High efficacy of nitric oxide generating dressing (EDX) in the management of Buruli ulcer disease: Result of a small-sized pilot study

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Background
The introduction of antibiotic treatment over the past ten years has transformed the outcomes of Buruli ulcer disease, however this is far from ideal. Given the increasing global threat of antimicrobial resistance, the current recommended regimen of a combination of oral rifampicin and clarithromycin for 8 weeks poses a challenge. Healing rates are highly variable in patients with seemingly similar lesions though the disease is cured in patients who adhere to the regimen. Two factors from previous studies account for this variability, the baseline bacterial load and the development of paradoxical reactions. The antibiotics used as the first line therapy were chosen for its bactericidal potency but these will need to be improved upon because studies have confirmed the persistence of viable organisms in some patients (more than 50%) weeks after the therapy. An alternative approach proposed is the concurrent treatment with a novel nitric oxide (NO) generating wound dressing (EDX dressing) developed by Edixomed Ltd, UK to provide all the properties of an advanced wound dressing and for the established roles of NO in wound healing involving the vascular component, the inflammatory component and the potent, broad spectrum antimicrobial activity. the results of a pilot study to determine the ability of the EDX dressing combined with the antibiotics regimen to improve healing outcomes in Buruli lesions in comparison with the current standard treatment and dressing are presented here.

Methods
Using an open-label study design, 23 BU confirmed cases were randomized into two wound dressing arms; 11 receiving NO dressings and 12 with standard routine gauze dressings. Swab / FNA samples were collected from patients after informed consent at baseline and weeks 2,4,8 and 12,16 when lesion persisted for the combined 16SrRNA /IS*2404* assays and the fTLC and Mu culture. Lesion measurements were done at each visit and time for healing was noted. Demographic data was collected using standard BU01 forms and photographic data was also collected. Clinical and laboratory variables were entered in excel and analysis was done using excel and GraphPad prism version 5 to compare healing outcomes and rate of killing of bacteria between the two arms.

Principal Findings
The median (Range) age of participants who received the NO dressings was 11 (3-50) comparable to those who received standard dressings 12 (5-51). The participants in both arms had similar lesion characteristics; same proportion of nodules, plaques and ulcers and category of lesions. There were 6 (50%) category I lesions and 6 (50%) category II lesions. The median time to healing for the NO patients was 4 weeks in comparison to 24 for the standard patients (log-rank test, p=0.0002). Clearance rate of viable organisms was faster in NO group compared to the standard dressings (8 weeks vrs 16 weeks) with a significance difference in the proportion of patients with detectable viable organisms and copies of IS*2404* at weeks 4 and 8.

Discussion/Conclusion

There is the need to conduct a larger population-size study to confirm the bactericidal activity of the EDX nitric oxide dressing which was higher in combination with antibiotics compared to standard dressing with antibiotics. Success in this would have a major impact on the management of Buruli ulcer, with faster healing leading to shorter treatment duration for many patients and further economic and social benefits.