

PROPHYLAXIS AGAINST *STAPHYLOCOCCUS AUREUS* PERITONITIS IN CONTINUOUS AMBULATORY PERITONEAL DIALYSIS

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Summary

To achieve prophylaxis for *Staphylococcus aureus* peritonitis, we vaccinated 15 patients with a specific Staphylococcal vaccine (Staphypan Berna) containing Staphylococcal anatoxin.

Subsequently these patients had no episodes of *Staphylococcus aureus* peritonitis, a significant increase in plasma anti-staphylolysin, an increased concentration in peritoneal effluent of some opsonic active proteins such as IgA and complement (C₃ and C₄), inhibition of growth of *Staphylococcus aureus* by dialysate fluid from vaccinated patients and negative *Staphylococcus aureus* cultures from various skin areas previously positive.

Introduction

Continuous ambulatory peritoneal dialysis (CAPD) is widely accepted in the treatment of end-stage renal disease but is associated with a high rate of peritonitis, occurring at least once in over half of the patients with an incidence of 1.3 episodes per patient year.

The incidence has been reduced but not eliminated by new techniques, patient education, development of better equipment and various devices such as microfilters [1], improved connections and ultraviolet light [2]. The organisms [3] responsible for peritonitis are usually *Staphylococcus epidermidis* and *Staphylococcus aureus*, often cultured from various skin sites of CAPD patients. *Staphylococcus aureus* peritonitis runs a protracted and serious clinical course [4] requiring prolonged antibiotic therapy and hospitalization. Exit-site infection is a major precipitating cause often requiring removal of the peritoneal catheter.

Although many factors operate in the pathogenesis of peritonitis in CAPD patients, various studies indicate that alterations in the host defences of the peritoneal cavity may play an important role, mainly in the case of Staphylococcal peritonitis [5]. In order to achieve prophylaxis of *Staphylococcus aureus* peritonitis by measures that enhance local defence mechanisms, we have vaccinated our CAPD patients with a specific Staphylococcal vaccine (Staphypan Berna) containing Staphylococcal anatoxin.

Patients and methods

From February 1982 to February 1985 a total of 21 patients (12 females and 9 males) with a mean age of 55.25 ± 15.2 years, have been treated by CAPD in the Department of Nephrology of the 'SS Annunciata Hospital, Taranto, Italy. The cumulative duration of treatment was 225.6 months.

Peritoneal access was gained by the curled Tenckhoff peritoneal catheter. CAPD was carried out using the Closter Double-bag System[®] manufactured by Bieffe Grossotto, Italy.

All patients were dialysed with three to five daily exchanges, seven days per week. The fluid was allowed to dwell for five hours in the daytime and eight hours overnight.

Twelve patients received CAPD as a first choice, nine were transferred from haemodialysis because of cardiovascular (two patients) or vascular access problems (seven patients).

The vaccine protocol was six 1ml vials of increasing concentration i.m. every other day with a booster dose every three months.

During the period from February 1982 to February 1985 26 episodes of peritonitis were documented — an overall incidence of one episode per 8.6 patient months.

The organisms responsible were:

<i>Staphylococcus epidermidis</i>	(9 cases: 34%)
<i>Staphylococcus aureus</i>	(5 cases: 18%)
<i>Escherichia coli</i>	(4 cases: 15.3%)
<i>Streptococcus</i>	(3 cases: 11.5%)
<i>Acinetobacter</i>	(3 cases: 11.5%)
<i>Staphylococcus saprophiticus</i>	(1 case: 3.8%)
<i>Enterobacter</i>	(1 case: 3.8%)

The clinical symptoms of peritoneal infection included cloudy effluent, nausea, vomiting and abdominal pain; chills were rare.

Results

Table I shows the incidence of peritonitis in the vaccinated group during February 1984 to February 1985.

TABLE I. Incidence of peritonitis in the vaccinated group (February 1984—February 1985)

Patients submitted to anti- <i>Staphylococcus aureus</i> vaccination	15
Cumulative follow-up	120 months
Episodes of peritonitis	6
Peritonitis rate/patient month	1 in 20
	(0.6 episodes/patient year)

Organisms cultured in peritoneal effluent

<i>Staphylococcus epidermidis</i>	1	16.6%
<i>Escherichia coli</i>	2	33.3%
<i>Acinetobacter</i>	2	33.3%
<i>Streptococcus</i>	1	16.6%

