Nasal carriage and antibiotic susceptibility of *Staphylococcus aureus* in general practice

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SUMMARY. The incidence of nasal carriage of *Staphylococcus aureus* and the *in vitro* susceptibility of isolates to fusidic acid, penicillin, erythromycin, methicillin and tetracycline was determined in 204 patients who had been treated previously with a short course of a topical preparation of Fucidin for acute skin sepsis, and in an equal number of control subjects. *Staphylococcus aureus* was isolated from 36 per cent and 34 per cent of patients in the Fucidin and control groups respectively. Only one of the 144 isolates was resistant to fusidic acid. Short, single courses of topical therapy in general practice are unlikely to be epidemiologically hazardous in the long term. Evidence of possible cross-infection in general practice was obtained.

Introduction

ALTHOUGH opportunistic Gram-negative bacilli have replaced *Staphylococcus aureus* as the principal hospital pathogen, this organism is still a major cause of morbidity and mortality in hospitalized patients. *Staphylococcus aureus* is also one of the most common pathogens encountered in general practice, particularly in patients with acute skin sepsis.

The correct management of patients with acute superficial staphylococcal skin sepsis, such as impetigo or boils, is a matter of debate. Particular attention has been given to the role of topical antibiotics. *Staphylococcus aureus* has shown an unfortunate ability to develop resistance to many antibiotics. Because of the fear of resistance developing when antibiotics are applied topically, it has been suggested that, ideally, no antibiotic that is used systemically should be applied to the surface of the body.[1]

Fusidic acid is a valuable systemic agent in the management of patients with severe staphylococcal sepsis.[2] Topical use of the drug is also employed widely in general practice.[3,4] In theory, this might prejudice its use systemically, if, as has been suggested, such usage of fusidic acid promotes resistance to the antibiotic among strains of *S. aureus*.

This study was conducted to see if there was evidence that prior use of fusidic acid topically resulted in an increased incidence of resistance in the long term. To answer this question we chose to look at the resistance profile of staphylococci isolated from the nares of patients who had been treated some time previously with topical Fucidin preparations.[3] We also investigated a similar number of patients who had not been treated for any skin complaint during the same period to act as a control group.

Method

A total of 204 patients, who had been treated during the previous 8–15 months (mean 12 months) with a short course of a topical Fucidin preparation for superficial acute skin sepsis, participated in this study. All had been treated with either an ointment containing 2 per cent sodium fusidate (Fucidin ointment) or a cream containing 2 per cent fusidic acid (Fucidin cream), and had been included in a multicentre study in general practice throughout Great Britain comprising a total of 487 patients.[3] Their involvement in our study was based on the willingness of their own general practitioners to participate in the investigation and on their assurance that they would return to the surgery when asked to do so. No attempt was made to select patients from the original trial on any other basis. They were representative of those participating in the original study (Table 1).

An equal number of control patients, matched for age (± 1 year), sex and general practitioner they attended, who had not been treated in the previous 12 months for any skin condition, but were visiting the surgery for other reasons, were studied. It was not known whether systemic antibiotics had been given for other reasons during this period.

The incidence of nasal carriage of *S. aureus* among the 408 subjects studied was determined as follows. A sterile swab was inserted carefully into one nostril, pushed to the back of the nares, rotated and then withdrawn. The swab was then pushed

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into the other nostril and the procedure repeated. The swab was then replaced in its holder and sent to the laboratory and cultured for the presence of *S. aureus*. The sensitivity of all staphylococcal isolates to fusidic acid, penicillin, tetracycline, methicillin and erythromycin was determined by the disc diffusion technique.[5] Sensitivity to methicillin was determined at 30°C. Isolates of *S. aureus* were also phage-typed. Only reactions occurring at routine test dilution were recorded.

Results

The incidence of nasal carriage of *S. aureus* in both the Fucidin-treated and control groups is shown in Table 2. There was no significant difference in the carriage rate between the two groups (McNemar's test).

Details of the *in vitro* sensitivity profile of all the isolates is depicted in Table 2. No isolate was resistant to more than two of the antibiotics tested. The majority (85 per cent) of the organisms exhibiting antibiotic resistance were resistant solely to penicillin. Only one of the 144 isolates of *S. aureus* was resistant to Fucidin.

Nine staphylococcal isolates (five Fucidin group, four control group) died before they were phage-typed. While most of the 135 isolates that were phage-typed appeared to be epidemiologically distinct, in two instances staphylococci of the same phage-type, coupled with a specific profile of antibiotic sensitivity/resistance, had been isolated from the patients of two general practitioners. All seven (five Fucidin group, two control group) of the 15 phage-type 29 strains that were resistant to penicillin and erythromycin had come from practitioner A. Three other patients from practitioner A (one Fucidin group, two control group) carried staphylococci of different phage-types (all resistant to penicillin only). Similarly, all seven isolates of phage-type 29/52/80 that were fully sensitive to all of the antibiotics tested came from practitioner B. Five of these patients were in the Fucidin-treated group and two subjects were controls. No other staphylococci were isolated from patients seen by practitioner B. These observations indicate that cross-infection may have taken place.

