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Treatment of familial staphylococcal infection—comparison of mupirocin nasal ointment and chlorhexidine/neomycin (Naseptin) cream in eradication of nasal carriage

D. A. Leigh and G. Joy

Department of Microbiology, Wycombe General Hospital, High Wycombe, Bucks HP11 2TT, UK

Twenty-six families with recurrent staphylococcal infections were treated with either mupirocin nasal ointment (group M) or chlorhexidine neomycin (Naseptin) cream (group N) to the anterior nares, each combined with chlorhexidine soap for washing and chlorhexidine powder applied to other possible carriage sites. Patients receiving mupirocin following failure with chlorhexidine/neomycin (group M/N) were also treated. Treatment was given for seven days to 99 patients, 32 index (infected) patients and 67 family members. Follow-up swabs were collected by a study nurse 8, 14, 28, and 91 days after starting treatment. The carriage of *Staphylococcus aureus* in the anterior nares was 67%, in the axillae 22%, in the groin 23%, and perianal 19%. The carriage rates in the index patients was higher than family members, in all sites. The eradication of *S. aureus* from the nasal carriage site after therapy at 8 days was 95% in group M, 85% in group M/N and 61% in group N. Recolonization during the follow-up period was much less in those treated with mupirocin: 57% of patients in group M and 42% in group M/N were not carriers at 91 days, whereas 89% of patients group N were again colonized. Assessment clinically and in terms of prevention of further infective lesions showed that there was a higher response to mupirocin than to chlorhexidine/neomycin. Mupirocin nasal is a successful therapy for removing nasal carriage of *S. aureus* and has a prolonged effect on recolonization.

Introduction

Familial staphylococcal infection is common and represents a significant workload for general practitioners. Whilst one member of a family may be subject to recurrent infections, the carriage of *Staphylococcus aureus* in other members of the family is important in reinfections (Leigh, 1979). Microbiological investigation of the infected members of the family should include documentation of the major carrier sites such as anterior nares, axillae, groin and perianal areas. In recurrent infections, the possible carrier sites should also be examined in all family and household members. Many staphylococcal infections, particularly of the skin, are self-limiting and may not require antimicrobial chemotherapy. The positive carrier sites can be treated with antibiotic or antiseptic creams or powders. It is important to follow up the whole family after treatment to check eradication of carriage.

Mupirocin (Bactroban) is a local antimicrobial agent with great activity against staphylococci (Casewell & Hill, 1985; Sutherland *et al.*, 1985; Parenti, Hatfield & Weyden, 1987). Whilst the skin preparation is suitable for the treatment of infected skin

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lesions and staphylococcal carriage in general skin sites, another formulation of mupirocin—the calcium salt in a white soft paraffin base (Bactroban nasal)—is available for the treatment of carriage in the anterior nares. This preparation has been used successfully in elimination of nasal carriage from medical and nursing staff and patients (Casewell & Hill, 1986; Bulanda, Gruszka & Heizke, 1989; Holton *et al.*, 1991), but there is little published information on its use in familial staphylococcal infection.

We report here a study carried out in families with recent staphylococcal infections where mupirocin was compared to chlorhexidine/neomycin in treating carriage in the anterior nares; other carrier sites were treated with chlorhexidine powder (Hibitane) after washing with chlorhexidine soap solution (Hibiscrub).

Patients and methods

The families with recurrent superficial staphylococcal skin infections, such as furunculosis, styes and boils, were referred directly to the Microbiological Outpatients at Wycombe General Hospital by their general practitioners.

Clinical examination of the infected patients was carried out, and swabs were taken from the infected lesions and potential carrier sites (e.g. anterior nares, axillae, groin and perianal regions). All members of the family and other relatives living in the household were screened by swabbing these sites. Infected patients with pre-existing infected eczema were excluded, although those with mild atopy were included. Patients whose family members were not staphylococcal carriers were also excluded. Patients who had failed to respond to previous treatment with chlorhexidine/neomycin were treated with mupirocin, and these non-randomized patients were studied as a separate group.

