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NOTES FROM THE FIELD

The experience of bedaquiline implementation at a decentralised clinic in South Africa

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Multidrug-resistant tuberculosis (MDR-TB) is a serious public health problem, but the new drugs bedaquiline (BDQ) and delamanid offer hope to improve outcomes and minimise toxicity. In Khayelitsha, South Africa, patients are routinely started on BDQ in the out-patient setting. This report from the field describes BDQ use in the out-patient setting at the Nolungile Clinic. The clinic staff overall report a positive experience using the drug. Challenges have been based largely on the logistics of drug supply and delivery. BDQ can be started successfully in the out-patient setting, and can be a positive experience for both patients and providers.

Multidrug-resistant tuberculosis (MDR-TB), defined as strains of *Mycobacterium tuberculosis* with in vitro resistance to at least isoniazid and rifampicin, is a growing public health problem,[1] and current treatment regimens result in both poor outcomes and high rates of adverse events.[2] There is some reason for optimism, however, with the introduction of two new drugs—bedaquiline (BDQ) and delamanid (DLM)—for the treatment of MDR-TB under programmatic conditions.[3,4] South Africa has a high burden of MDR-TB,[5] and in 2012 introduced an expanded access programme for BDQ.[6] Excellent early outcomes, combined with the approval and registration of the drug by the Medicines Control Council in 2014, has led to the widespread use of BDQ, with almost 1100 patients started on BDQ in 2015.[7]

Although patients in the majority of sites across the country were hospitalised to initiate their BDQ-containing regimens, in the peri-urban township of Khayelitsha patients were initiated on BDQ in decentralised out-patient clinics, due to previous decentralisation of MDR-TB services there. This report from the field highlights the experience of community-based BDQ initiation at one clinic in Khayelitsha.

SETTING

Khayelitsha, with a population of approximately 500 000, is located outside Cape Town, South Africa. The setting has a high burden of MDR-TB, with approximately 200 newly diagnosed patients started on treatment each year.[8] The Western Cape Government Health and the City of Cape Town, with support from Médecins Sans Frontières (MSF), provide decentralised MDR-TB services at 11 primary health care clinics, and a recent World Health Organization programme review noted major successes in MDR-TB care as a result.[9] Nolungile Clinic, one of the primary clinics in Khayelitsha, currently has 50 MDR-TB patients undergoing treatment. A multidisciplinary TB team consisting of one doctor, two nurses and two auxiliary care workers started the first patient on BDQ in November 2013, and to date have started 10 patients on BDQ-containing regimens.

FINDINGS

Preparation for introduction of BDQ

Before BDQ was provided at Nolungile Clinic, the doctor and nurses underwent an initial training session offered by the National Department of Health (NDOH) and supporting partners, including MSF. The training emphasised new management practices necessary for BDQ treatment, including the need to replace antiretroviral treatment regimens containing efavirenz and the need for baseline and monthly electrocardiography (ECG) to assess QTc intervals.

Process for starting BDQ

Nolungile Clinic provides out-patient access to BDQ following the guidelines set forth by the NDOH. Once an individual who meets these criteria is identified, the doctor at Nolungile Clinic completes an application form that is submitted to a clinical advisory committee (CAC). The CAC is composed of at least 10 expert clinicians from around the country with experience treating MDR-TB. Applications are submitted to the CAC electronically and reviewed daily. The CAC reviews the request, provides input on an optimal regimen and the management of comorbid conditions, and recommends additional testing or follow-up if needed. If three physicians agree that the patient should be given BDQ, the treating clinician can then request the drug. Turnaround time is usually within 48–72 h, although it can be longer if the information submitted is incomplete or the case is complicated.

