Pharmacokinetic Modeling of Intranasal Scopolamine in Plasma, Saliva and Urine

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ABSTRACT

An intranasal gel dosage formulation of scopolamine (INSCOP) was developed for the treatment of Space Motion Sickness (SMS). The bioavailability and pharmacokinetics (PK) were evaluated under IND guidelines. The aim of the project was to develop a PK model that can predict the relationships among plasma, saliva and urinary scopolamine concentrations, using data collected from the IND clinical trial with INSCOP, and estimate the PK parameters of INSCOP described from a multiple compartmental PK model.

METHODS

Subjects and Treatments:
- Twelve healthy human subjects (6 male/6 female) participated in the study, with an average age of 38.9 ± 8.1 yr., height of 175.6 ± 11.3 cm and weight of 80.8 ± 14.3 kg.
- A randomized double blind crossover study design was used with a seven-day washout period between treatments.
- All subjects were administered at three dose levels (0.1, 0.2 and 0.4 mg) of INSCOP.

PK Evaluation
- Serial blood samples (7 ml) were collected at 0, 0.083, 0.25, 0.5, 0.75, 1, 2, 3, 4, 6, 8, 10, 12, 24 h after each treatment.
- Saliva samples (0.4-2 ml) were collected at 0, 0.25, 0.5, 0.75, 1, 2, 3, 4, 6, 8, 10, 12, 24 h after each treatment.
- Urine samples for PK analysis were collected over the following intervals: Pre-dose (single void) and at intervals of 0-3, 3-6, 6-10, 10-12, 12-24 hours.
- Plasma saliva and urine samples were assayed for concentrations of INSCOP using a validated LC/MS/MS method.

A Waters Acquity UPLC system combined with Micromass Quattro MicroTM API MS/MS detector was used, and concentrations range were between 100 and 1000 pg/mL with LLOQ of 50 pg/mL.

CONCLUSIONS

The PK model developed for INSCOP satisfactorily estimated the PK of scopolamine in plasma, saliva and urine after administration.

The model can be utilized to predict scopolamine plasma concentrations from saliva and urine data, which will be useful for the assessment of PK of scopolamine in space and other remote environments without requiring invasive blood sampling.

A future objective is to use the validated model to fit data from the bed rest study to predict PK changes of scopolamine after INSCOP administration.

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