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Therapeutics

High levels of fusidic acid-resistant *Staphylococcus aureus* in dermatology patients

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Summary

Background Antibiotic resistance is a significant problem both in hospitals and the community. Topical antibiotics are widely used for dermatological problems and this may be leading to the emergence of resistant bacteria.

Objective To assess the level of fusidic acid-resistant *Staphylococcus aureus* inpatients with dermatological problems.

Methods All microbiology samples over a 4-month period were tested for antibiotic sensitivities. Patients with cultures positive for *S. aureus* were studied.

Results The study shows 50% of *S. aureus* isolates from dermatology patients were resistant to fusidic acid. This figure rose to 78% inpatients with atopic eczema. Of patients with fusidic acid-resistant *S. aureus* isolates, 96% had used a fusidic acid-containing preparation within the previous 6 months. The level of fusidic acid resistance in *S. aureus* samples cultured from nondermatology patients was only 9·6%, a level significantly below that for dermatology patients ($P < 0{\cdot}001$).

Conclusions High levels of fusidic acid-resistant *S. aureus* are found in dermatology patients. Inappropriate use of topical antibiotics in dermatology patients leading to fusidic acid resistance may threaten the efficacy of systemic fusidic acid for the treatment of serious *S. aureus* infections. Education of health professionals and restriction of the use of fusidic acid is needed.

Key words: antibiotic resistance, fusidic acid, *Staphylococcus aureus*

Antibiotic resistance is becoming an increasing problem in both community and hospital medicine.[1] In particular, resistant *Staphylococcus aureus* is responsible for many infections in primary and secondary care.[2] Fusidic acid is an antibiotic with good antimicrobial activity against *S. aureus* infections, and has been widely used for over 20 years. Topical fusidic acid-containing preparations are extensively used for a range of dermatological problems, especially infected atopic eczema and skin infections, such as impetigo. The antibiotic is also available as a topical therapy, combined with hydrocortisone or betamethasone for the treatment of eczema.

It is well recognized that topical antibiotic therapy may lead to the emergence of resistance. In our hospital fusidic acid has always been on a restricted drugs list to be used only under advice. It was not the practice of the microbiology department to test *S. aureus* isolates routinely for sensitivity to fusidic acid. However, the increased incidence of methicillin-resistant *S. aureus* (MRSA) infections in recent years has necessitated routine testing for all *S. aureus* isolates. Sensitivity to fusidic acid was not routinely reported before this study. This restricted reporting had been in place to control inappropriate use. During 2001 we noticed increasing numbers of patients with infected eczema failing to respond clinically to fusidic acid-containing topical preparations. In September 2001 we started to report *S. aureus* strains for fusidic acid resistance.

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Methods

Forty-eight patients under the care of the Dermatology Department at Dewsbury & District Hospital (Dewsbury, West Yorkshire, U.K.) between September and

December 2001 were identified from microbiology records. In each case, *S. aureus* infection was identified by positive culture. Skin swabs taken in the dermatology department were cultured on to agar plates. Microorganisms were tested for resistance to a standard battery of antibiotics including fusidic acid by the modified Stokes disc diffusion method. Results are interpreted as sensitive, intermediate or resistant according to the zone size. During the period of study, results obtained were clear-cut, either sensitive or resistant. The results were compared with those of samples taken from other outpatient departments, hospital wards and from primary care over the same 4-month study period.

Results

The age range of the dermatology patients was 6 months to 75 years with a mean age of 6·7 years. Twenty-six of the patients (54%) were male. Samples from 24 patients (50%) showed *S. aureus* resistant to fusidic acid. The commonest medical conditions of the patients were atopic eczema (48% of patients), hand and/or foot dermatitis (10%), impetigo (10%) and leg ulcers (10%). The remaining patients had superficial skin infections. The use of fusidic acid was extensive; 62% of all patients had used a topical preparation within the previous 6 months. In patients whose culture showed fusidic acid-resistant *S. aureus*, 96% had used a fusidic acid-containing preparation compared with only 29% of patients whose culture showed fusidic acid-sensitive *S. aureus*.

In the 23 patients with atopic eczema, 18 (78%) showed cultures with *S. aureus* resistant to fusidic acid. All of these 18 had used topical fusidic acid within the previous 6 months. The remaining five (22%) grew *S. aureus* still sensitive to fusidic acid, of whom three had previously used topical preparations.

Hospital inpatient and outpatient statistics and results from primary care were used as control groups. Over the 4-month study period 9% (11 of 119) of samples of *S. aureus* from primary care were found to be resistant to fusidic acid, 10% (11 of 111) from hospital inpatients and 10% (7 of 71) from non dermatological outpatients. This compares with 50% (24 of 48) fusidic acid resistance in samples of *S. aureus* taken from the dermatology outpatients.

When we examined prescribing data for the community from figures provided by the pharmaceutical advisor for the local Primary Care Trust (PCT), we noted a constant level of prescriptions for fusidic acid preparations in the community over the last 36 months. An average of 8200 prescriptions per annum were written over this period for topical fusidic acid preparations (excluding ophthalmic preparations). This figure was for a population of approximately 200 000. The PCT monitors only numbers of prescriptions, not the quantities of treatment dispensed. This may be important as fusidic acid-containing preparations are now being marketed in larger pack sizes. Over the same period the hospital pharmacy had dispensed significantly fewer topical fusidic acid preparations. There was an average of 41 prescriptions per month for fusidic acid-containing preparations (excluding ophthalmic preparations) in mid-1999. By mid-2001 this figure had reduced to an average of 16·3 prescriptions per month.