The patient is then referred to a dedicated MDR-TB counsellor who provides information and education as well as adherence support to identify any potential issues that need to be addressed before starting treatment. The dedicated MDR-TB counsellor is based at Nolungile Clinic and supported by an MSF counsellor who specialises in the use of BDQ. The patient is usually seen at Nolungile or another location of their choosing if that is more comfortable. All patients are contacted within 24 h of being approved by the CAC,

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and counselling sessions usually take place within 2–3 days. After the counselling session, the patient signs an informed consent form and begins treatment with BDQ, usually in the out-patient setting.

Patients on BDQ are supplied with the complete MDR-TB treatment regimen recommended by the CAC and their treating clinicians. The drugs, including BDQ, are stored at a central pharmacy and Nolungile Clinic is provided with a monthly supply of medications. For BDQ, however, they are given a 2-week supply for the first 14 days of treatment, as the dosing of the drug changes after 14 days. The drugs for new patients are supplied to Nolungile on a daily basis, but there can be a delay from the time the clinician requests the medication to when it is logged in the Nolungile Clinic pharmacy and available for use. To date, there have been no stock-outs of BDQ, but there have been some challenges with the companion medications linezolid and clofazimine. Ancillary medications for the management of adverse events are provided by the City of Cape Town and the Province of the Western Cape, and are available to MDR-TB patients free of charge.

Ongoing clinical support for providers using BDQ in the out-patient setting is established through monthly clinical forums, during which the case notes of all patients initiated on BDQ are discussed. This meeting, held at a conference hall in Khayelitsha, is attended by the treating physicians, nurses, and counsellors, the MSF physician and counsellors and the chief medical officer for the City of Cape Town. MSF and the consulting service for infectious diseases at the district hospital provide ongoing telephone and on-site mentorship.

Baseline and follow-up testing for patients undergoing BDQ treatment are undertaken at Nolungile Clinic, which has the capacity to perform ECGs and also accepts patient referrals for ECG from other decentralised clinics in Khayelitsha where ECG is not available. A formal referral system was developed for patients needing ECG monitoring; the test is provided free of charge, and any transport costs incurred by patients are supported by MSF.

Benefits

Although there were initial concerns about providing BDQ in the community setting, providers became familiar with the drug after initiating three patients with extensively drug-resistant (XDR) TB on BDQ in one week. The staff found the drug not nearly as challenging to use as they thought it would be, and patients reported minimal side effects attributable to BDQ compared to the other drugs in the standard MDR-TB regimen. Being able to access and initiate BDQ at the out-patient level meant there was a faster initiation time, as there was no need to wait for an in-patient bed.

Anecdotally, clinical staff have had an overall positive experience with BDQ. They report that their workload has not increased compared with the management of patients on standard MDR-TB treatment. They note that patients with highly resistant forms of TB undergoing BDQ treatment at Nolungile seem to be doing well clinically. They also report that the drug is an excellent option for managing toxicity and makes treating MDR-TB more straightforward compared to before BDQ became available, when limited options meant patients had to continue taking medications that caused serious and severe adverse events. Finally, the clinic has reported renewed enthusiasm among staff and patients.

The clinic staff also report using a variety of measures to help support patient adherence. All patients started on BDQ are seen by a facility-based MDR-TB counsellor as well as an MSF counsellor who has expertise in BDQ use. The clinic encourages patients to come and speak with the staff at any time and to be proactive about reporting any symptoms or problems they might have. BDQ patients receive more information about this medication than they do for standard treatment, and thus are more empowered to be part of their TB care.

Challenges

The primary challenges with administering BDQ in an out-patient setting have been the logistics involved in obtaining supplies of the drug and delayed turnaround time for feedback from the CAC. Both of these issues have improved dramatically since the wider rollout of the Clinical Access Program across the country. Although there was initial concern about added workload for patients taking BDQ, the clinic has found that the workload is actually the same as for routine MDR-TB patients. The lack of clinical drug susceptibility testing for BDQ is also of concern, as it is unclear if patients are developing resistance to BDQ or if they have baseline resistance. Optimal use of BDQ is ensured by use in combination with other drugs, ongoing counselling, and consultation with the monthly clinical forum.

