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EDITORIAL

Atorvastatin to reduce bacillary load and attenuate lung damage in TB patients

There has been significant progress in the battle against TB over the past 30 years, but challenges persist, especially in the realm of treatment effectiveness and outcomes.[1] However, recent studies have shed light on a potential game-changer: the use of statins, known primarily for their role in managing cardiovascular conditions, as an adjunctive therapy in anti-TB treatment.[2,3] *Mycobacterium tuberculosis* (Mtb) uses cholesterol in the host macrophage membranes to bind and enter these cells, to promote replication and surveillance.[4] Immediately after infection, macrophages accumulate lipid bodies, which serve as a source of nutrition for bacteria.[5] Statins, such as the widely used atorvastatin, are prescribed to reduce cholesterol levels.[3] and thus may make it difficult for the pathogen to bind and enter the immune system cells, thereby aiding Mtb control.[6] In addition, as these drugs regulate cytokine responses and control autophagy and apoptosis, they could act as a potentially interesting adjuvant for anti-TB therapy.[7] On this basis, several studies tested the association of statins with anti-TB therapy, which highlighted their benefits, including a decrease in the Mtb burden,[6] a reduction in mycobacterial severity and enhanced permeability of granulomas to first-line drugs.[8] However, the use of statins might also increase the risk of adverse events (AEs), potentially leading to non-adherence and unsuccessful treatment.[9] This highlights the need to study their safety and effectiveness before more widespread use in patients with TB. If proven to be beneficial in clinical studies, their low cost and wide availability would allow rapid adoption in clinical practice.

A study published in this issue of the *Journal* has assessed the safety, tolerability and efficacy of atorvastatin during anti-TB therapy of uncomplicated, drug-susceptible pulmonary TB in Nigeria.[10] The phase IIB open-labelled randomised clinical trial (NCT04721795) was performed with 150 TB participants in a multicentre approach. As a first result, the two treatment regimens were found to be safe and well-tolerated. A comparison of those who received the adjuvant and those who did not revealed no differences in the severity of adverse events. Of note, the majority of participants in both groups experienced grade I severity AE, while the remaining had grade II severity AE. However, although it is important to note that those who received atorvastatin presented with muscle pain more frequently, this did not limit drug administration. One of the most promising outcomes of this study was the significant improvement in early sputum conversion after 8 weeks of treatment in the group receiving anti-TB drugs along with atorvastatin.[10] Sputum conversion reflects the transition from a state of infectiousness to non-infectiousness. Delayed sputum conversion is associated with a higher risk of treatment failure, drug resistance and TB transmission. Thus, this improvement in early sputum conversion in association with atorvastatin not only curtails the spread of the disease, reducing the TB transmission cascade, but also significantly improves the prognosis for patients.[11] Moreover, the authors noted a substantial decrease in chest X-ray severity scores in the trial group compared to controls. This marked disparity not only indicates an enhancement in the overall condition of the participants, but also strongly suggests that statins are effective at mitigating long-term pulmonary damage associated with TB. These findings highlight the potential of atorvastatin to address both the immediate symptoms and to offer significant benefits in terms of long-lasting pulmonary health. This would be a pivotal advance in our battle against TB-related complications and post-TB lung disease.[12]

Table Clinical trials investigating statins for therapy in pulmonary TB*

ID	Phase	Drug	Country	Participants *n*	Status
NCT03882177	2b	Atorvastatin	Nigeria	150	Completed
NCT03882177	2b	Pravastatin	South Africa	16	Completed
NCT04147286	2	Atorvastatin	South Africa	220	Recruiting
NCT04504851	2	Rosuvastatin	Singapore, Vietnam, Uganda and the Philippines	154	Unknown

* There are currently four clinical trials registered that investigate the use of statins in anti-TB therapy on the National Institute of Health Clinical Trial platform (clinicaltrials.gov). These include two trials related to atorvastatin, one related to pravastatin and one related to rosuvastatin use. Of these, only two have been completed, but their results have not yet been published.

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However, although we celebrate this newfound potential, it is important to expose these findings to further scientific scrutiny and rigorous research. There are more ongoing clinical trials on the use of statins as an adjuvant for anti-TB therapy (see Table).[13] These will help to build on the findings of this study and determine the optimal dosage, treatment regimens and potential side effects associated with this drug class in TB treatments. Furthermore, efforts must be intensified to ensure equitable access to this promising therapy, particularly in resource-limited settings where the TB burden is most severe.

In conclusion, the integration of statins, especially atorvastatin, into anti-TB therapy protocols is potentially a step towards combating this ancient scourge. If we can transform these findings into practical solutions, it will bring us closer to a future where TB is no longer a threat to global public health.

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