BACKGROUND

Namibia is a sparsely populated country located in Southern Africa with a population of 2.1 million inhabitants. In 2011, Namibia reported 11,694 cases (589/100000) of all forms of TB. A drug resistance survey (DRS) held in 2008 showed a multi-drug resistant (MDR) TB prevalence of 3.8% among new TB cases and 16.5% among previously treated cases. Since the implementation of PMDT, 1,180 patients have been treated for DR TB under a government funded programme. 245 patients were commenced on treatment for DR TB in 2011 alone. Although national guidelines recommend monthly electrolyte and renal monitoring of patients during the initial phase of treatment, this is often poorly implemented due to reduced staff capacity and distances from the laboratory. In the event that the tests are done, there is often suboptimal documentation and follow-up. We present the prevalence of life-threatening electrolyte disturbances in patients being treated with 2nd line anti-TB drugs as well as the prevalence of renal and hepatic impairment while on treatment. It is hoped that the final results will inform the National TB and Leprosy Programme on the value of frequent monitoring, and alert clinicians to the magnitude of frequently missed adverse events.

The Namibian guidelines in 2010 and 2011 recommended individualised treatment regimens based on drug susceptibility results and treatment history. For some patients, a standardised empiric regimen was applied as follows:

- Intensive phase with Kanamycin, Levofloxacin, Ethionamide, Cycloserine, Pyrazinamide with or without Ethambutol for at least 6 months and 4 months post culture conversion
- A continuation phase of up to 18 months with oral medicines Levofloxacin, ethionamide and cycloserine

METHODS

A retrospective review of patient records for patients enrolled for DR TB treatment and receiving 2nd line anti-TB injectable at Katutura TB Unit (Windhoek) in 2010 and 2011 was conducted. 70 records were included. The period analysed was limited to the first 8 months of treatment, consisting mainly of the intensive phase. All the patients included had been subjected to clinical screening for adverse events, as well as monthly monitoring of serum electrolytes and renal function. Variables collected included serum potassium, sodium, urea, creatinine clearance, as well as age, sex, HIV status, TB resistance profile, comorbidities, current medications and regimen being analysed. There were 43 confirmed MDR cases (including 1 XDR): 9 polyresistant; 5 rifampicin monoresistant cases and 13 cases treated as suspected MDR TB without DST confirmation.

RESULTS

70 records were analysed, of which 40 (57%) were males. The median age, also the mean, was 33 years. Mean baseline weight was 46.5 kg. 34 patients were HIV positive, while 3 had an unknown HIV status (HIV prevalence 51%). All those with HIV were either already on antiretroviral therapy or were put on antiretroviral therapy during treatment for TB. Apart from HIV, the only other comorbidities reported were diabetes (1) and asthma (2). All the patients were on an injectable, of which 57 (81%) were on kanamycin while 13 (19%) were on capreomycin. All the patients were on levofloxacin. 31 (44%) of the patients received the standardised regimen for MDR TB, recommended by the WHO and consisting of kanamycin, levofloxacin, ethionamide, cycloserine and pyrazinamide.

Of note, some patients reported clinically significant adverse events, including some hearing loss in 24% of the patients; skin rash, neuropathy and nausea and vomiting. 3 of the patients had clinical syndromes, later attributed to electrolyte wasting (2/57 on kanamycin and 1/13 on capreomycin)

30 (43%) had at least one episode of hypokalemia (defined as a K+ < 3.6 mmol/L) during first 8 months of treatment. Hyponatraemia occurred in 40/68 (59%) patients, while ureaemia occurred in 17/70 (24%) of patients. 46 patients (66%) had renal insufficiency (estimated CrCl=97ml/min for males or 88ml/min females). 17 (19%) patients had hyper-bilirubinemia and 5 (7%) patients had elevated ALT (>45)2670 (37%) patients had elevated thyroid stimulating hormone (TSH) suggesting a level of hypothyroidism

CONCLUSION AND RECOMMENDATIONS

Serum abnormalities, particularly electrolyte and renal impairment, are common in patients on treatment for DR TB. This may be responsible for some unexplained morbidity and mortality among this group of patients. While this study requires follow-up and further validation with a larger patient sample, clinicians should strengthen monitoring for subclinical adverse events, and respond appropriately. The results also point to the need for serum monitoring even in ambulatory based models of treatment for DR TB.

ACKNOWLEDGEMENTS

The Ministry of Health and Social Services would like to acknowledge the support and contribution made by the following:

United States Agency for International Development (USAID); Management Sciences for Health - Systems for Improved Access to Pharmaceutical Services (MSH-SIAPS); the Therapeutics Information & Pharmacovigilance Centre (TIPC); the United States Centers for Disease Control and Prevention (CDC); the Global Fund to fight AIDS, TB and Malaria (GFATM); the World Health Organisation (WHO); Namibia Institute of Pathology; all the community based organisations and care providers in the field of TB and HIV/health care workers, and all our patients.