CONCLUSIONS

Nolungile Clinic has successfully implemented community-based treatment with BDQ for 10 patients, and the overall experience has been positive. After receiving focused and intensive training at the start of the BDQ introduction, the clinic team is now able to initiate and manage patients on the drug. Community-based initiation and management of patients on BDQ has led to rapid initiation of effective therapy, viable options for managing resistance and toxicity and increased enthusiasm among patients and providers.

References

1 World Health Organization. Global tuberculosis report, 2015. WHO/HTM/TB/2015.22. Geneva, Switzerland: WHO, 2015.
2 Ahuja S D, Ashkin D, Avendano M. Multidrug resistant pulmonary tuberculosis treatment regimens and patient outcomes: an individual patient data meta-analysis of 9,153 patients. PLOS Medicine 2012; 98: e1001300.
3 World Health Organization. The use of bedaquiline in the treatment of multidrug-resistant tuberculosis: interim policy guidance. WHO/HTM/TB/2013.6. Geneva, Switzerland: WHO, 2013.
4 World Health Organization. The use of delamanid in the treatment of multidrug-resistant tuberculosis: interim policy guidance. WHO/HTM/TB/2014.23. Geneva, Switzerland: WHO, 2014.
5 Farley J E, Ram M, Pan W, et al. Outcomes of multi-drug resistant tuberculosis (MDR-TB) among a cohort of South African patients with high HIV prevalence. PLOS ONE 2011; 6: e20436.
6 Ndjeka N, Conradie F, Schnippel, K, et al. Treatment of drug-resistant tuberculosis with bedaquiline in a high HIV prevalence setting: an interim cohort analysis. Int Tuberc Lung Dis 2015; 9: 979–985.
7 Furin J, Brigden G, Lessem E, Rich M, Vaughan L, Lynch S. Global progress and challenges in the implementation of new medications treating multidrug-resistant tuberculosis. Emerg Infect Dis 2016; 22: e151430.
8 Stinson K, Goemaere E, Coetzee D, et al. Cohort profile: the Khayelitsha antiretroviral programme, Cape Town, South Africa. Int J Epidemiol 2016; May 20. Epub ahead of print.
9 Noeske J. Drug Resistant TB Review: Western Cape Province Feedback Report. Cape Town, South Africa: National Department of Health, October 12, 2015.

La tuberculose multirésistante (TB-MDR) est un problème de santé publique grave, mais les nouveaux médicaments que sont la bédaquiline (BDQ) et le délamanide apportent un espoir d'améliorer les résultats tout en réduisant la toxicité. A Khayelitsha, Afrique du Sud, les patients démarrent leur traitement par BDQ en consultation externe en routine. Ce rapport du terrain décrit l'utilisation de la BDQ à la consultation externe du dispensaire Nolungile. Dans l'ensemble, le personnel du centre de santé exprime une expérience positive du médicament. Les défis ont surtout été liés à la logistique de l'approvisionnement et de la distribution du médicament. La BDQ peut être mise en route avec succès dans le cadre d'une consultation externe et peut constituer une expérience positive pour les patients et les prestataires de soins.

La tuberculosis multirresistente (TB-MDR) representa un grave problema de salud pública, pero la utilización de nuevos medicamentos como la bedaquilina (BDQ) y el delamanid ofrece perspectivas de mejores desenlaces terapéuticos y disminución de la toxicidad asociada. En Khayelitsha, Suráfrica, se inicia de manera sistemática el tratamiento ambulatorio con BDQ. En el presente informe del terreno, se describe la utilización de BDQ en tratamiento antituberculoso ambulatorio en el centro de atención Nolungile. En general, los miembros del personal del centro refirieron una experiencia positiva con la administración del medicamento. Las dificultades surgieron en gran parte con respecto a aspectos logísticos del suministro y la administración del medicamento. Es posible iniciar un tratamiento eficaz con BDQ en condiciones ambulatorias, y represente una experiencia positiva para los pacientes y los profesionales de salud.

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