How MSF operational research in a neglected disease (Buruli ulcer) treatment programme can impact international management guidelines

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Introduction

Buruli ulcer (BU), a neglected tropical disease, is caused by infection with *Mycobacterium ulcerans* and results in debilitating skin and soft tissue lesions. MSF has implemented a BU treatment programme with the Ministry of Health in Akonolinga, Cameroon since 2002; rates of BU/HIV coinfection are high. Guidance for management of this coinfection has been lacking. Here we describe how analysis of data from the BU programme provided the scientific basis for development of guidance principles for BU/HIV coinfection.

Methods

A retrospective analysis of clinical data from the MSF BU programme in Cameroon, from 1 January 2002 to 27 March 2013, was carried out. The findings were published in an international medical journal and used to inform an expert panel guidance process for management of BU/HIV coinfection. Ethics approval was granted by the Humanitarian Committee of the University of Geneva Hospitals.

Results

1130 patients with a first episode of BU were included in the analysis; thirteen patients died. HIV prevalence in BU patients was higher than regional HIV prevalence (37% vs 7% women; 20% vs 5% men; and 4% vs 0.7% children). HIV-positive adults had significantly more multiple BU lesions at diagnosis than HIV-negative adults (24% vs 11% respectively; p=0.004). Main lesion size significantly increased with decreasing CD4 cell counts (p=0.02). 80% of patients with category 2 or 3 BU lesions had CD4 <500 cells/mm³ compared with 55% of those with category 1 (less serious) lesions. CD4 >500 cell/mm³ was associated with reduced time to heal lesions (hazard ratio 2.39; 95%CI 1.44-3.98). Mortality was higher among HIV-positive than HIV-negative patients (11% vs 1%; p<0.001). Median CD4 cell count among the eight deceased HIV patients was 229 cell/mm³ (IQR 98-378); none were on antiretroviral therapy (ART). Median duration from HIV diagnosis until death was 41.5 days (IQR 16.5-56.5).

The expert panel guidance for management of BU/HIV coinfection included the following steps. All BU patients should be offered quality provider-initiated HIV testing and counselling. Combination antibiotic treatment for BU should be commenced before starting ART. ART should be initiated in all coinfectected patients with symptomatic HIV disease (WHO clinical stage 3 or 4) regardless of CD4 cell
count and in asymptomatic individuals with CD4 count \( \leq 500 \text{ cells/mm}^3 \). If CD4 count is not available, BU/HIV coinfected individuals with category 2 or 3 BU lesions should be offered ART. For eligible individuals, ART should be commenced as soon as possible within 8 weeks after commencing BU treatment, and as a priority in those with advanced HIV disease (CD4 \( \leq 350 \text{ cells/mm}^3 \) or WHO stage 3 or 4).

**Conclusions**

The clinical practice and study of observational data in an MSF BU programme allowed improved understanding of the clinical and epidemiological interactions between BU and HIV disease. This evidence was important in building preliminary international guidance for the management of BU/HIV co-infection.