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New short-course regimen in multidrug-resistant tuberculosis control- A need of the hour

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Drug resistant TB (DR-TB) has threatened the global TB control efforts [1]. A growing number of such cases could be attributed to the ever increasing population and to the increased awareness about the disease, due to a large scale IEC activities and advertisements in the media [2].

The routine treatment of DR-TB like multidrug-resistant TB (MDR-TB) is associated with a high pill burden, multiple adverse drug reactions (ADR's) and longer treatment duration [3-5]. This has led to a number of lost to follow-up cases, treatment failures, deaths and even development of extensively drug resistant (XDR-TB) cases [5].

To overcome this problem on May 2016, a new regimen shorter in duration of 9-12 months is endorsed by the WHO based on the meta-analysis studies done by the Union, Damien Foundation, Medecins Sans Frontieres and the Antwerp Institute of Tropical Medicine in Belgium, involving a large number of patients with uncomplicated MDR-TB [6-9].

This short-course regimen also famous as 'Bangladesh regimen' being started post initial studies in Bangladesh is intended for the Rifampicin resistance (RR-TB) and MDR-TB cases who have not been previously treated with second-line drugs and in whom resistance to fluoroquinolones and second-line injectable agents has been excluded or is considered highly unlikely [10]. WHO recommends a detailed work-up for detecting resistance to fluoroquinolones and injectable second-line anti-TB drugs [11].

The short-course MDR regimen involves an intensive phase of four months (extended to six months in case of delayed sputum smear conversion) containing high-dose Gatifloxacin or Moxifloxacin, Kanamycin, Prothionamide, Clofazimine, high-dose Isoniazid, Pyrazinamide and Ethambutol followed by a continuation phase of five months containing Clofazimine, Gatifloxacin or Moxifloxacin, Pyrazinamide and Ethambutol and can be started in uncomplicated MDR-TB children, adults and people living with HIV who meet the inclusion criteria [12]. However, this regimen is not recommended for extrapulmonary TB cases and in pregnant women [12].

The benefits of this regimen are a lot as the short duration leads to greater compliance and adherence of the patients to the treatment, thereby reducing the number of lost to follow-up cases [12]. It also has a remarkable impact on the number of toxic effects of drugs, as the total duration of treatment is almost halved and the ADR's have always been a major contributor to the treatment failure or lost to follow-up cases [13]. Also, it is a much cheaper regimen and costs less than USD1000 per patient [13]. The published literature shows that the treatment success rate of this shorter regimen is 89.9% as compared to78.3% in the conventional regimen [12].

Besides, this regimen will also reduce the burden on the already overburdened health staff working in the DR-TB care [12]. The shorter treatment duration will be a boon to the already grave situation in the high TB burden countries like India [12]. And one of the very important aspects of this regimen is that it can be given in HIV prevalent settings as well [14]. The resources freed by the short-course regimen may be utilized to increase the reach and accessibility of the TB control program, thus having an impact on the health budget of the high TB burden countries [12].

However, there are certain snags associated with this newer short-course regimen [13]. There is a need of rapid DST and in many settings such fast results of DST may not be available and this could hamper the initiation of this regimen [13]. Also, this may lead to higher chances of decreased effectiveness and diminished short-term benefit, as well as long-term risk of amplified second-line drug resistance [13]. The regimen relies on a number of drugs to which baseline resistance has been reported in certain populations [15,16]. There is a baseline resistance to fluoroquinolones or second-generation aminoglycosides to the extent of 10%, thus depriving these groups from this highly beneficial regimen [13]. The reliance on Pyrazinamide in the new regimen with an evidence of a baseline resistance to the extent of 35-81% in MDR strains needs to be taken care of especially in high burden settings as the majority of such cases will be excluded from the new short-course regimen [15,17].

Thus, a shorter, cheaper, more effective, and more tolerable new regimen is the need of the hour and might prove to be a solution to the ever growing MDR-TB cases. The new regimen may reduce the TB incidence by 20%, however, before coming to such major conclusions, evidence from multiple randomized controlled trials with a sizeable data from endemic countries is imperative. Furthermore, in the fight

against TB this short-course regimen is a big ray of hope and may prove to be helpful in reducing the mortality and morbidity associated with the disease.

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