

Linezolid directly affects the ability of the mitochondria to produce energy

By Sachin Jagdale on October 21, 2016

Dr Salil Mehta, Volunteer and Consultant Ophthalmologist with MSF, recently published a paper on optic neuropathy in DR-TB patients in Mumbai. He discusses key takeaways of his research with **Sachin Jagdale**

Any specific reason behind selecting patients from Mumbai for Linezolid associated optic neuropathy in DR-TB patient study?

There is a combination of reasons. Firstly, MSF has an excellent and a well-established TB/ HIV clinic in Mumbai. Hence, the expertise is available. Secondly, and more importantly, Mumbai is a global hot spot for tuberculosis (TB). A perfect storm of several factors including extreme population densities, incorrect treatment and poor compliance are leading to high incidence of primary drug sensitive TB and subsequent drug resistance. Worryingly, an increasing number of patients are presenting with primary drug resistant tuberculosis. This makes Mumbai an ideal city to undertake such a study.



Dr Salil Mehta

Can you take us through this entire study. (How and why was it started? Have you managed to achieve your targets?)

Ever since the use of linezolid became wide spread, available literature suggested potential ocular toxicity. Accordingly, the staff and doctors of MSF conducted primary screening and evaluation for all these patients. Suspect cases were then referred for further evaluation. These patients were fully evaluated, treated and followed up till resolution. It's an ongoing process and hopefully in a few years we will have more data for more research.

What was the role of Lilavati Hospital and Research Centre in this study?

As I mentioned previously, MSF referred suspect cases for further evaluation. These patients were sent to Lilavati Hospital which provided the facilities for treating these patients.

How does HIV as a co-infection decide/ affect the level of optic neuropathy?

HIV per se can cause optic nerve disease. This most likely is due to a direct effect of the virus on the cellular components of the nerve. While HIV positive patients have a very high rate of developing systemic TB, the development of optic nerve disease in these patients is due to either TB meningitis, encephalitis or due to drug toxicity caused by ethambutol or linezolid. However, exact correlates will need a larger sample size.

Will the outcome of this study have a universal application, since the patients with varied gene pools and ethnicity will be showing different response to linezolid?

We believe it will. With alarming levels of drug resistance, the use of linezolid will increase and also the number of patients potentially at risk of toxicity. So far, world wide data suggests that all ethnicities are at risk. We need more research to suggest whether certain ethnicities or geographies may be more at risk due to genetic influences or local factors such as nutrition etc.

Linezolid has come off the patent and its consumption is definitely going to increase in future. What are the chances of TB strains becoming resistant to linezolid as well?

Mumbai is a hot spot for the development of resistance to a wide range of antibiotics which is not only restricted to anti-TB drugs. The development of resistance leads to poor recoveries, which act as demotivating factors for patients to continue the treatment even after therapeutic measures have been undertaken. Given this scenario resistance to linezolid is very likely. Various factors including poor compliance, resource depletion and even systemic factors contribute to resistance to linezolid.

Is optic neuropathy a Linezolid-specific adverse effect? Which are the alternatives to this antibiotic?

Linezolid directly affects the ability of the mitochondria to produce energy. This is most apparent in the optic nerve but affects a wide range of tissues. Commonly affected are the nerves, especially the peripheral nerve where neuropathy occurs. Alternatives will have to be chosen based on the results of culture studies.

How are you going to use the results of this study to frame the future course of treatment?

Patients on linezolid need regular visual screening, early interception and treatment. Early screening allows us stop the drug, initiate treatment early and follow up with the patient. The early detection of patients in our case helped full recoveries. With this protocol, it may be possible to reduce the incidence and severity of toxicity. Staff at outreach clinics should be trained to conduct basic visual screening. This may be during the follow-up interview or by the use of simple devices.

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