The full treatment was given to all members of the family, whether or not they were staphylococcal carriers. This consisted of applying a nasal preparation—either mupirocin nasal ointment, containing 2% mupirocin (Bactroban Nasal, SmithKline Beecham) or 0·1% chlorhexidine +0·5% neomycin cream (Naseptin, ICI). A cotton bud was used to apply the medication to the anterior nares morning and evening for seven days. Treatment was selected by means of a random code. All patients also used 4% chlorhexidine gluconate (Hibiscrub soap solution, ICI) for washing, and 1% chlorhexidine as a powder (Hibitane powder, ICI) applied to the axillae, groin and perianal regions twice daily. The treatment was carried out for seven days.

A State Registered Nurse was employed to interview all families during and after treatment, and to collect all the follow-up swabs. The latter were taken from all potential carrier sites 8, 14, 28 and 91 days after starting treatment. Any infective lesions appearing during or after treatment were swabbed where possible.

Table I. Details of families studied

Treatment	Group	No of families	patients	Index members	Family Total
Mupirocin	M	9	9	23	32
Chlorhexidine/neomycin	N	9	11	23	34
Mupirocin, after failure with chlorhexidine/neomycin	M/N	8	12	21	33
Total		26	32	67	99

Swabs were transported to the laboratory in nutrient broth supplemented with 5% NaCl. Direct culture was carried out immediately and the salt broth was incubated for 24 h and cultured again. All strains of *S. aureus* were phage-typed and their susceptibility to mupirocin and neomycin determined by the disc method. Treatment was assessed in two main ways. First, by the eradication of strains from carrier sites and second by the prevention of recurring infective lesions.

Results

The families

Thirty-one families were entered initially into the study but five were excluded, three because of negative bacteriology results in the non-infected members of the family, one due to infected acne, and one due to inadequate therapy. Details of the 26 families studied are shown in Table I. Nine families each received mupirocin (group M), and chlorhexidine/neomycin (group N), and eight families received mupirocin after treatment with chlorhexidine/neomycin had failed (group M/N). Two families were included twice, having received unsuccesful treatment with chlorhexidine/neomycin before mupirocin; the interval between treatments was over three months and the phage types of the infecting staphylococci were different.

There were 99 patients included in the study, 32 index cases with episodes of active infection, and 67 family contacts. The average family size was similar in all three groups.

Infections and initial staphylococcal carriage

When first seen as outpatients, three of the nine index patients in group M had active infections from which *S. aureus* was isolated. Five did not have any current infection and one in culture from lesions was negative. There were 11 index cases in group N, six

Table II. Carriage of *S. aureus* at pre-treatment examination

		Group	Patients	*S. aureus* present (%)	% isolation Index patients	% isolation Family members
Anterior		M	32	21 (66)	56	70
Nares		N	34	18 (53)	64	49
		M/N	33	27 (82)	64	49
	Total		99	66 (67)	72	64
Axillae		M	32	10 (31)	33	30
		N	34	3 (9)	18	4
		M/N	33	9 (27)	33	24
	Total		99	22 (22)	28	19
Groin		M	32	6 (19)	33	13
		M	34	5 (15)	9	17
		M/N	33	12 (36)	58	24
	Total		99	23 (23)	34	18
Perianal		M	32	9 (28)	44	22
		N	34	3 (9)	9	9
		B/N	33	6 (18)	42	5
	Total		99	18 (18)	31	12

with active infection, one had no current infection, and four were culture negative. In group M/N, five of the 12 index patients had current infection, six were culture negative and one did not have a current infection.

The pre-treatment isolation of *S. aureus* from the carriage sites is shown in Table II. The highest carriage rate was found in the anterior nares, where 66 (67%) of the 99 patients were carriers. More patients in group M (66%) than in group N (53%) were nasal carriers. The carriage rate in group M/N was very high (82%), indicating the complicated nature of patients in this group. Positive nasal carriage was found in 72% of the index cases and 64% of family cases. In the index patients with negative nasal carriage, positive carriage in other sites was found in 63%. Rates of carriage in the other sites (axillae, groin and perianal areas) were much lower than in the nose, and varied between 18 and 23%. The carriage rates in all sites generally were highest in group M/N and index patients of all treatment groups. The carriage rates in all patients treated with chlorhexidine/neomycin were generally lower than those treated with mupirocin. Multiple site carriage (two or more sites) occurred in 34% of all the patients in the study, with no significant difference between the index patient and family members. However, carriage in all four sites was twice as common in index patients in group M (42%) and group M/N (42%), than group N (18%). Carriage of *S. aureus* in the axillae, groin and perianal regions was over twice as likely if nasal carriage was positive (48% vs 21%) and it was higher in index cases than family cases.

