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Why isn't cefadroxil used more often?

Cephalexin is the most commonly prescribed oral first-generation cephalosporin in the United States. In 2013, there were 4.77 million Medicare Part D claims for cephalexin prescriptions, making it the fourth most commonly prescribed oral antibiotic overall.[1] Cephalexin is commonly prescribed for the treatment of skin and soft tissue infections as well as uncomplicated urinary tract infection (UTI). In the case of skin and soft tissue infections, the Infectious Diseases Society of America recommends that cephalexin be dosed four times daily.[2] Cefadroxil, an oral first-generation cephalosporin, has been available for over 30 years. It has the same spectrum of coverage as cephalexin,[3] a similar adverse-effect profile,[4] and similar efficacy[4] but a dosing frequency half that of cephalexin. Susceptibility cutoff values and methods for determining them are available for cefadroxil, but the former can be extrapolated from values determined for other first-generation cephalosporins, such as cefazolin and cephalexin.

Both cephalexin and cefadroxil are readily absorbed after oral administration and primarily excreted unchanged in the urine. In patients with normal renal function, cephalexin is usually given four times daily; twice-daily dosing can be used for treating a UTI. Cefadroxil, whose 1.5-hour half-life exceeds that of cephalexin (1 hour), has a recommended dosage of 500–1000 mg twice daily in patients with normal renal function or 1000 mg daily for uncomplicated UTI. The reduced frequency of administration for cefadroxil should result in higher medication adherence, compared with cephalexin. The absolute increase in adherence associated with twice-daily dosing, compared with more frequent administration, can be as high as 30%.[5]

The adverse-effect profile of cefadroxil is similar to that of cephalexin. Specifically, diarrhea, nausea, vomiting, and abdominal pain have been reported to occur in 2–4% of patients taking cefadroxil.[4] Both medications have been available generically for some time. At our institution, the cost to our inpatient and outpatient pharmacies for a 10-day course of therapy is $3.20 for cefadroxil (20 500-mg capsules) or $4.27 for cephalexin (40 500-mg capsules). The average copayment for a patient with insurance is $3.23 for cefadroxil or $4.65 for cephalexin. According to Medicare Part D prescription data for 2013, the average retail cost for a cephalexin prescription was $7.74, compared with $17.87 for cefadroxil.[1]

Medicare prescription data indicate that cephalexin is prescribed 23 times more frequently than cefadroxil.[1] Nevertheless, it would appear that cefadroxil and cephalexin are quite similar and that cefadroxil has no apparent dis-

advantages compared with cephalexin. Since the less-frequent administration of cefadroxil should enhance medication adherence, compared with cephalexin, we suggest that cefadroxil may be a superior choice when first-generation cephalosporin therapy is indicated.

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Incompatibility between irinotecan and fluorouracil injections

Colorectal cancer is considered to be the world's leading cause of cancer death,[1] and more than 1 million individuals are diagnosed with this disease each year.[2] The standard chemotherapy for colorectal cancer includes fluorouracil, leucovorin calcium, irinotecan, and oxaliplatin.

No literature has appeared on an incompatibility that we observed while a patient was receiving simultaneous infusions of irinotecan hydrochloride 2 mg/mL in 0.9% sodium chloride injection and fluorouracil 25 mg/mL through the same i.v. line. A faint yellow color and a precipitate appeared where the two drugs came into contact. When the drugs were given at different times through the same line, no such phenomenon was apparent.

We investigated this incompatibility by mixing the two drugs in clear glass tubes. Commercially available irinotecan hydrochloride (40 mg/2 mL; Qilu Pharmaceutical Co., Ltd., China; lot B1E1212007) appeared as a light yellow transparent liquid; its excipients included sorbitol, lactic acid, and sodium hydroxide. Commercially available fluorouracil (250 mg/10 mL; Shanghai Xudong Haipu Pharmaceutical Co., Ltd., China; lot FA121004) was a colorless transparent liquid; its excipients included sodium hydroxide and edetate disodium. The mixed solution consisted of 5 mL of a 2-mg/mL dilution of irinotecan hydrochloride (prepared by mixing 1 mL of irinotecan hydrochloride 20-mg/mL injection with 9 mL of 0.9% sodium chloride injection) and 5 mL of undiluted fluorouracil 25-mg/mL injection. The separate drug solutions were clear, but a faint yellow precipitate appeared 10 minutes after they were mixed and was present 24 hours later. The same phenomenon occurred after repeated tests.

To our knowledge, this is the first report of an incompatibility between irinotecan and fluorouracil injections. Although this incompatibility is not mentioned in the package insert for either drug, our clinical experience and our experiment demonstrate that the two drugs should not be infused simultaneously. Patients receiving infusions of irinotecan, leucovorin calcium, and fluorouracil should receive the drugs in sequence with a precision infusion set. Further research is needed to identify the composition of the precipitate and its effects on the human body.

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