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LETTER TO THE EDITOR

Directly observed therapy with azithromycin for skin and soft tissue infections in injection drug users

To the Editor:
The prevalence of skin and soft tissue infections (SSTIs) among injection drug users (IDUs) is estimated to be between 21% and 32% (1,2). Several studies (3) indicate that SSTIs are a leading cause of morbidity and hospitalization among IDUs. In the field of HIV infection, the directly observed therapy (DOT) program is one strategy that has been proposed to address issues of adherence and to increase access to treatment (4). Several studies (5) have demonstrated the feasibility and efficacy of the DOT programs in community-based clinics. In the present study, we sought to evaluate the efficacy of a three-day course of oral azithromycin within a methadone-based DOT program for the outpatient treatment of SSTIs in IDUs.

The study was a prospective, observational study in a clinical setting conducted at the Pender Community Health Centre in Vancouver, British Columbia, between 2001 and 2003. IDUs who were enrolled in a methadone treatment program were eligible to participate if a SSTI diagnosis was made, and for whom outpatient treatment with azithromycin was appropriate according to the treating physician. Azithromycin (Zithromax, Pfizer Canada Inc) was prescribed at 500 mg/day for three days, to be given by a pharmacist within a DOT program, beginning on the day the diagnosis was made. The antibiotic was coadministered with methadone, and adherence was reported as a function of the number of witnessed doses. In addition, appropriate drainage of subcutaneous abscesses was undertaken.

As a usual component of methadone treatment, urinalyses were performed every two weeks to detect the ongoing use of recreational drugs, including cocaine and opiates. The evaluation of clinical efficacy was the main end point of the study. Clinical cure was defined as the resolution of all signs and symptoms of infection or sufficient improvement such that additional or alternative therapy was not required. Clinical failure was defined as a lack of clinical response, the use of additional antibiotics or a recurrence of the same condition within eight weeks. All statistical evaluations were performed using an intent-to-treat methodology, using the $\chi^2$ or Fisher’s exact test, as appropriate. All statistical tests were two-sided, with statistical significance established at $\alpha=0.05$.

There were 62 subjects (42 male and 20 female) enrolled in the study: 26 (42%) with cellulitis, 16 (26%) with cellulitis and abscesses, and 20 (32%) with other SSTIs (nine with skin lesions and ulcerations, four with impetigo, four with furuncles, and three with wounds and burns). All were receiving methadone as part of the long-term management of their addiction, while 58 (94%) were also infected with hepatitis C virus. At eight weeks, a clinical response to azithromycin was achieved in 54 of 62 (87%) cases. Considering only the HIV-positive subjects, a clinical response was observed in 38 of 45 (84%) cases, while in HIV-negative subjects, a clinical response was observed in 16 of 17 (94%) cases ($P=0.43$). In the overall group, 16 of 22 (73%) subjects nonadherent to methadone during the three days of antibiotic treatment were cured, compared with 38 of 40 (95%) subjects who were adherent to methadone ($P=0.019$). Moreover, 32 of 40 (80%) subjects known to be active IDUs during the study period were treated successfully with azithromycin compared with 22 of 22 (100%) subjects who were not active IDUs ($P=0.042$).

The results of the present study demonstrate that a three-day, once daily oral course of azithromycin within a DOT setting leads to clinical response rates in 87% IDUs with SSTIs for whom outpatient treatment is appropriate. These results are consistent with those of clinical trials of azithromycin in adult populations at far less a risk of nonadherence to medications, in whom cure rates of 76% to 99% have been reported (6). The main limitation of the study is that it was not a randomized controlled trial in which patients were required to have microbiological confirmation of the diagnosis. It should be remembered that, as in the cases included in the present study, the diagnosis of SSTIs is often a clinical one. Without the benefit of microbiological data, it is difficult to assess the role of macrolide resistance on any clinical failures observed in our cohort. This is certainly an issue that has to be monitored prospectively if we are to implement a strategy for the management of SSTIs in IDUs using short-course macrolide therapy.

In conclusion, a three-day course of azithromycin within a DOT program can be clinically effective in treating acute SSTIs in IDUs with a degree of therapeutic success that equals or exceeds that which is associated with the use of this agent in the general population. Our data suggest that DOT may be an appropriate method of combining acute medical therapy with addiction treatment and mirrors the success of DOT for chronic medical conditions such as HIV. However, surveillance programs to monitor the evolution of azithromycin resistance will have to be maintained to ensure that the intervention remains effective over time, particularly in the era of methicillin-resistant *Staphylococcus aureus*.

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