Results of treatment

Clinical assessment. The clinical assessment of families with recurrent staphylococcal infection is difficult, as the use of nasal preparations does not prevent those infections that are already developing at the start of treatment. The important factor in success of therapy is to prevent further infective lesions after treatment. The overall assessment showed the highest clinical success rate in group M, where five (56%) of the nine families had no further infections (Table III). Success was observed in 33% of families in the M/N group, and in 27% of those in group N.

Five of the nine index patients in group M, did not have any more lesions during long-term follow-up, three developed lesions after one month and one after three months. In group N (11 index patients), lesions developed within one month in seven patients, two months in one, and only three patients did not develop any more lesions during the follow-up period. In group M/N only four of the 12 index patients remained free of infection; seven developed infections within one month and one in three months.

Table III. Clinical results in the index patients

	Group	No. of index patients	No further infection	Failure and reinfection
Mupirocin	M	9	5 (56%)	4–3 at 1 month 1 at 3 months
Chlorhexcidine/neomycin	N	11	3 (27%)	8–7 at 1 month 1 at 2 months
Mupirocin after failure with chlorhexidine/neomycin	M/N	12	4 (33%)	8–7 at 1 month 1 at 3 months

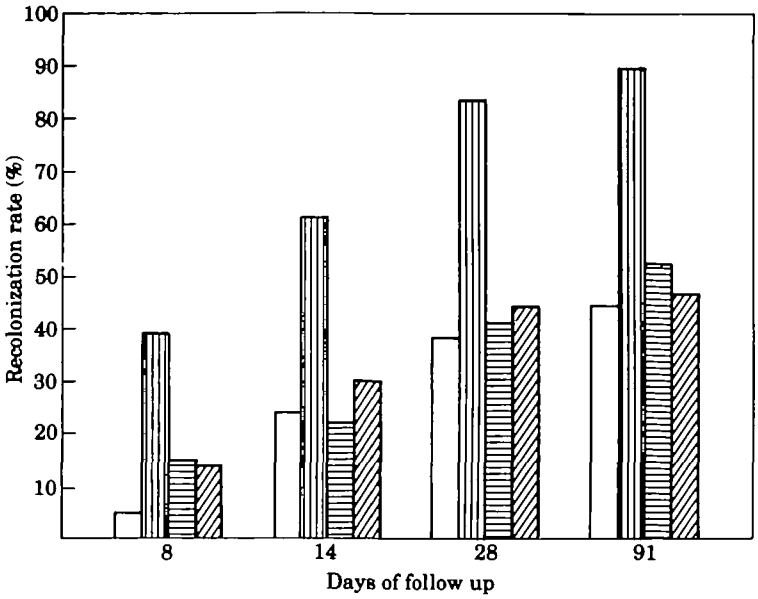

Figure 1. Recolonization of carrier sites during the follow-up period. □, mupirocin (group M); ▥, chlorhexidine/neomycin; ▤, mupirocin, after failure with chlorhexidine/neomycin (group M/N); ▨, combined sites of axillae, groin, perianal.

Skin atopy was present in five families in the study. This resulted in a poor response rate: four who had first received chlorhexidine/neomycin all failed therapy and only one of the families (which contained two index patients) responded to mupirocin. The application of both mupirocin ointment and chlorhexidine/neomycin cream to the anterior nares was well tolerated by all patients and no side-effects were reported.

Mupirocin therefore was significantly better than chlorhexidine/neomycin in clearing the carriage of nasal staphylococci and preventing subsequent infections.

