Pharmacokinetic Modeling of Intranasal Scopolamine in Plasma Saliva and Urine

Wu L1, Tam VH1, Chow DSL1 and Putcha L2

1University of Houston College of Pharmacy; 2NASA Johnson Space Center

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 hr after each treatment.
- Serial 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 hr 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 LC/MS/MS method.

BACKGROUND

- An intranasal gel dosage formulation of scopolamine (INSCOP) was developed for space motion sickness (SMS), and bioavailability and pharmacokinetics (PK) were evaluated under approved protocol in IND guidelines.
- Understanding the PK of INSCOP is crucial for the use of this drug in space.
- Pharmacokinetic modeling can be used to describe the PK of INSCOP in plasma as well as in saliva and urine over time.

RESULTS

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.

Acknowledgements

The clinical trials were supported by a grant from the National Space Biomedical Research Institute, Houston. Partial funding for data analysis was provided by NASA through SAA partnership with the Navy.