Is mixing of tobramycin and colistimethate-sodium containing inhalation solutions a good idea?

A. Bucholzki1, R. Egle1, G. Lang1, O. Denk1, M. Knoch1, 2PARI Pharma GmbH, Gräfelfing, Germany

Objective: Patients suffering from bacterial infections of the lungs are frequently treated by alternating or combining the inhaled antibiotics tobramycin (aminoglycoside) and colistimethate-sodium (CMS, i.e. polymyxin E). Therefore, patients might feel encouraged to mix solutions of both antibiotics in order to inhale the mixture in one single inhalation session. As the effects of preparing such a mixture on physical and chemical stability of the solution are not known, an evaluation was triggered.

Methods: Vials of tobramycin solution (170mg/1.7ml) were mixed with reconstituted CMS (2 Mio. IU CMS dissolved in 4 ml of 0.9% saline) and physico-chemically characterized with respect to osmolality, viscosity, surface tension and pH. Additionally, the tobramycin content and possible tobramycin related impurities were assayed by HPLC.

Results and Conclusion: Mixtures of the antibiotics did not show obvious signs of physicochemical incompatibilities. However, the measured content of tobramycin in the mixture decreased to 70−75% of the initial amount within about 12 hours. Already 10 minutes after mixing a marked decrease of tobramycin content (approx. −7%) was observed indicating a fairly rapid reaction or decomposition immediately after preparation and during treatment. Therefore, mixing of tobramycin containing solutions with CMS prior to inhalation cannot be recommended.

The effectiveness of nebulised tobramycin over a 3 year period

D. Nazareth1, R. Sapina-Vivo1, J. Gallagher1, S.M.H. Kazmi1, J. Greenwood1, M.J. Ledson1, M.J. Walshaw1, 1PARIPharmaGmbH, Gräfelfing, Germany

Objectives: Patients with cystic fibrosis and Pseudomonas aeruginosa infection have been shown to improve lung function. The relative efficacy of inhaled tobramycin is not known, as few comparative studies are available. The efficacy of tobramycin inhalation powder capsules (TIP), tobramycin inhalation solutions (TIS-T and TIS-B), colistimethate sodium (Colistin) and aztreonam lysozyme for inhalation (AZLI) was compared.

Methods: A systematic search found seven relevant randomised controlled trials in CF patients with moderate to severe lung function impairment. Percent change from baseline in FEV1% predicted was assessed using network meta-analysis techniques, combining indirect and direct evidence. Several covariates including prior exposure to active drug, considered as a potential treatment effect modifier, were included in the analysis.

Results: Two studies had patients with mean age <18 and five with mean age >18 years. Two studies had patients previously exposed to active drug, and five had naive to study drug patients. Mean baseline FEV1% predicted was between 50% and 64%. TIP TIS-T and TIS-B had comparable efficacy in improving FEV1% predicted at 4 weeks. TIP was comparable to all treatments, although point estimates may suggest a trend for better efficacy than Colistin and AZLI for this endpoint: TIP versus Colistin: −5.8 (CrI: −12.8; 1.2) and TIP versus AZLI: −3.6 (CrI: −8.3; 1.0).

Conclusion: The analysis suggests that TIP is at least as efficacious as other inhaled antibiotics for lung function improvement at 4 weeks of treatment.

Efficacy of tobramycin inhalation powder (TIP) versus other inhaled antibiotics in cystic fibrosis (CF) patients with chronic P. aeruginosa infection: a network meta-analysis

M.-M. Balp1, G. Capkun-Niggli1, K. Littlewood2, G. Döring3, G. Angyalosi1, 1Novartis Pharma AG, Basel, Switzerland; 2Mapi Consultancy, Houten, Netherlands; 3University of Tübingen, Tübingen, Germany

Objectives: Inhaled antibiotics prescribed to treat CF patients with chronic P. aeruginosa infection have been shown to improve lung function. The relative efficacy of inhaled tobramycin is not known, as few comparative studies are available. The efficacy of tobramycin inhalation powder capsules (TIP), tobramycin inhalation solutions (TIS-T and TIS-B), colistimethate sodium (Colistin) and aztreonam lysozyme for inhalation (AZLI) was compared.

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