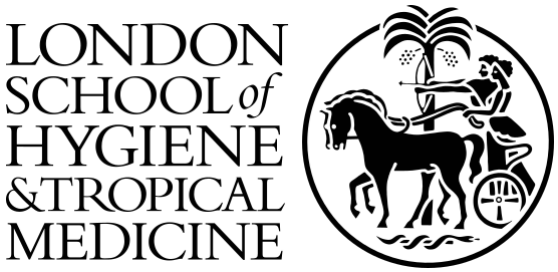

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Linezolid for children with tuberculous meningitis: more evidence required.

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Linezolid for children with tuberculous meningitis: more evidence required

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A Letter to the Editor in response to:

Li H, Lu J, Liu J, Zhao Y, Ni X, Zhao S. Linezolid is Associated with Improved Early Outcomes of Childhood Tuberculous Meningitis. Pediatr Infect Dis J. 2016 Jun;35(6):607–10.

To the editors:

Tuberculous meningitis (TBM) is a devastating disease. With the currently available treatment regimens one in five children die and only a third of surviving children escape neurological sequelae.[1] If there was any way of improving these outcomes significant mortality and morbidity would be averted. We were greatly interested, therefore, to read the study by Li *et al* regarding the use of linezolid in children with TBM in Beijing.[2]

In many ways linezolid is an attractive therapeutic option given its good bioavailability, excellent CSF penetration and proven efficacy against *M. tuberculosis*. However, three major obstacles currently limit the use of linezolid in the treatment of pediatric TBM: efficacy, safety and current high cost. Until this report the only described use of linezolid in pediatric TBM had been in the successful treatment of a South African case of extensively drug-resistant TBM.[3]

Caution is warranted in interpreting the efficacy of linezolid in the treatment of pediatric TBM from this report. The retrospective design, unrandomised nature of group allocations, and unblinded ascertainment of outcomes limit how much can be inferred. In terms of patient selection, children were given linezolid if they remained febrile after two weeks on conventional treatment and had no neurological improvement in that time. It is therefore unclear why over 50% of children in the control group had a fever clearance time of greater than 4 weeks. It would be useful for the authors to further clarify on what criteria the decision to use linezolid was made, and from what common reference point during therapy fever clearance time

comparisons were made. Persistent fever following initiation of anti-tuberculous therapy with confirmed drug susceptible strains of *M. tuberculosis* is a recognized, although unusual, clinical phenomenon.[4]

It would also be important to know if the improved outcomes were due to linezolid improving the treatment of TBM generally, or if the advantage was the result of improved treatment in cases with drug resistance. Understanding this would allow clinicians to evaluate whether this drug should be reserved only for cases with drug resistance. It would therefore be interesting to know if there are any molecular or phenotypic drug resistance results available from either the 14 microbiologically confirmed TB cases, or from the TB source cases identified in 50 of the children.

Regarding safety, the authors report no significant difference in adverse events (GI disturbance, hepatotoxicity, rash, peripheral neuropathy or thrombocytopenia) between the 36 children treated with linezolid and those who received standard treatment. However, it is unclear from the report how the children were evaluated for these and whether they may have experienced any other side effects (such as lactic acidosis, optic neuropathy, impaired renal function, raised amylase or hypoglycemia[5]).

We commend the authors on reporting these cases and providing some much-needed data where so little exists. We look forward to learning from their experiences in even more depth. In our opinion however, there is currently still insufficient evidence to warrant use of linezolid in paediatric TBM without information strongly suggestive of drug resistance.

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