van 10µg via een patiënt gecontroleerde analgesie (PCA) pomp. Er werden geen andere sedatieven gegeven. De frequenties van PCA aanvragen en toezeggingen werden geregistreerd. Arteriële bloeddruk, zuurstofsaturatie en ademhalingsfrequentie werden gedurende de gehele procedure geregistreerd. Postoperatieve misselijkheid en braken (PONV), duizeligheid, jeuk, agitatie en ademhalingsdepressies werden gemeten na afloop van de behandeling. Visueel analoge schaal (VAS) pijn scores werden preoperatief, direct postoperatief en 30 minuten postoperatief afgenomen. Er zijn geen statistisch significante verschillen in de frequentie van aanvragen en toezeggingen van PCA- bolussen of de peri-operatieve VAS scores gevonden. De omvang van de PONV en de frequentie van de duizeligheid en jeuk direct

postoperatief en de duizeligheid 30 minuten postoperatief zijn significant verminderd in de groep met de lage dosis. Wij concluderen dat remifentanil in een dosis van 0.05µg .kg-1. min-1 met een PCA bolus systeem van 10 µg remifentanil de voorkeur geniet boven een remifentanil dosis van 0.1 µg. kg-1. min-1 met een PCA bolus systeem van 10 µg remifentanil. Dit is gebaseerd op het feit dat er geen verschillen waren in de VAS-pijn scores die voor beide groepen genoteerd werden. Bovendien werd in deze groep patiënten een lagere incidentie van bijwerkingen gevonden.

Hoofdstuk 6. Modafinil reduceert vermoeidheid na de combinatie sedatie/analgesie.

Het doel van deze studie was om te onderzoeken of modafinil, een slaapreducerend medicijn dat wereldwijd gebruikt wordt bij de behandeling van narcolepsie en obstructief slaap apnoe/ hypapnoe syndroom, het herstel na sedatie/analgesie verbetert. 67 patiënten die gepland stonden voor een extracorporele shock wave lithotripsie (niersteenvergruizing) werden door loting in een van de vier studiegroepen geplaatst.

Twee groepen ontvingen een combinatie van fentanyl/ midazolam met modafinil of een placebo. De twee overgebleven groepen ontvingen een combinatie van remifentanil/ propofol met modafinil of een placebo. De groepen werden vergeleken door gebruik te maken van de Digitale Symbool Substitutie Test (DSST), Trail Making Test (TMT), observeerders schaal van sedatie en analgesie OAA/S) en de Aldrete score. Verbale Rating Score (VRS) voor energie, eetlust, misselijkheid, rusteloosheid, vermoeidheid, ontspannenheid, duizeligheid, pijn, slaperigheid, agitatie, zenuwachtigheid, opgewondenheid, eetlust, hoofdpijn en jeuk werden ook genoteerd.

De modafinil en de placebo groepen ontvingen gelijke hoeveelheden sedatie en analgesie middelen.

Er werden geen statistisch significante verschillen gevonden voor de DSST tussen de groepen die met modafinil of een placebo werden behandeld. Gemiddelde waarden voor de VRS voor vermoeidheid was echter minder in de modafinil groep die met midazolam/fentanyl behandeld werden in vergelijking met de placebo groep ($P < 0.05$). Zo'n verschil werd niet gevonden tussen modafinil versus placebo in de remifentanil/propofol groep. De VRS voor duizeligheid was groter in de met modafinil behandelde remifentanil/propofol groep in vergelijking met de placebo groep ($P < 0.05$). Er traden geen andere significante bijwerkingen op in relatie met het gebruik van modafinil. Er werden geen significante verschillen gevonden tussen de modafinil en de placebo groepen voor wat betreft de TMT, OAA/S en Aldrete scores. Concluderend heeft deze studie aangetoond dat modafinil de hersteltijd verbetert bij het gebruik van langwerkende vormen van sedatie/analgesie in de subjectieve waarneming van de patiënt betreffende de gemelde vermoeidheid. Desalniettemin verbetert de psychomotorische functie, als gemeten in de objectieve testen, niet. Vervolgonderzoek is nodig om vast te stellen of specifieke patiënten groepen, zoals diegenen met een obstructief slaap apnoe/ hypapnoe syndroom, baat hebben bij het gebruik van modafinil betreffende de hersteltijd na sedatie/ analgesie.

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Curriculum Vitae.

Eilish Galvin was born in Kerry, Ireland. She commenced medical school in October 1987 in the Royal College of Surgeons in Ireland, National University of Ireland, and received her medical degree in June 1993. She rotated through surgery, internal medicine and emmergency medicine before commencing anesthesia specialisation in 1995. Following successful completion of the primary and final fellowship examinations, she became a fellow of the college of anesthetists, RCSI in 1999. She became an advanced trauma life support instructor in 2003. Following completion of the senior specialist registrar rotation, she worked as fellow in ambulatory anesthesia at Erasmus University Medical Center (EMC) for 1 year. Since September 2004, she has been working as a staff anesthesiologist in the EMC. From December 2004, she has been the medical co-ordinator of the ambulatory surgical unit in EMC.