

Safety of Prolonged Intraventricular Administration of Olistin Methanesulphonate

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Opinion

The recommended duration of intraventricular therapy is between 2 and 56 days [1]. Nevertheless, there have been concerns related to the intraventricular therapy due to the possibility of local or systemic antibiotic toxicity. Direct instillation of colistin to meninges could induce irritation and necrosis of tissues if colistin reaches high CSF concentrations. The most common form of toxicity is chemical ventriculitis, manifested by CSF leukocytosis despite negative cultures [1,2], with a reported incidence of 13% [3]. No clinical adverse effects related to leukocytosis were reported, but colistin was discontinued or the dose was reduced in three cases. In all cases the reduction or discontinuation of intraventricular colistin did not lead to failure of treatment [1-3].

In other cases of intravenous and intraventricular / intrathecal colistin therapy, the treatment was associated with seizures controlled with anticonvulsants plus in one case intrathecal dose reduction. Seizures were not reported when intraventricular treatment was administered as monotherapy [1-3]. Therefore, it could be hypothesized that seizures might have been triggered by increased concentrations of colistin during combined intravenous/local treatment and not by the mode of treatment (i.e. intrathecal/intraventricular). Unfortunately, colistin levels were not reported and therefore, this hypothesis could not be confirmed.

Only two studies sought to characterize pharmacokinetic parameters of intraventricular colistin in adults by obtaining serial colistin concentrations. A previous study in our institute measured CSF colistin concentrations 1, 4 and 8 h after intravenous/intraventricular colistin methanesulphonate (CMS) administration of 10 mg [4] and Imberti et al administered 2.61 to 10.44 mg daily

intraventricularly (as monotherapy or combined with intravenous CMS) [5]. Notably, CSF colistin concentrations in Imberti's study were five to ten times higher than in our previous study. Although the increased levels of CSF colistin in Imberti's study could have been due to carryover of colistin during sampling, these levels were not associated with toxicity.

In conclusion, we believe that combined i.v. and intraventricular colistin may be a feasible and well-tolerated treatment alternative in gram-negative ventriculitis.

References

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