Practitioner A worked in a three-partner practice, and he and one of his colleagues prescribed erythromycin frequently. Two patients in the Fucidin group had been given erythromycin in the previous 12 months. An erythromycin-resistant organism was isolated from one patient. Neither of practitioner A's colleagues had participated in this study. Subsequently, erythromycin-resistant staphylococci were isolated from the nose of practitioner A and the practice sister, although these isolates were not phage-typed. Practitioner B worked in a three-partner practice. A different phage-type was isolated from one of his partner's patients.

Table 1. Characteristics of patients given Fucidin preparations.

	Original multicentre study	Nasal swab study (% relative to multicentre study)	
Number of patients	487	204*	*(41.9)*
Males	216	90	*(41.7)*
Females	271	114	*(42.1)*
Mean age (years)	28.7	27.4	
Original diagnosis (no. of cases)			
Abscess/boil	123	48	*(39.0)*
Impetigo	143	56	*(39.2)*
Paronychia	47	17	*(36.2)*
Secondary infection of acute lesions	174	83	*(47.8)*
Mean duration of topical Fucidin therapy (days)	7.4	7.9	

*Control group in nasal swab study matched for age (± 1 year), sex and general practitioner.

Table 2. Incidence of nasal carriage and *in vitro* sensitivity of isolates.

	Fucidin-treated group	Control group
Total number of patients	204	204
Number of patients (%) with S. aureus in nares	*74 (36.3)*	69** *(33.8)*
Number of patients not carrying S. aureus	130	135
Number of isolates (%) resistant to:		
Penicillin	61 *(82.4)*	52 *(74.3)*
Methicillin*	0	1 *(1.4)*
Fusidic acid*	1 *(1.3)*	0
Tetracycline*	2 *(2.7)*	5 *(7.1)*
Erythromycin*	5 *(6.8)*	3 *(4.3)*

*Isolates also resistant to penicillin.
**One patient harboured two distinct strains, therefore 70 isolates.

Discussion

The original aim of this study was to ascertain whether the use of topical preparations of Fucidin to treat patients in the general community with acute superficial skin sepsis was associated with a marked increase in the number of fusidic acid-resistant isolates of *S. aureus* in the long term. The design of our study may be criticized on the grounds that we studied staphylococci from the nares and conducted the investigation some time after therapy with topical Fucidin had been completed. However, nasal carriage of staphylococci has been shown to be a major source of sepsis,[6] and we wished to see whether resistance to fusidic acid might be a problem in the long term. Our choice of a control group may

also be criticized as not being representative of the general population. However, the results obtained were similar to those of other studies involving healthy adults.[6,7]

The mean incidence of nasal carriage among the patients studied was 35 per cent. It was 36.3 per cent in the Fucidin-treated group and 33.8 per cent among the controls.

A large number of different phage-types were isolated in this study, as was anticipated since the patients studied came from throughout the country. However, the most frequently isolated types, namely 29, 29/52, 29/52/80, 95, 42E and 94/96, were also among the major phage-types obtained from patients in a district hospital.[8] Phage-types 29 and 94/96 were also isolated frequently from the nares of members of a British Antarctic Survey team in the late 1970s,[9] and produced septic lesions in six of the 13 subjects studied. Therefore, it seems reasonable to conclude that the organisms we isolated are representative of those prevalent in the general community at the present time.

Only one fusidic acid-resistant isolate was found in the group who had received the antibiotic previously, and no such organisms were isolated from the control group. Overall, the level of resistance to Fucidin among staphylococci isolated from the nares of patients in general practice was found to be low, and similar to that associated with methicillin. Resistance to tetracycline (4.0 per cent) and erythromycin (5.6 per cent) was greater. Seventy-eight per cent of the isolates exhibited *in vitro* resistance to penicillin. These figures are similar to those reported recently in this country.[10]

Although we found only one fusidic acid-resistant isolate among the patients who had been treated topically, the possibility that resistance had been lost in some strains cannot be ruled out, as it may be unstable.[11] The development of resistance to fusidic acid during therapy with the antibiotic has been recorded previously.[12] Resistance has been shown to increase when topical therapy is used widely in a closed epidemiological situation, such as dermatology ward, where cross-infection is the major hazard.[12] As with some other antibiotics, the use of topical Fucidin in such a setting cannot be recommended. However, the situation in the general community may be different, as any selection pressure is less intense. As Lacey pointed out,[13] and as our observations and those of others confirm, resistance to fusidic acid is still uncommon,[10,14] despite many years of widespread use. Our results indicate that short, single courses of topical therapy in general practice are unlikely to be epidemiologically hazardous in the long term.

We found evidence that cross-infection may be taking place in general practice. In one case (practitioner A) there was evidence of possible dissemination of a penicillin- and erythromycin-resistant strain from either the general practitioner and/or the practice nurse. Investigations were not conducted in the other case (practitioner B) to ascertain whether the practitioner was implicated or not. This was an unexpected finding and warrants further prospective investigation.

It is not our intention here to advocate an increased usage of topical Fucidin preparations, but solely to try to assess the bacteriological implications of such therapy. It would appear that the use of a single, short course of topical Fucidin for patients with acute staphylococcal skin sepsis in the general community, and where the risk of cross-infection is low, is unlikely to be epidemiologically hazardous in the long term.

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