SPORANOX® (itraconazole) Capsules
SPORANOX Capsules - Dosage and Administration - Opening Capsule

SUMMARY

- A literature search did not find any citations pertaining to opening itraconazole capsules and sprinkling the beads onto food.
- Case reports have stated that opening itraconazole capsules and putting the beads directly into a nasogastric (NG) tube will clog the tube.[1,2]
- Additional case reports described dissolving itraconazole beads into different liquids and administering the extemporaneous preparation to patients with mixed results.[1-6]
- Itraconazole oral solution and itraconazole capsules should ***not*** be used interchangeably. This is because drug exposure is greater with the oral solution than with the capsules when the same dose of drug is given. In addition, the topical effects of mucosal exposure may be different between the 2 formulations. Only the oral solution has been demonstrated effective for oral and/or esophageal candidiasis.[7]

CASE REPORTS

Ong et al (1996)[1] described various attempts to administer itraconazole via an NG tube in an adult male patient with cystic fibrosis who was being treated for suspected pulmonary aspergillosis. Opening up the capsules and putting the beads directly into the NG tube clogged the tube. They tried to dissolve the beads in Coca-Cola, which was unsuccessful. They next prepared and attempted to administer the itraconazole formulation described by **Jacobson et al (1995)**[8], which they state also clogged the NG tube. They were finally successful when they placed the itraconazole beads from the capsules in 15-30 mL of cranberry juice and allowed them to dissolve over 3 hours prior to administration. After receiving 18 days of itraconazole 200 mg 3 times daily, the patient's blood itraconazole level was 1.5 µg/mL (therapeutic range listed as 0.1-2.2 µg/mL). The authors concluded that this preparation did not clog the NG tube and was absorbed.

Jacobson et al (1995)[8] described the preparation of an extemporaneously compounded oral liquid of itraconazole. A liquid preparation was prepared from the beads contained in 24 itraconazole capsules (100 mg each). The beads were softened with a small amount (4-5 mL) of 95% Ethyl Alcohol, USP in a glass mortar which allowed them to be ground to a fine powder. Simple Syrup, NF was added gradually for a final volume of 60 mL. The resultant formulation (40 mg/mL) was found to be stable for 35 days when refrigerated in an amber bottle. Please note that the bioavailability of the formulation has not been evaluated. The authors state that this formulation should be used only when no alternative for oral administration is available.

Kintzel et al (1995)[3] described 2 critically ill mechanically ventilated allogenic bone marrow transplant recipients who received extemporaneous preparations of an itraconazole suspension through an orogastric tube. Itraconazole was initially prepared as a suspension intravenous lipid emulsion 20% to provide a lipophilic carrier for the dissolved itraconazole. Itraconazole beads were first pulverized for 10 minutes and placed in 10 mL of sterile water that had been heated to 80-90°C. The resultant liquid was "cloudy" and some solid material remained undissolved in the mortar, so it was rinsed 2 times with 10 mL intravenous lipid emulsion 20% and transferred to a 60 mL syringe. The suspension was administered via an orogastric tube and was preceded and followed with warm water flushes. Blood samples were obtained immediately before and 4 hours after the fifth dose of itraconazole to determine serum concentrations. In patient 1, who was receiving itraconazole 400 mg/day, predose itraconazole concentrations were undetectable and the postdose concentration was only 5 ng/mL. In patient 2, who received 600 mg/day, predose and postdose concentrations were 19 and 18 ng/mL, respectively.

An alternative preparation was administered to patient 1 later in his treatment course. The contents of itraconazole capsules (600 mg) were placed into a mortar with 10 mL of citric acid 1.5% in 5% dextrose in water (D5W) and allowed to dissolve for 20 minutes at 25°C. The suspension was then transferred to a syringe and administered through the feeding tube with pre- and postdose flushes of 30 mL warm tap water. Blood samples were obtained immediately before and 3 hours after the fifth dose; serum concentrations were 72 ng/mL and 97 ng/mL, respectively. Although this formulation had better bioavailability than the lipid formulation, itraconazole serum levels were notably lower than those reported in the literature for equivalent doses. Other factors which may have contributed to the low serum concentration with the formulations included impaired gastrointestinal function in patient 1, concomitant use of ranitidine in both patients (gastric pH was not measured), and presence of diarrhea and mucosal damage secondary to graft-versus-host disease and possibly also due to Crohn's disease in patient 2. The authors also noted that these 2 formulations lacked compatibility, stability and bioavailability data.

Seay et al (1995)[4] described the use of an extemporaneously prepared itraconazole suspension for use in a 4-year-old cancer patient with *Alternaria* sp sinusitis. The 100 mg/5 mL itraconazole suspension was formulated by emptying the contents of 5 itraconazole capsules (100 mg each) and combining them with 15 mL 0.1 N hydrochloric acid. After allowing the mixture to stand for 5-10 minutes, the beads were levigated in a glass mortar until smooth. Cherry syrup (10 mL) was added. Each dose was followed by a cola beverage, and the patient's mouth was rinsed afterwards. The patient tolerated the suspension with no complaints. A blood sample was obtained 4 hours following the fifth dose to determine itraconazole concentrations. The serum concentration was 13.8 µg/mL. Following several nasal and sinus debridements, the patient fully recovered from the infection.

In a subsequent case report, **Villarreal et al (1995)**[5] described the administration of the formulation developed by **Jacobson et al (1995)**[8] to a 50-year old female patient with invasive aspergillosis via a jejunostomy tube. On day 5, blood samples were obtained 30 minutes prior to and 90 minutes after a dose and sent to a laboratory for analysis. Itraconazole levels in both samples were undetectable. The authors state that the drug may not have been absorbed since it was administered into the jejunum, where the pH is basic. In addition, the patient was receiving rifampin, which may have resulted in decreased concentrations of itraconazole.

Bhandari et al (1992)[6] reported administration of itraconazole via an orogastric tube in a neonate with disseminated candidiasis. The drug was removed from the 100 mg capsule, ground to a fine powder and dissolved in 10 mL of warm double distilled water. The requisite amount was administered via an orogastric tube in 2 divided doses mixed with expressed breastmilk feeds. The neonate was treated for 4 weeks and was clinically and microbiologically cured. The investigators stated that they were unable to monitor the blood levels of itraconazole in the patient.

Denning et al (1989)[2] described the use of itraconazole to treat invasive aspergillosis in 21 patients. In their report, they described 2 patients with low serum concentrations of itraconazole. The first patient was semiconscious and could not swallow medication. His capsules were therefore crushed and delivered via either an NG or gastrostomy tube. The formulation of itraconazole caused agglutination of particles clogging even a large-caliber tube, and intestinal absorption was impaired. Another patient also received itraconazole by NG tube and, despite a dose of 200 mg 3 times daily, only achieved a maximum serum level of 0.6 µg/mL after 5 days of therapy.

OTHER RELEVANT LITERATURE

Additional citations identified during a literature search are included in the References section for your review.[9]

LITERATURE SEARCH

A literature search of MEDLINE®, Embase®, BIOSIS Previews®, and Derwent Drug File (and/or other resources, including internal/external databases) pertaining to this topic was conducted on 06 December 2024.

REFERENCES

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