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NASAL CARRIAGE AND PERITONITIS BY *STAPHYLOCOCCUS AUREUS* IN PATIENTS ON CONTINUOUS AMBULATORY PERITONEAL DIALYSIS: A PROSPECTIVE STUDY

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♦ ***Objective***: **To establish whether or not patients on continuous ambulatory peritoneal dialysis (CAPD) using current infection control measures who are nasal carriers of *Staphylococcus aureus* are at risk for the development of *S. aureus* peritonitis.**

♦ ***Design***: **A prospective 22-month study analyzing nasal and skin/nasal (i.e., nasal and/or exit-site) carrier status for *S. aureus* and peritonitis episodes. Nasal swab cultures for *S. aureus* were taken with 1- to 3-month intervals; swab cultures from the catheter exit site were taken only when infection was suspected.**

♦ ***Setting***: **Renal unit, tertiary-care center.**

♦ ***Patients***: **All patients on CAPD at our center that could be observed during at least 2 months.**

♦ ***Interventions***: **None.**

♦ ***Main Outcome Measures***: **Nasal and skin/nasal carrier status, occurrence of peritonitis.**

♦ ***Results***: **Of 54 enrolled patients, 31 (57%) were nasal carriers for *S. aureus*: 6 of these 31 developed *S. aureus* peritonitis as opposed to none of 23 non-carriers ($p = 0.03$). The *S. aureus* peritonitis rate in 28 skin/nasal carriers was increased when compared to non-carriers ($p = 0.02$), but there was no difference between chronic and intermittent skin/nasal carriers ($p = 0.63$).**

♦ ***Conclusions***: **In our population, nasal carriers are at increased risk for the development of *S. aureus* peritonitis. Further studies should evaluate the effect of eradication of nasal carriage of *S. aureus* and the effect of additional preventive hygienic measures on the occurrence of peritonitis by *S. aureus*.**

KEYWORDS: nasal carriage; peritonitis; skin carriage; *Staphylococcus aureus*

Patients on dialysis are susceptible to bacterial infection, and *Staphylococcus aureus* constitutes a major pathogen within this patient category (1,2). The anterior nares are the main reservoir for *S. aureus*, and nasal carriage can maintain skin infections and thus increase the risk for subsequent invasive infections (3,4). Furthermore, *S. aureus* tends to adhere to the synthetic CAPD catheters, and therefore, it is the pathogen most frequently associated with catheter-tunnel and exit-site infections in CAPD treatment (5,6). According to the literature, *S. aureus* is the cause for CAPD-associated peritonitis in up to 24% of all cases (7,8). A retrospective study demonstrated that this complication represents a serious threat to both patient and technique survival in our patients (5). The association of *S. aureus* nasal carriage, infection of the catheter exit-site, and peritonitis has already been suggested (2,9–12). Luzar *et al.* (2) reported that although overall peritonitis rates between nasal carriers and non-carriers were not different, all cases of *S. aureus* peritonitis occurred in carriers. Sesso *et al.* (9) reported that chronic and intermittent *S. aureus* skin (i.e., nasal and/or exit site) carriers would develop *S. aureus* peritonitis more often than non-carriers.

Measures to eradicate nasal carriage by means of topical bactericidal ointments or antibiotics to prevent infectious complications are effective in patients on hemodialysis, but results from studies in CAPD patients have been contradictory (1,13–19). At our center, the introduction of hygienic measures [a new fluid exchange system (Twin Bag) and alcohol disinfection of hands] in 1988 was accompanied by a decreased incidence of gram-positive and gram-negative peritonitis and exit-site infections, but patient, technique, and catheter survival did not improve (5). To establish the need for investigations concerning the effect of *S. aureus* nasal carriage eradication on peritonitis incidence, we prospectively studied the relation of nasal carriage and peritonitis in our CAPD population.

METHODS

PATIENTS

All of the patients on CAPD at our center with an observation period of at least 2 months, from Novem-

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ber 1993 to September 1995, were enrolled in the study. Nasal swabs were taken with 1- to 3-month intervals on all patients. Swab cultures from the pericatheter skin (exit-site) were prepared whenever infection was suspected. Sex, age, CAPD treatment time, observation period, diabetic status, and previous *S. aureus* infections were taken into account in the analysis.

MICROBIOLOGY

For the preparation of nasal cultures, a swab moistened with sterile 0.9% saline solution was rotated in both anterior nares, placed into Amies medium (Eurotubo, Barcelona), and transported to the laboratory. Thereafter, the specimens were inoculated onto a blood plate and incubated for 48 hours at 37°C. Colonies macroscopically suspect for *S. aureus* and consisting of acinar gram-positive cocci microscopically were agglutinated with Stafaurex (Murex, Weesp). In positive agglutination tests, the strains were identified as *S. aureus*.

