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A randomized, controlled trial of tea tree topical preparations versus a standard topical regimen for the clearance of MRSA colonization

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KEYWORDS

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Summary Two topical MRSA eradication regimes were compared in hospital patients: a standard treatment included mupirocin 2% nasal ointment, chlorhexidine gluconate 4% soap, silver sulfadiazine 1% cream versus a tea tree oil regimen, which included tea tree 10% cream, tea tree 5% body wash, both given for five days. One hundred and fourteen patients received standard treatment and 56 (49%) were cleared of MRSA carriage. One hundred and ten received tea tree oil regimen and 46 (41%) were cleared. There was no significant difference between treatment regimens (Fisher's exact test; $P = 0.0286$). Mupirocin was significantly more effective at clearing nasal carriage (78%) than tea tree cream (47%; $P = 0.0001$), but tea tree treatment was more effective than chlorhexidine or silver sulfadiazine at clearing superficial skin sites and skin lesions. The tea tree preparations were effective, safe and well tolerated and could be considered in regimens for eradication of MRSA carriage.

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Introduction

It is common practice to attempt to clear methicillin-resistant *Staphylococcus aureus* (MRSA) carriage in hospital patients with topical antimicrobials and antiseptics. Our routine practice is to isolate and barrier-nurse all patients known to be colonized with MRSA and administer topical

eradication therapy. The aim of this approach is to reduce the risk to the patient of infection with a resistant pathogen, reduce transmission of MRSA to other patients and staff, and if eradication is successful, to remove the need for barrier nursing or isolation of the patient. While it has been argued that this is not an efficient process,¹ UK national guidelines recommend an attempt to eradicate MRSA in most hospital patients.²

The oil of the tea tree (*Melaleuca alternifolia*) is a popular 'natural' antiseptic with a broad spectrum of anti-microbial activity including MRSA,³⁻⁵

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suggesting that this agent may be useful for skin antiseptics. Australian aborigines have used the plant medicinally for millennia.³ The oil is a complex mixture of agents but the main active ingredient is terpinen-4-ol. It has been incorporated in a wide variety of domestic products including soap, shampoo and household antiseptic creams. There is little published evidence on the value of its use in contemporary medical settings. Its use has been advocated in past decades for furunculosis,⁶ superficial fungal infections,^{7,8} anaerobic vaginosis,^{9,10} and eradication of head lice. In November 2000, a review of evidence for the efficacy against MRSA¹¹ failed to include any clinical data. Since then one study showed that topical tea tree preparations were more effective than standard regimens for eradicating MRSA carriage, but the numbers of patients were very small.¹²

The aim of the present study was to compare the efficacy of topical tea tree preparations with the standard regimen for the eradication of MRSA colonization in patients in a 550 acute-bedded hospital and to assess their safety. At the time the standard eradication regimen was application of mupirocin (Bactroban) cream to the anterior nostrils and small open skin lesions, silver sulfadiazine ointment to open skin lesions and ulcers, and chlorhexidine washes to axillae and groin areas for five days.

Methods

Patients

The study, which was approved by the local research ethics committee, was conducted in the Royal Hampshire County Hospital, Winchester between March 2001 and May 2002. All patients colonized with MRSA were considered eligible for entry, but those unable to give informed consent; known to be sensitive to tea tree oil; under the age of 16; pregnant or breast feeding were excluded. Patients who consented were randomly allocated either regimen by a balanced randomization method (block size of 10; SAMPSIZE v 2.0, Blackwell Science, Oxford, 1997).

Treatment was prescribed by the main investigator (M.D.). Treatment was delivered by nursing staff on the wards. Compliance with treatment regimens was not closely monitored by the investigating team. Nursing staff and patients were asked to report any problems with delivery of the treatment regimens or any adverse events.

Treatment regimens

The standard treatment (ST) regimen comprised mupirocin 2% nasal ointment applied to the anterior nares three times a day for five days, chlorhexidine gluconate 4% soap applied all over the body at least once a day for five days, silver sulfadiazine 1% cream to skin lesions, wounds, leg ulcers once a day for five days.

The tea tree oil regimen (TT) comprised tea tree 10% cream (Ord River Tea Tree Oil Pty Ltd, Warners Bay, New South Wales, Australia) applied to the anterior nostrils three times a day for five days; tea tree 5% body wash all over the body at least once a day for five days; tea tree 10% cream to skin lesions, wounds and ulcers, and also to axillae or groins as an alternative to the body wash (Table I).

Microbiology and outcome measures

Before starting treatment all patients had swabs for MRSA detection collected from nose, throat, axillae, groin creases and any open skin lesions. The same sets of swabs were collected after the second day and on day 14 post-treatment. Eradication was defined as the absence of MRSA in both sets of post-treatment swabs.

Persistence of MRSA in any site was regarded as a failure of eradication. The effectiveness of the two treatments (mupirocin and tea tree cream) on nasal carriage was analysed separately.

Results

Two hundred and thirty-six patients were entered in the study; follow-up swabs were not received for 12, so 224 were evaluable. One hundred and fourteen patients received ST of which 56 (49%) were cleared of MRSA carriage. One hundred and ten received TT and 46 (41%) were cleared (Table II). There was no significant difference between treatment regimens ($P = 0.0286$ Fisher's exact test)

Seventy-four ST patients had nasal carriage and 58 (78%) had carriage eradicated by intra-nasal mupirocin. Six (8%) were clear on day two after treatment, but positive on day 14, and 10 (14%) remained MRSA positive on both days. Seventy-six TT patients had nasal MRSA carriage and 36 (47.3%) were cleared with tea tree nasal cream. Eight (10.5%) were clear on day two, but positive on day 14, and 32 (42.1%) remained positive on both days (Table III). Mupirocin was significantly more effective at clearing nasal carriage than tea tree cream ($P = 0.0001$ Fisher's exact test).

