The Biogun® A Novel Way of Eradicating MRSA colonization in Diabetic Foot Ulcers.

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Introduction

Diabetic foot ulceration remains a common problem in diabetic patients with peripheral neuropathy with an annual incidence of over 7% and it precedes 80% of non traumatic lower limb amputations. The prevalence of Methicillin resistant staphylococcus aureus (MRSA) infection continues to increase and is around 30% to 40% in infected diabetic foot ulcers and is associated with significant morbidity [1,2]. We have previously demonstrated that this doubles foot ulceration healing time [1] which has been shown to increase the cost of care [3]. Whilst the pathogenic relevance of MRSA colonisation remains debatable we have previously demonstrated that MRSA even in clinically infected ulcers may take over six month to disappear [2]. Furthermore, there is increasing evidence that MRSA colonization of chronic ulcers is associated with an increased risk of bacteraemia, invasive intervention and longer hospital stay [4]. Therefore there is a need to effectively eradicate MRSA. The aim of this pilot study was to determine the efficacy of a novel method of MRSA eradication using the Dentron Biogun®.

Patients and Methods.

A prospective study of fifteen consecutive diabetic patients without clinically infected foot ulceration but with MRSA colonization was undertaken in a specialized diabetic foot clinic. All patients received standard treatment with debridement by a podiatrist and appropriate off loading. All patients received topical MRSA eradication as per hospital protocol for colonisation (initial 5 days, then 10 days and then 15 days if required of Tisept shampoo, Oilatum Plus for bath/shower, Bactroban nasal ointment and Corsydyl

mouthwash) and treatment with the Denton Biogun®. The probe was moved at a distance of 2-10mm above the ulcer surface at a speed of not less than 60s per square centimetre. Patients were treated until MRSA was eradicated or up to a maximum of three times with each episode at least 2 days after completion of the standard hospital MRSA eradication program.

An MRSA swab was taken from the wound after debridement of superficial exudate using sterile instruments and MRSA swabs were also taken from the hairline, nostril, throat, axilla, and perineum.

Patient with a clinically infected diabetic foot ulcer and pacemaker was excluded from the study.

Results

Fifteen patients with non infected diabetic foot ulcers colonised with MRSA were treated using the Dentron Biogun®. There was a 60% successful eradication of MRSA colonisation with the majority, 6 requiring only one course and 3 requiring a second course of treatment. There were no significant differences between the groups that had successful MRSA eradication and those that were unsuccessful in term of age, type of diabetes, duration of diabetes, duration of foot ulceration or the proportion of neuroischaemic ulcers. The HbA1c was significantly greater in the group that had MRSA eradicated (9.9%) compared to those in whom MRSA persisted (7.8%), ($p<0.05$).

The only factor that influenced the success of treatment is the ulcer size with those ulcers where MRSA eradication was unsuccessful being significantly larger than the successful group, $843.3\pm254.4mm^2$ vs. $294.8\pm104.6mm^2$ ($p<0.05$). Surprisingly there was no significant difference between the duration that the foot ulceration was colonised with MRSA and the success of MRSA eradication although the success of MRSA eradication at non ulceration sites almost reaches significance ($p=0.06$). The proportion of patients who cleared other sites of MRSA was greater in those who cleared their foot ulcer.

There was no significant side-effect with only one patient noticing a mild tingling sensation.

Discussion.

This pilot study was undertaken to see if we can improve the success of MRSA eradication in patients with diabetic foot ulceration colonised by MRSA using a novel method. We have demonstrated that using the Dentron Biogun® it is possible to eradicated MRSA colonisation in uninfected diabetic foot ulcers in the majority of patients after only 2 courses of treatment. In our previous report the mean duration of MRSA colonisation in infected foot ulceration was 28.3 weeks [2] which we have now reduced to less than 4 weeks for most of our patients.

The most important factor in determining the success of the Biogun® appears to be the size of the foot ulcer. This reflects the mechanism of action of the Biogun® which was originally designed to reduce the number of micro organisms in dental caries [5]. The bactericidal effect is achieved with the tip of the Biogun® delivering a stream of electrons which binds the surrounding molecules of oxygen forming hydrated superoxide anion. The superoxide anion acts on the phospholipids bi-layer of the micro-organism causing de-esterification of the fatty acid and weakening and disrupting the cell membrane resulting in cell death [6]. The tip is able to eradicate MRSA *in-vitro* in a zone of 2-3mm after 60 seconds. The Biogun® probe was applied at a rate to cover 1 cm^2 and so most ulcers required 5 to 10 minutes of treatment. To improve the success rate the length and frequency of treatment needs to be increased. More importantly a means of delivering the charged ions over a greater surface area requires further development.

With the continual rise in the prevalence of MRSA in the diabetic foot clinic and the likely implication on resources it is time to consider alternative methods of MRSA eradication. We propose that the Dentron Biogun® should be considered for this purpose.

References.

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Table 1. Biogun® treatment results comparing diabetic foot ulcers with MRSA colonisation which were successfully eradicated vs persistent colonisation.

	MRSA cleared	MRSA positive
Total number	9	6
Sex M : F	3 : 6	3 : 3
Age (yrs)	54.7±3.4	51.1±3.8
Type 1 DM	44.4 %	50%
Duration of DM (yrs)	16.8±2.9	24.5±6.0
HbA1c (%)	9.9 ±1.4	7.8±1.4 *
Neuroischaemic ulcers	33.3	50.0
Duration of ulcers (weeks)	11.1±4.3	9.5±4.0
Ulcer size (mm^2)	294.8±104.6	843.3±254.4 *
MRSA duration in ulcers	10.8±4.3	8.5±4.2
MRSA duration non ulcer sites (weeks)	11.7±4.3	69.7±40.0
MRSA non ulcer sites cleared (%)	66.7	16.7
Number Biogun treatment	1.33±0.2	3.0±0.0