DEFINITIONS

S. aureus nasal carriage was defined by a positive nasal culture. *S. aureus* peritonitis was defined as a cloudy dialysate with leukocyte count $> 0.1 \times 10^9$ and >50% neutrophils in the differentiation and a positive culture for *S. aureus*. *S. aureus* exit-site infection was defined by the presence of a purulent secretion in combination with local erythema of the skin at the catheter-epidermal interface and a positive culture for *S. aureus*.

S. aureus skin/nasal carriage was classified according to the criteria by Sesso *et al.* (9) as chronic (positive culture for *S. aureus* from nose or exit site 75% or more of the time) or intermittent (positive culture more than once but less than 75% of the time). Non-carriers either had no positive culture or had only one isolate.

STATISTICAL ANALYSIS

The Mann-Whitney U test was used for analysis of continuous variables; in case of categorical variables, Fisher's Exact Test (two-tailed) was applied. Values are expressed as mean ± standard deviation. A p value < 0.05 was regarded as significant.

RESULTS

Overall, 58 patients were treated with CAPD during an observation period of 724 patient-months. During this period, 15 peritonitis episodes occurred in 14 patients, resulting in a peritonitis incidence of 1 episode per 48.3 patient-months. Four patients were excluded because of an observation period of less than 2 months. The remaining 54 patients were included in the study and observed during 13.4 ± 7.1 treatment months per patient (range, 2–23 months). Of these patients, 31 (57%) were nasal carriers. Demographic data of *S. aureus* nasal carriers compared to non-carriers were not different (Table 1). Four patients who had had a *S. aureus* peritonitis before the observation period were all nasal carriers, but none developed *S. aureus* peritonitis during the study period. Seven other patients (of which 4 were nasal carriers during the study) had a history of *S. aureus* exit-site infection, and 1 patient (non-carrier) had a history of *S. aureus* wound infection of the hand. One peritonitis episode (by *S. aureus*) resulted in catheter loss during the study period.

Patients with a negative nasal-carrier status (n = 23) did not develop *S. aureus* peritonitis, whereas 6 of 31 nasal carriers developed seven *S. aureus* peritonitis episodes (p = 0.03, Table 2). One diabetic nasal carrier developed *S. aureus* peritonitis twice during the observation period. Culture results during all peritonitis episodes are shown in Table 3.

In 18 of the 31 nasal carriers, the initial nasal culture was positive; in 13 a conversion from negative to positive nasal-carrier status took place during a

TABLE 1
Demographic Data of CAPD Patients with Positive or Negative Nasal Culture for *S. aureus*

	Nasal culture result			
	Negative	Positive	Total	p value
Number of patients	23 (43%)	31 (57%)	54	
Male/female	16/7	15/16	31/23	0.12
Age	56.3±15.5	54.5±14.3	55.3±14.7	0.31
CAPD treatment time (yr)	2.7±1.9	3.2±2.1	3.0±2.0	0.23
Cultures per patient	7.6±4.9	9.8±3.7	8.9±4.4	0.11
Observation time (mo)	11.1±7.8	15.1±6.2	13.4±7.1	0.10

TABLE 2
S. aureus Peritonitis Compared to Nasal Carrier versus Non-carriers Rates (p = 0.03)

Nasal Carriage	Peritonitis No	Yes	Total
No	23	0	23
Yes	25	6	31
Total	48	6	54

TABLE 3
Culture Results in 14 CAPD Patients Developing 15 Peritonitis Episodes during the Observation Period

Culture Result	Peritonitis Episodes
S. aureus	7
S. epidermidis	2
S. epidermidis and *Corynebacterium* sp.	2
Diphtheroid rod	1
Escherichia coli	2
Bacteroides sp.	1

mean observation period of 6.5 ± 6.1 months (range, 1 – 19 months) and after a mean of 4.8 ± 2.7 nasal cultures (range, 2 to 9).

Nine of 54 patients (17%) were diabetics; 7 of these 9 were carriers and 2 of these 7 developed *S. aureus* peritonitis. *S. aureus* nasal carrier status and peritonitis rate were not different for diabetic CAPD patients (p = 0.27 and p =0.26, respectively) when compared to nondiabetics, but diabetic patients developed a peritonitis caused by organisms other than *S. aureus* significantly more often than did nondiabetic patients (4 of 9 vs. 4 of 45, respectively; p = 0.02).