Clearance of carrier sites. All strains of *S. aureus* isolated from infections and the carriage sites before and after treatment were fully sensitive to both mupirocin and neomycin. Eradication of *S. aureus* from the positive nasal carrier sites and recolonization is shown in Figure 1. The results show a high eradication rate (95%) at eight days in group M, a similar result in group M/N (85%) and a less favourable outcome in group N (61%). Recolonization occurred more readily and earlier after chlorhexidine/neomycin, and at the 91 day follow-up only 11% of patients were not recolonized. The recolonization rate in group M was much lower 57% of patients remaining free of colonization. The complicated group (N/M) resembled group M, 48% of all patients not being recolonized at 91 days. However, the rate in index patients in group M/N was much lower (27%), probably as a direct consequence of the complicated nature of these patients and their previous treatment failures. In the 33 patients who were negative before treatment nasal carriage was acquired by only 8 (24%) over the 91 day follow-up period. The eradication of *S. aureus* from the axillae, groin and perianal carriers in all three groups was efficient, with a combined rate of 86% at eight days and recolonization was moderate, 54% at 91 days. There was no significant difference between the clearance of the three sites. Recolonization in all treatment groups was usually by the original phage-type, 69% in the nose and 76% at other sites. However,

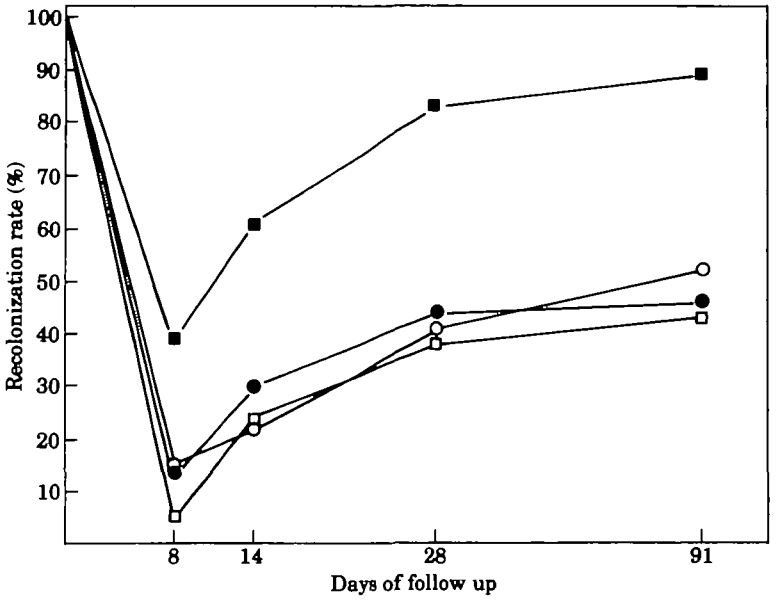

Figure 2. Recolonization of carrier sites during the follow-up period. □, mupirocin (group M); ■, chlorhexidine/neomycin (group N); ○, mupirocin, after failure with chlorhexidine/neomycin; ●, combined sites of axillae, groin, perianal.

in the nose patients in group N were to be recolonized by the same phage type (94%), at all follow-up times. The figure for group M was 44%, and in group M/N 57%. There was a wide distribution of phage types (Table IV), with group III (31%) the commonest. The phage types isolated from infective lesions were generally found in one or more carrier sites of the patient (71%) and in positive sites in 53% of other members of the family. Patients with multiple carriage (two or more sites) usually had the same

Table IV. Phage types isolated from the infected patients & carriage sites at entry to study

Phage type group	Previous infected lesions	Carriage sites nose	axillae	groin	perianal	Total
Total strains typed	18	61	22	23	18	120
Group 1	5 (28%)	16	3	3	2	24 (20%)
Group 2 (4%)	—	7	3	5	3	18 (15%)
Group 3	5 (28%)	12	11	7	7	37 (31%)
Mixed groups	5 (28%)	10	2	2	—	14 (12%)
Non-typable	3 (17%)	16	3	2	6	27 (23%)

Details of phage types

Group 1	29, 29/52, 29/52/52A 29/52/80, 29/52/52A/80, 29/52/80, 29/52/52A/80 29/79, 52/80, 79	Group 3	6/42E/77, 6/42E/75, 75, 6/47/53/75/83A, 42E/81, 42E, 53, 53/75, 96, 94/96
Group 2	3A/3C/55/71, 3C, 55, 55/71, 71/95	Mixed	29/52/52A/80/85, 52/42E, 29/52/52A/80/84/85/81,
	29/52/80/81		29/52/80/81

phage type in all sites (70%) and none had more than two phage types. The phage types carried by members with positive carriage in a family were the same in 38% of families, and 31% carried either two or three phage types. The carriage rate of the same phage type in family members varied from one to four members. No family had carriage in all members. Acquisition of phage types after treatment showed the same phage type in 58% of family members.

