Use of an electronic monitoring system to generate objective information on patients’ adherence to taking treatments of a novel inhaled tobramycin solution (VANTOBRA)

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Objective: Patient adherence to inhaled medications is important to interpret clinical trial results. Self-reported diaries have a high potential for manipulation. To provide a reliable tool to assess patient adherence to treatment, a monitoring feature was developed and incorporated into a specific eFlow technology nebulizer. VANTOBRA/Tolero was compared prospectively in a randomised study in cystic fibrosis patients with TOBI/PARI LC PLUS.

Methods: The configuration’s key feature is an electronic chip card recording date, time and duration of each nebulization session and cause for termination. The nebulizer operates only by insertion of a valid chip card. Recorded data were processed using PARI’s Patient Monitoring Software. Adherence is calculated as the ratio of actual/planned inhalations and shown graphically per study day or cumulatively.

Results: Data of 54/58 patients were analysed. Mean adherence was 99% for all evaluable patients, 98% in patients >13 years and 99% in patients of 7–13 years of age. The adherence rate was comparable in all treatment cycles, independent whether the patient was randomized to receive VANTOBRA as the first or second treatment cycle. As per patient diary, the compliance in the TOBI group was 99%.

Conclusion: The eFlow technology nebulizer with patient monitoring function provides objective adherence data. The monitoring feature offers the potential to distinguish whether an observed treatment failure is based on lack of drug efficacy or non-adherence to the prescribed treatment regimen.

Pharmacokinetics of nasal administered tobramycin in patients with cystic fibrosis

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Recent studies showed that the paranasal sinuses can constitute a niche for bacteria. To date no effective treatment for these bacteria is available. Off label administration of nasal antibiotics may be an option. However, first safety of this treatment has to be established.

Objectives: With this pilot study in two patients the pharmacokinetic parameters of nasal administered tobramycin were investigated.

Methods: In two hospitalised CF-patients, treated with intravenous tobramycin, after a wash-out period, 320 mg of tobramycin, dissolved in 200 ml isotonic saline, was administered to the nose using nasal lavage. Eleven venous blood samples were collected and with a Liquid Chromatography Tandem Mass Spectrometer (LC-MSMS) method, serum tobramycin concentrations were determined. Tobramycin pharmacokinetic parameters were calculated using the MWPharm software pack-age. Systemic absorption was calculated by dividing AUC after nasal administration by AUC after intravenous administration corrected for the administered dose.

Results: In patient 1, a female of 32 years old, the maximum concentration (Cmax) of tobramycin was 0.027 mg/L. This Cmax was reached 30 minutes after the nasal lavage with tobramycin (tmax). In total 0.20% (0.62 mg) of the tobramycin was systemically absorbed. In patient 2, a male of 36 years old, the Cmax was 0.029 mg/L. The tmax was 45 minutes and in total 0.16% (0.51 mg) of tobramycin was absorbed.

Conclusion: Nasal lavage with 320 mg tobramycin did not result in toxic serum levels. The results of two patients showed a fast absorption of tobramycin and a slow elimination. Approximately 0.20% of the tobramycin was absorbed by the sinonasal mucosa.