When patients were classified according to skin/nasal carriage, the *S. aureus* peritonitis rate was 11% (1/9) in chronic carriers and 26% (5/19) in intermittent carriers (Table 4). The *S. aureus* peritonitis incidence in chronic skin/nasal carriers was not different from that in intermittent carriers (p = 0.63). Skin/nasal carriage was associated with an increased risk for *S. aureus* peritonitis (p = 0.02). According to the criteria for skin/nasal carriage, *S. aureus* peritonitis did not occur in noncolonized patients.

DISCUSSION

As previously reported, the *S.aureus* peritonitis incidence within the CAPD population at our center decreased significantly from 0.26 ± 0.63 (period 1982–1988) to 0.08 ± 0.31 episodes per treatment year (period 1988–1994; p = 0.01). This decrease coincided with the introduction of the Twin-Bag system and ethanol hand disinfection from 1988 on, but was not accompanied by an improvement in patient or catheter survival (5). Therefore, additional hygienic measures with respect to infection control are mandatory. *S. aureus* nasal carriage in our CAPD patients was not determined regularly before the observation period in this study. Although conclusions based on an observation period of only 22 months should be regarded with care, it is clear that in our population, the nasal carriage rate for *S. aureus* (57%) during the observation period was high compared to data from previous studies (32% – 45%) (2,9,11,14). But most importantly, only *S. aureus* nasal carriers developed *S. aureus* peritonitis during the observation period. This is in accordance with a study by Luzar *et al.*, in which all *S. aureus* peritonitis episodes developed in nasal carriers, although the overall peritonitis rate of carriers was not different from non-carriers (2). Sesso *et al.*(9) and Pignatari *et al.* (10) demonstrated that CAPD patients who are nasal carriers of *S. aureus* are at higher risk of developing *S. aureus* peritonitis. Lye *et al.* (20) found *S. aureus* nasal carriage to be the

TABLE 4
Peritonitis and Skin/Nasal Carrier Status for *S. aureus* in 54 CAPD Patients

	Skin/Nasal Carriage n	Peritonitis Patients n	Episodes n
Chronic carriers	9	1[a]	1
Intermittent carriers	19	5[b]	6
Overall carriers	28	6[c]	7
Non-carriers	26	0	0
Total	54	6	7

The difference between carriers and non-carriers (Fisher's Exact Test) is indicated as follows:
[a] p = 0.26
[b] p = 0.01
[c] p = 0.02
The difference between chronic and intermittent carriers was not significant (p = 0.63).

most important predictive factor for *S. aureus* peritonitis. *S. aureus* infectious complications in patients on CAPD are attributed to the same strains that colonize the nose in some but not all studies (2,10,21,22). Although Sesso *et al.* suggest that it may be important to distinguish chronic from intermittent *S. aureus* skin/nasal carriers, in our study, the *S. aureus* peritonitis rate in chronic carriers was not different from that in intermittent carriers. Carriage of *S. aureus* can be defined as nasal or as skin/nasal. In our opinion, for clinical practice, the definition of nasal carriage is more helpful as it can be used prospectively, while the skin/nasal carrier status as defined by Sesso *et al.* can only be determined in retrospect.

In a multicenter study by Luzar *et al.* (2), diabetic patients were *S. aureus* nasal carriers at the start of CAPD in 77% of cases, and they developed exit-site infections more often. In this study, the nasal carrier rate was 78% in diabetics. *S. aureus* peritonitis did not occur more often compared to nondiabetics (2 of 9 vs. 4 of 45, $p = 0.26$). We found no obvious explanation why peritonitis not caused by *S. aureus* was more frequent in diabetics (4 of 9 vs. 4 of 45, $p = 0.02$).

In our study, the carriage of *S. aureus* was detected by placement of nasal and exit-site swabs into Amies medium, followed by inoculation onto blood plates. Van Ogtrop (23) reported that the exclusion of an enrichment procedure in broth may result in a false-negative culture rate of 44.6%. Whether or not the inclusion of a broth enrichment medium would have altered our study results can neither be proven nor ruled out, but it seems mandatory that such a medium should be included when determining carrier status or evaluating the effect of eradication of carriage of *S. aureus*.

In conclusion, *S. aureus* nasal and skin/nasal carriage within the CAPD population at our center is associated with an increased risk for *S. aureus* peritonitis. There is a need for prospective randomized studies evaluating the effect of additional preventive hygienic measures and carriage eradication of *S. aureus* on the occurrence of infectious complications by *S. aureus* in patients on CAPD.

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