New infections occurred in four index patients (44%) in the mupirocin group, and two (50%) were due to different phage types. In group N, eight index patients (73%), had new infections, but four (50%) were due to the same phage type. In those patients in group M/N who failed treatment, 12 index patients showed a high level of reinfection, and eight (67%) new infections occurred, six (75%) due to the same phage types.

Use of salt broth. Enrichment of staphylococci using salt broth considerably increased isolation rates. Two hundred and thirty-six strains were isolated on direct culture, and 164 (42%) additional strains were isolated from subcultures. This advantage was shown continuously throughout the study.

Discussion

The aetiology of recurrent familial staphylococcal infection is very complex. The incidence of carriage in the known carrier sites can be very high, although the anterior nares is the commonest positive site. It is very important that all members of the family or household are screened, as the removal of carriage in all family members is an essential aspect of treatment. The strain causing the recurrent infection in the index case was carried by 38% of other family members in one or more sites. Although the treatment is superficially simple i.e. nasal cream or ointment, antiseptic soap solution and antiseptic powder, patients do not find it easy to follow the procedure accurately. It is very important that detailed instructions are given to the families, particularly for the nasal preparations, which must be applied to the anterior nares with a cotton bud rather than a finger tip. Asymptomatic carriers need encouragement to apply the treatment on a regular basis for the whole length of treatment.

The employment of a nurse to interview patients and collect swabs on the correct follow-up day is essential to the success of the study. Swabs from all members of a family must be collected at the same time to avoid missing new acquisition of carriage.

Swabs from the anterior nares must be carefully taken and it is essential to use a selective medium for transport. Enrichment by means of salt broth resulted in an increase in the isolation rate of *S. aureus* of 42%.

S. aureus carriage in the nose and other sites was generally higher in patients given mupirocin in group N, despite the random allocation of all families. Patients failing treatment with both chlorhexidine/neomycin had the highest carriage rate in most sites.

Although eradication of *S. aureus* during treatment occurred frequently —post-treatment swabs at 8 days showed an eradication rate from the anterior nares of 91% in group M and 61% in group N—recolonization can occur quickly. In many instances this was with the original phage-type, which suggests that environmental contamination may be the source of the strain. Mupirocin was consistently better than chlorhexidine/neomycin in eradication and had a more prolonged effect. After 91 days of follow-up recolonization had occurred in 43% and 52%, respectively, of patients receiving mupirocin groups M and M/N, and 89% in group N. The effect of Hibitane

powder and Hibiscrub soap solution was good, and eradication was 86% at eight days and 46% at 91 days. In patients where new infections occurred after treatment, the same phage type was involved in a similar incidence in groups M and N, whereas the complicated group (M/N) showed a higher incidence, confirming the difficult therapeutic problem in these patients.

Nasal carriage is important in these families and was the primary carriage site. Where it was positive, carriage of *S. aureus* in the secondary carriage sites was much higher. This finding was more common in the index cases than family members.

The results of treatment showed a clinical success rate of 56% with index patients treated by mupirocin, and only 27% treated by chlorhexidine/neomycin. Of the index patients who had failed naseptin therapy (group M/N), only four (33%) responded to mupirocin.

This study shows that eradication of *S. aureus* carriage can be achieved using a simple treatment regimen, but the effect is likely to be short-lived and reinfection in the index cases will occur in many instances. Although the mechanism is unknown, families who acquire recurrent infection appear to be abnormal in their degree of carriage, and this has an effect on the success of treatment. However, it is possible to lengthen the interval between the episodes of infection, and this is of value to the families. This study has shown that mupirocin is more successful in removing nasal carriage of staphylococci, and its effect on recolonization is more prolonged than after the use of chlorexidine/neomycin.

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