Comment on "Bedaquiline-related QTc Prolongation in Multidrug Resistant Tuberculosis Patients: A Prospective Study"

Reshmi Bhattacharya[1], Nitin Chintaman Gawari[2], Bhalchandra Tryambak Rane[3], Sujata Prakash Shingare[4]

[1]Junior Resident; [2]Assistant Professor; [3]Associate Professor; [4]Assistant Professor, Department of Pharmacology, Dr. D.Y. Patil Medical College, Hospital & Research Centre, Pune, Maharashtra, India

Dear Sir,

We read with considerable interest the article titled "Bedaquiline-related QTc Prolongation in Multidrug Resistant Tuberculosis Patients: A Prospective Study."[1] The authors should be commended for addressing an important safety concern regarding the use of bedaquiline in patients with multidrug-resistant tuberculosis (MDR-TB). Cardiac safety, particularly QT interval prolongation, remains a key issue during treatment with newer antitubercular agents, and studies focusing on this aspect are highly valuable. However, we would like to share a few observations regarding the findings reported.

In the present study, the authors reported an overall prevalence of QTc prolongation of 37.25%, with 13.7% of patients developing significant QTc prolongation. These rates appear somewhat higher than those reported in earlier studies.

For instance, Khan et al. conducted a large prospective cohort study involving MDR/rifampicin-resistant tuberculosis (RR-TB) patients from 16 countries who were treated with regimens containing bedaquiline and/or delamanid between April 2015 and September 2018.[2] The study evaluated the occurrence of clinically relevant QT prolongation (grade III or higher) or serious adverse events associated with QT changes. Among the 2,553 patients included in the study, 59% received bedaquiline and/or delamanid for more than 6 months. QT prolongation was observed in 579 patients (20.9%); however, most of these cases (95.5%) were mild, corresponding to grade I or grade II prolongation. Clinically significant QT prolongation was noted in only 64 patients (2.5%), while more severe prolongation occurred in 12 patients (0.5%). Notably, the majority of clinically relevant QT prolongation events were reported within the first 6 months of therapy.

Similarly, studies conducted in India have indicated that moderate to severe QT prolongation most commonly occurs around the third month of treatment. When compared with these findings, the overall incidence reported in the current study appears relatively higher (37.25% vs 20.9%).

The cardiac safety profile of bedaquiline has also been reviewed extensively by Gavras and Schluger.[3] Their analysis included studies evaluating bedaquiline both as monotherapy and in combination regimens. When administered alone in doses ranging from 100 to 400 mg per day, no QTcF increases >60 ms were observed, and QTcF values exceeding 500 ms were not reported.[4]

In recent years, bedaquiline has frequently been used together with delamanid in the management of drug-resistant tuberculosis. A multicountry cohort study conducted across 14 countries involving 472 patients assessed the safety of this combination therapy.[5] QTcF prolongation was observed in only seven patients (1.5%). Among them, two patients had QTcF values exceeding 500 ms without symptoms, while four experienced QT intervals >500 ms accompanied by clinical symptoms. These findings further support the generally acceptable cardiac safety profile of this combination regimen.

We concur with the authors that careful cardiac monitoring is essential when prescribing bedaquiline-containing regimens, particularly during the early months of treatment. Continued surveillance and larger prospective studies would be valuable in further clarifying the true magnitude of QT prolongation risk associated with these therapies.

Orcid

Reshmi Bhattacharya https://orcid.org/0009-0007-9762-9735
Nitin Chintaman Gawari https://orcid.org/0009-0006-4241-8909
Bhalchandra Tryambak Rane https://orcid.org/0000-0001-7093-6654
Sujata Prakash Shingare https://orcid.org/0009-0002-5260-364X

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Reflections on Prosthetic Valve Thrombosis: Prevention and Evolving Therapeutic Strategies

Fidel Manuel Caceres-Loriga[1], Humberto Morais[2]

[1]Cardiologist Specialist, Department of Case Management, Doctors HealthCare, Miami, Florida, United States; [2]Cardiologist Specialist, Department of Cardiology, Hospital Militar Principal/Instituto Superior, Luanda, Angola

Dear Editor,

The recent article by Machigar et al., "Prosthetic Valve Thrombosis: Fibrinolysis, Surgery, or Percutaneous Manipulation?" offers an insightful and practical review of therapeutic strategies for prosthetic valve thrombosis (PVT).[1] The authors should be commended for addressing a complex and often life-threatening condition that continues to challenge clinicians worldwide. Beyond the valuable discussion on fibrinolysis, surgery, and emerging percutaneous options, this topic also invites reflection on the upstream and preventive aspects that remain pivotal in reducing the global burden of PVT.

Prevention of Rheumatic Fever and Rheumatic Heart Disease

In many low- and middle-income countries, rheumatic heart disease (RHD) remains the leading indication for valve replacement. This epidemiological reality underscores that the ultimate solution to the PVT burden lies not only in technological or procedural advances but also in the primary and secondary prevention of rheumatic fever. Sustained public health programs providing benzathine penicillin prophylaxis, early diagnosis of streptococcal pharyngitis, and community awareness can drastically reduce new cases of RHD and, consequently, the number of young patients who require mechanical prostheses. This preventive perspective—briefly alluded to in the authors' work—deserves renewed emphasis as the most cost-effective strategy for reducing PVT incidence globally.