Incidence of *Staphylococcus aureus* peritonitis in vaccinated group = 0

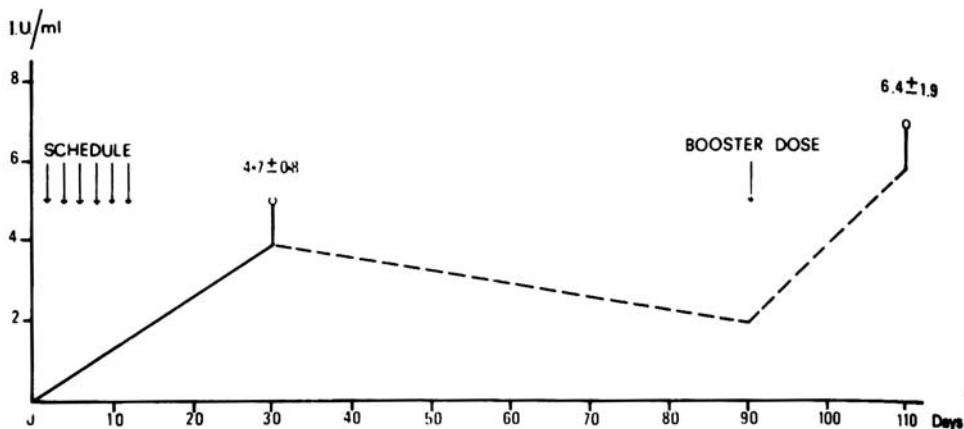


Figure 1. Increase of anti-staphylolysin serum levels after schedule and booster-doses of vaccine in 15 patients (mean \pm SEM)

It is interesting to note that there were no episodes of *Staphylococcus aureus* peritonitis. No reactions to the vaccine have been seen. Moreover the patients have shown a significant increase in plasma anti-staphylolysin (Figure 1) measured by the Behringwerke analysis. Cultures from all sites (skin exit, nasopharynx, nail beds) in all the patients were negative and there was quick recovery in two cases of *Staphylococcus aureus* tunnel infections. The growth of *Staphylococcus aureus* inocula (10^5 colony forming units/ml) was inhibited when cultured in Baird-Parker-Agar broth with dialysate fluid from vaccinated patients (80% of cases) while there was the usual growth [7,8] on incubation with fluid from unvaccinated patients (100% of cases).

Discussion

Although many factors contribute to the pathogenesis of peritonitis in CAPD patients, such as exogenous contamination or gastrointestinal disease, alterations in host defences of the peritoneal cavity may play an important role, mainly in the case of Staphylococcal peritonitis [5]. Various studies have shown that the instillation of dialysate suppressed the phagocytic and bactericidal activity of polymorphonuclear leucocytes and peritoneal macrophages. Phagocyte cells recognize micro-organisms by complex processes which include such phenomena as opsonization. This mechanism involved immunoglobulin and complement, particularly IgA, IgG, and C_3 . These opsonic molecules function as ligands, facilitating the attachment of bacteria to the surface of phagocytic cells. After attachment, micro-organisms are ingested, killed and degraded. Human observations and experimental studies of animal models of peritonitis support the concept that phagocytic function is the first line of cellular defence against bacterial invasion and this function requires the presence of the opsonic molecules [6] which facilitate the ingestion of micro-organisms. Although normal peritoneal fluid contains opsonic molecules, such as IgG and C_3 comparable to that found in serum, peritoneal effluent from CAPD patients contains only about

one per cent of these critically important opsonic molecules and some authors propose the addition of purified IgG to the dialysate to increase the opsonic activity of this fluid [5]. The passive immunization of the peritoneal cavity would reduce the incidence of peritonitis in CAPD patients. Our experience suggests that anti-staphylococcal vaccination could enhance local defence mechanisms with the increased concentration in peritoneal effluent of some opsonic active proteins such as IgA, C₃, C₄ while IgG and IgM only slightly increase (Table II). This active immunization of the peritoneal cavity has reduced the

TABLE II. Daily opsonic active proteins removed before and 60 days after in 15 vaccinated patients (mean \pm SEM)

IgA	IgG	IgM	C ₃	C ₄	Average daily drainage volume (ml)
<i>Before vaccination</i>					
27.3 \pm 5.9	167.2 \pm 42.6	15.1 \pm 3.5	13.8 \pm 1.6	2.4 \pm 10.5	7620 \pm 1022
<i>After vaccination</i>					
46.4 \pm 7.8	180.7 \pm 137.3	19.1 \pm 9.7	27 \pm 1.9	6.5 \pm 1.9	8219 \pm 887
S	NS	NS	S	S	NS

incidence of *Staphylococcus aureus* peritonitis in our vaccinated patients (Table I) and inhibited the growth of *Staphylococcus aureus* colony in dialysate fluid in 80 per cent of cases. In addition, the increased serum anti-staphylolysin (Figure 1) improves the systemic defences against *Staphylococcus aureus* infections and results in negative *Staphylococcus aureus* cultures from various skin areas previously positive. Recent reports refer to the favourable results of anti-staphylococcal vaccination in children with ventriculo-peritoneal shunts, a condition resembling CAPD [9]. Also increased levels of IgA and IgG can be seen both in the serum and in the bronchial secretions and sputum of vaccinated children suffering from chronic bronchitis [10].

In conclusion our experience suggests that anti-staphylococcal vaccination could be a useful approach to the prevention of *Staphylococcus aureus* peritonitis but our preliminary results need further evaluation. Moreover, we intend to continue anti-staphylococcal vaccination and to extend this method to the use of a polyvalent vaccine against other gram-positive and gram-negative organisms, maybe formulated specifically for this purpose, and, in the case of relapsing peritonitis, with prepared autovaccine.

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