SPORANOX® (itraconazole) Capsules/Oral Solution
SPORANOX - Administration via a Nasogastric Tube

SUMMARY

- No clinical studies have been conducted evaluating the administration of SPORANOX capsules and oral solution via a nasogastric (NG) tube.
- The in vitro compatibility of itraconazole (ICZ) oral solution with different NG tube plastics has not been evaluated.
- Data on file and case reports have shown low serum concentrations of ICZ following NG tube administration.[1-4]
- The opening of ICZ capsules and dispersing in water for administration via a NG tube is not recommended due to low water solubility of the active ingredient.[5]
- One case study reports the administration of ICZ beads removed from a capsule, administered in a cranberry juice solution, which resulted in therapeutic plasma levels.[6]

PUBLISHED LITERATURE

Simon et al (2007)[1] conducted an open-label, prospective, observational study in which ICZ capsules or liquid were given to pediatric cancer patients.

- In the period 2001 to 2005, 39 pediatric patients received 44 prophylactic ICZ cycles in which trough plasma concentrations were measured with high liquid chromatography following at least 7 days of oral treatment.
- Results showed that patients who received the oral solution without a feeding tube had significantly higher trough concentrations vs patients who received the ICZ capsule (P=0.02).
- In comparison, patients in whom ICZ was administered through a feeding tube (to overcome compliance problems or difficulties in swallowing) had significantly lower trough concentrations than patients who were able to swallow the oral medication (P=0.049).
- In the dosing range of 7–10 mg/kg/day, protective trough concentrations were reached in most patients despite which oral formulation had been used (solution vs capsule, P=0.119; solution through feeding tube vs capsule P=0.52).
- Nonetheless, the bioavailability of the solution was still significantly lower in patients in whom ICZ was administered through a feeding tube (solution with no tube vs solution through feeding tube, P=0.030).

Kintzel et al (1995)[2] report two cases where ICZ suspension was administered via orogastric feeding tubes.

- Two male patients, aged 38 and 29 years old, both recipients of allogeneic bone marrow transplant, were treated with oral ICZ suspension for fungal infections.
- Preparation of ICZ suspension was initially done as an intravenous lipid emulsion 20% and later on as a suspension in citric acid 1.5% in D5W USP.
- Serum concentrations of ICZ were measured by high liquid chromatography, with predose concentrations undetectable to 72 ng/mL.
- Following dosing, serum concentrations were shown to be 5-97 ng/mL.
    - These levels were shown to be significantly lower than serum concentrations seen in literature for similar doses administered to "fed" patients.

Ralph et al (1999)[3] described a patient who presented with life-threatening, severe community-acquired pneumonia due to *Blastomyces dermatitidis* who was immediately commenced on ICZ 200 mg twice daily, administered via an NG tube.

- After five days, his condition deteriorated and amphotericin B (50 mg once daily) was added to his treatment.
- The patient developed hepatotoxicity associated with amphotericin B and it was subsequently discontinued (total dose received 175 mg).

- ICZ treatment was continued at the initial 200 mg twice daily dose via an NG tube and liver enzymes returned to baseline after six days.
- Sputum cultures remained positive until day 29, and the patient remained on mechanical ventilation until day 36.
- The patient was discharged home at day 49 and continued treatment with itraconazole capsules.

Klang et al (2010)[5] discusses feeding tube administration and the potential issues that can arise amongst different medication formulations such as the crushing or opening of drugs intended for extended release and those with a low solubility and low bioavailability, such as ICZ.

- The authors discuss the preparation of an ICZ suspension by opening the capsule and dispersing the beads in water before the oral solution was available.
- An assay was conducted to confirm the stability; however, serum values were not measurable as little drug was actually delivered to the patient.
- This was attributed to the formulation of ICZ capsules, which are formulated with the drug sprayed onto sugar granules; the sugar acts to increase the surface area, enhancing the dissolution and absorption of the active pharmaceutical ingredient, ICZ.
- Opening the capsules and dissolving the contents resulted in the separation of the excipient and active drug, which in turn resulted in the drug precipitating to the bottom and little being absorbed.

Ong et al (1996)[6] discusses the administration of ICZ (200 mg three times daily) to a 31-year old man with cystic fibrosis who had an NG tube.

- The authors report that opening the capsules and putting the ICZ beads directly into the NG tube caused it to block.
- Trying to dissolve the beads in Coca-Cola was also unsuccessful.
- An extemporaneous preparation of ICZ solution, prepared according to the procedure of Jacobson et al. (1995)[7] (i.e. the beads from 100 mg of ICZ capsules mixed with sufficient 'Simple Syrup' to make a volume of 60 mL; the final concentration of ICZ in the suspension being 40 mg/mL) also clogged the tube.
- A final successful formulation was found in which the beads were dissolved in 15-30 mL of cranberry juice for 3 hours.
- After administration, the blood concentration of ICZ was measured at 1.5 µg/mL (within the recommended therapeutic range of 0.1-2.2 µg/mL).

DATA ON FILE

An open-label phase 2 trial described the pharmacokinetics of ICZ and hydroxy-itraconazole in 12 patients (7 female and 5 male) in an intensive care unit (ICU) setting.

- Patients received a single dose of 2.5 mg/kg ICZ oral solution on an empty stomach via a NG tube for 5 days.
- Blood samples were taken prior to ICZ administration and at 1, 2, 4, 6, 8, 12, 24, 32, 48, 72 and 96-hours post dose.
- A single-dose of 2.5 mg/kg ICZ oral solution administered via an NG tube in ICU patients resulted in relatively low plasma concentrations with a high degree of pharmacokinetic variability.[4]

LITERATURE SEARCH

A literature search of MEDLINE®, EMBASE®, BIOSIS Previews®, DERWENT® (and/or other resources, including internal/external databases) pertaining to this topic was conducted on 08 February 2024.

REFERENCES

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