Table I Treatment regimens

Standard treatment	Tea tree treatment
Mupirocin 2% to anterior nares tds for five days	10% Tea tree cream to anterior nostrils tds for five days
Chlorhexidine gluconate 4% soap applied all over the body at least once a day for five days	5% Tea tree body wash applied all over the body at least once a day for five days
Silver sulfadiazine 1% cream to skin lesions, wounds, leg ulcers once a day for five days	10% Tea tree cream to skin lesions, wounds and ulcers once a day for five days and as an alternative to body wash for axillae and groins

Table IV lists clearance rates by site of colonization. Although the numbers are small, it appears that tea tree cream or body wash is more effective than chlorhexidine or silver sulphadiazine in clearing MRSA from superficial skin sites and wounds.

Safety and tolerance of topical treatments

There were no reports of adverse effects or of intolerance from the nurses applying the topical treatments, from the patients, or in the patient notes.

Discussion

MRSA challenges and, in some cases, exhausts the resources of infection control teams. In this hospital we maintain an active approach to MRSA control. Our strategy of limited screening of patients awaiting orthopaedic and vascular surgery before admission to hospital, inter-hospital transfers and nursing home admissions, and new admissions to the intensive care unit was aimed at identifying as many new admissions with MRSA as possible. By influencing their accommodation in the hospital the spread of MRSA in high-risk areas could be limited. Our policy was to barrier nurse carriers by isolation or cohort nursing on most general wards and to exclude patients with MRSA from certain higher-risk wards, for example orthopaedic and vascular surgical wards, and to offer topical eradication treatment to all MRSA carriers.

There was no significant difference between the two regimens when all patients and all colonized

sites were taken into consideration. However, mupirocin (an antibiotic) was significantly more effective than tea tree cream (an antiseptic) in the nostrils. Mupirocin resistance is increasing,¹³ and although the data are not shown in this study, none of our isolates were mupirocin-resistant. Tea tree cream may be useful as an alternative to mupirocin in areas of high mupirocin resistance. At other superficial body sites including open skin lesions tea tree preparations were more effective than chlorhexidine soap or silver sulfadiazine.

Patients vary considerably in the extent of MRSA colonization. It is usually relatively simple to clear acute localized MRSA colonization of a single anatomical site, such as nasal mucosa or superficial skin wound; but quite another matter to clear MRSA colonization from a patient with chronic carriage at multiple sites. Such patients may never become clear of MRSA, but topical treatment may be appropriate even in the chronically colonized to reduce the bacterial load and thereby the chance of transmission to other patients or staff.

This study included all consenting patients with MRSA at a general hospital and as such reflected a wide range of degree of colonization and of underlying general health. A debilitated patient colonized with MRSA at many sites, with a chronic illness, open skin lesions and prolonged hospital stay is unlikely to be cleared of MRSA by any therapeutic regimen.

The study reflected current practice in which any patient with MRSA is given topical clearance therapy, as well as being barrier nursed. A more selected patient group may have achieved higher

Table II The presence or absence of MRSA 14 days after receiving one or other MRSA eradication regime

Treatment	MRSA negative at any site day 14	MRSA positive at any site day 14	Total
Standard	56	58	114
Tea tree	46	64	110
Total	102	122	224

Table III The presence or absence of MRSA in the nose after treatment of nasal carriage

Treatment	MRSA negative day 14	MRSA positive day 14 (–ve day two but positive day 14)	Total
Standard	58	16 (6)	74
Tea tree	36	40 (8)	76
Total	94	56	150

Table IV MRSA carriage at different sites and the number and percentage cleared after treatment

	Standard total	Standard cleared (%)	Tea tree total	Tea tree cleared (%)
Nose	74	58 (78)	76	36 (47)
Throat	34	16 (47)	36	10 (28)
Axilla	4	2 (50)	14	8 (57)
Groin	14	4 (29)	10	8 (80)
Wound	26	8 (31)	34	16 (47)

rates of clearance. As it was, both treatment regimens achieved clearance rates in the 40–50% range. The question must be asked whether it is worth treating patients at all to achieve this level of clearance. We feel that eradication therapy serves several useful purposes: reduction in the likelihood of serious MRSA infection in the colonized patient; potential vacation of isolation beds; and any reduction in the microbial load and distribution of MRSA must help to reduce transmission, even if complete eradication is not achieved.

Tea tree creams and soaps appear to be safe and well tolerated, judging by the paucity of adverse events reported in this study and the other small published study.¹² Sensitivity to components of tea tree oil has been described.¹⁴

The optimal strength of tea tree oil for MRSA eradication is unknown. As topical application is required, it is likely that the higher the concentration the greater the killing of MRSA. Greater concentrations might result in more sensitivity reactions, but much higher concentrations of tea tree oil preparations (25%) are already used for cold sore treatments without appreciable adverse effects.

Tea tree preparations are effective, safe and well tolerated, and can therefore be considered in regimens for the eradication of MRSA carriage.

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