Discussion

Topical antibiotics are extensively used in community and hospital medicine. For chronic conditions such as atopic eczema, topical antibiotics may have been used for prolonged periods or on numerous occasions. *S. aureus* colonization and staphylococcal enterotoxins have been implicated in the exacerbation of atopic eczema.[3] This discovery may have led to the increased use of topical antibiotic preparations. Higher levels of fusidic acid resistance have been noted in areas using larger quantities of topical fusidic acid-containing preparations.[4] Increasing fusidic acid resistance does appear to be a significant problem. Other groups are recognizing the problem. A study in Bristol found a virtual doubling of fusidic acid resistance in methicillin-susceptible *S. aureus* over a 4-year period.[5] Recent data show the prevalence of fusidic acid-resistant *S. aureus* triples in children from infancy to school age.[6]

Over 90% of atopic eczema sufferers are colonized by *S. aureus*.[7] About a quarter of healthy children are similarly colonized.[8] Fusidic acid resistance seems to be a particular problem in children with atopic eczema, reflecting the chronicity of the problem, the extent of disease and high usage of fusidic acid. There is a risk of atopic children developing MRSA infection in the future. Increasing resistance to fusidic acid is already causing problems in a number of areas. The use of fusidic acid for eye and ear infections will be inappropriate for patients colonized with fusidic acid-resistant *S. aureus*. More importantly, the effective use of systemic fusidic acid therapy may be threatened for serious *S. aureus* infections, particularly in osteomyelitis,

septicaemia and postoperative infections. The fusidic acid resistance rates for MRSA have remained low despite the rise in rates in methicillin-sensitive *S. aureus*.[5] Fusidic acid is still a highly effective treatment for MRSA isolates sensitive to the drug. We are also worried that patients colonized and infected with fusidic acid-resistant *S. aureus*, particularly dermatological patients, pose a threat to both hospital inpatients and outpatients.[9–11]

The results from our study suggest there is an almost identical level of fusidic acid resistance in both non-dermatological hospital and community patients, which is 10%. This compares with a statistically significant different level of 50% for dermatological patients ($P < 0{\cdot}001$ when analysed using the *t*-test). Our results suggest that patients with eczema are more likely to show cultures of fusidic acid-resistant *S. aureus*. This may be as a result of inappropriate use of topical antibiotics.

Although topical fusidic acid has been available for over 20 years, we feel this rapidly emerging resistance is a recent phenomenon. The resistance rate is nearly 10% in our general population and 50% in dermatology patients. This seems to be the correct time to convey the message of restrictive use of fusidic acid to health care professionals. Restrictive antibiotic policies have worked well in countries such as Denmark where financial levers have been successfully used to reduce significantly antibiotic use by general practitioners.[12] In our own area we have reminded our general practitioner colleagues about the problems of antibiotic resistance and the need to restrict use of fusidic acid. We suggest that fusidic acid-containing preparations are used to treat acute skin infections in the short term only. Dermatologists and general practitioners should consider alternatives to topical antibiotics for treating chronic eczema. Topical fusidic acid should only be used for short periods and not on a regular or prolonged basis. If possible, topical antiseptic preparations should be used to treat skin infection. If action is not taken now, the future use of fusidic acid will be compromised.

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References

1 Select Committee on Science and Technology. *Resistance to Antibiotics and Other Antimicrobial Agents*. 7th Report. London: The Stationery Office, 1997–98.
2 Shanson DC. Antibiotic resistant *Staphylococcus aureus*. *J Hosp Infect* 1981; **2**: 11–36.
3 Leung DYM, Hauk P, Strickland I *et al.* The role of superantigens in human diseases: therapeutic implications for the treatment of skin diseases. *Br J Dermatol* 1998; **139**: 17–29.
4 Ravenscroft JC, Layton A, Barnham M. Observations on high levels of fusidic acid resistant *Staphylococcus aureus* in Harrogate, North Yorkshire, UK. *Clin Exp Dermatol* 2000; **25**: 327–30.
5 Brown EM, Thomas P. Fusidic acid resistance in *Staphylococcus aureus* isolates. *Lancet* 2002; **359**: 803 (Letter).
6 Arkwright PD, Daniel TO, Sanyal D *et al.* Age-related prevalence and antibiotic resistance of pathogenic staphylococci and streptococci in children with infected atopic dermatitis in a single-specialty center. *Arch Dermatol* 2002; **138**: 939–41.
7 Abeck D, Mempel M. *Staphylococcus aureus* colonization in atopic dermatitis and its therapeutic implications. *Br J Dermatol* 1998; **139** (Suppl. 53): 13–16.
8 Hussain FM, Boyle-Vavra S, Daum RS. Community-acquired methicillin-resistant *Staphylococcus aureus* colonization in healthy children attending an out-patient pediatric clinic. *Pediatr Infect Dis J* 2001; **20**: 763–7.
9 Norregaard C, Jensen I, Olesen J, Hagedorn S. Spread and control of methicillin resistant *Staphylococcus aureus* in a department of dermatology. *Ugeskr Laeger* 1998; **160**: 2257–60.
10 Farrell AM, Shanson DC, Ross JS *et al.* An outbreak of methicillin-resistant staphylococcus aureus (MRSA) in a dermatology day-care unit. *Clin Exp Dermatol* 1998; **23**: 249–53.
11 Andersen BM, Bergh K, Steinbakk M *et al.* A Norwegian nosocomial outbreak of methicillin-resistant *Staphylococcus aureus* resistant to fusidic acid and susceptible to other antistaphylococcal agents. *J Hosp Infect* 1999; **41**: 123–32.
12 Steffersen FH, Schonheyder HC, Tolboll Mortensen J *et al.* Changes in reimbursement policy for antibiotics and prescribing patterns in general practice. *Clin Microbiol Infect* 1997; **6**: 653–7.