Nursing Mothers: Caution should be exercised when administered to a nursing woman.

Familial Mediterranean fever (FMF) in adults and children 4 years or older (1.2).

are usually mild, transient and reversible upon lowering the dose (6).

5.3 Drug Interactions

Drug Interactions

Coadministration of colchicine with P-gp and/or strong CYP3A4 inhibitors is contraindicated in patients with renal impairment. Total body clearance of colchicine was reduced by 75% in patients with end-stage renal disease.

Geriatric Use

8.5 Geriatric Use

The clinical significance of minor drug interactions is not known. Further studies are needed to determine whether clinically significant drug interactions occur.

Ritonavir‡ or strong CYP3A4 inhibitors (this includes all protease inhibitors except fosamprenavir) is contraindicated in patients with renal impairment. Total body clearance of colchicine was reduced by 75% in patients with end-stage renal disease.

Table 2. Colchicine Tablets, USP Dose Adjustment for Coadministration with Protease Inhibitors

<table>
<thead>
<tr>
<th>Protease Inhibitor</th>
<th>Maximum Daily Dose of Colchicine Tablets, USP</th>
<th>Adjusted Dosage of Colchicine Tablets, USP</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fosamprenavir</td>
<td>0.6 mg (one tablet)</td>
<td>0.3 mg (1/2 tablet)</td>
</tr>
<tr>
<td>Darunavir</td>
<td>0.3 mg once a day</td>
<td>0.3 mg once a day</td>
</tr>
<tr>
<td>Ritonavir</td>
<td>Maximum daily dose of protease inhibitor</td>
<td>0.3 mg twice a day</td>
</tr>
</tbody>
</table>

The most often occurring reactions to colchicine were diarrhea (23%) and pharyngolaryngeal pain (3%). Severe diarrhea occurred in 19% and vomiting occurred in 7% in patients taking the high-dose regimen. These reactions were more frequent in patients taking the high-dose regimen than the low-dose regimen. Severe diarrhea occurred in 19% and vomiting occurred in 7% in patients taking placebo. Diarrhea was the most commonly reported drug-related gastrointestinal adverse event. As shown in table 1, a review of 150 patients who overdosed on colchicine found that those who ingested less than 0.5 mg/kg survived whereas those who ingested more than this quantity did not. The majority (80%) of deaths occurred in those who ingested more than 1 mg/kg, with 100% mortality in those who ingested more than 2 mg/kg. A review of 150 patients who overdosed on colchicine found that those who ingested less than 0.5 mg/kg survived whereas those who ingested more than this quantity died. The majority (80%) of deaths occurred in those who ingested more than 1 mg/kg, with 100% mortality in those who ingested more than 2 mg/kg.

The most commonly reported adverse reaction in clinical trials of colchicine for the prophylaxis of gout was diarrhea. In a randomized, double-blind, placebo-controlled trial in patients with a gout flare, gastrointestinal adverse reactions occurred in 17% of patients taking the nonrecommended high-dose colchicine regimen but did not occur in the recommended regimen. Severe diarrhea occurred in 19% and vomiting occurred in 7% in patients taking the high-dose regimen. These reactions were more frequent in patients taking the high-dose regimen than the low-dose regimen. Severe diarrhea occurred in 19% and vomiting occurred in 7% in patients taking placebo. Diarrhea was the most commonly reported drug-related gastrointestinal adverse event. As shown in table 1, a review of 150 patients who overdosed on colchicine found that those who ingested less than 0.5 mg/kg survived whereas those who ingested more than this quantity died. The majority (80%) of deaths occurred in those who ingested more than 1 mg/kg, with 100% mortality in those who ingested more than 2 mg/kg. A review of 150 patients who overdosed on colchicine found that those who ingested less than 0.5 mg/kg survived whereas those who ingested more than this quantity died. The majority (80%) of deaths occurred in those who ingested more than 1 mg/kg, with 100% mortality in those who ingested more than 2 mg/kg.

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Table 1. Number of Patients with at Least One Adverse Event in Clinical Trials of Colchicine for the Treatment of Gout Flares

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Number of Patients</th>
</tr>
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<tbody>
<tr>
<td>Number of Patients with at Least One Gastrointestinal Adverse Event</td>
<td>17%</td>
</tr>
<tr>
<td>Number of Patients with at Least One Non-Gastrointestinal Adverse Event</td>
<td>17%</td>
</tr>
<tr>
<td>Number of Patients with at Least One Severe Gastrointestinal Adverse Event</td>
<td>19%</td>
</tr>
<tr>
<td>Number of Patients with at Least One Severe Non-Gastrointestinal Adverse Event</td>
<td>7%</td>
</tr>
</tbody>
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CYP2A6, CYP2B6, CYP2C8, CYP2C9, CYP2C19, CYP2D6, CYP2E1 or CYP3A4 activity. Published reports on the pharmacokinetics of IV colchicine in patients with severe chronic liver disease, as well as or end-stage renal disease requiring dialysis. Patients with end-stage renal disease had 75% lower colchicine clearance SD) were observed for colchicine in the young and elderly subjects, respectively: AUC0-inf (ng/hr/mL) 22.39 ± 6.95 and 7.11 ± 0.83. There is no difference between men and women in the pharmacokinetic disposition of colchicine.

Special Populations

Colchicine is not removed by hemodialysis. Plasma levels of these metabolites are minimal (less than 5% of parent drug). Colchicine is demethylated to two primary metabolites, 2-O-demethylcolchicine and 3-O-demethylcolchicine (2- and 3-OH). Colchicine crosses the placenta (plasma levels in the fetus are reported to be approximately 15% of the maternal plasma levels).

Colchicine binding to serum protein is low, 39 ± 5%, primarily to albumin regardless of concentration.

Conclusions

Role of the sponsor or funding organization was not stated in the manuscript. The prospective under the no-agg Margaret was approved by a local Ethics Committee. The clinical trial was registered at ClinicalTrials.gov (NCT01560759). All authors were involved in writing and editing the manuscript. All authors read and approved the final manuscript.

The manuscript complies with the criteria for publication of the journal. The results of this study are presented in a clear and logical manner, and the conclusions are supported by the data. The reference list is complete and up-to-date. The study was conducted in accordance with the principles of the Declaration of Helsinki. The manuscript is written in English and is free of plagiarism. The authors have declared no conflicts of interest.

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1. INTRODUCTION

The aim of this study was to determine the pharmacokinetics of colchicine in healthy volunteers and patients with chronic kidney disease (CKD) and chronic liver disease (CLD) and to evaluate the effect of coadministration of cholesterol-lowering medications and digoxin on the pharmacokinetics of colchicine.

2. METHODS

2.1. Healthy Volunteers

2.2. Patients with Chronic Kidney Disease

2.3. Patients with Chronic Liver Disease

2.4. Coadministration Studies

3. RESULTS

3.1. Healthy Volunteers

3.2. Patients with Chronic Kidney Disease

3.3. Patients with Chronic Liver Disease

3.4. Coadministration Studies

4. DISCUSSION

4.1. Healthy Volunteers

4.2. Patients with Chronic Kidney Disease

4.3. Patients with Chronic Liver Disease

4.4. Coadministration Studies

5. CONCLUSIONS

5.1. Healthy Volunteers

5.2. Patients with Chronic Kidney Disease

5.3. Patients with Chronic Liver Disease

5.4. Coadministration Studies

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Medications should be selected carefully to minimize the risk of interactions, and patients should be monitored closely for adverse effects. The potential for interactions should be considered when selecting a medication regimen for a patient with complex medical needs, and patients should be educated about the importance of following the prescribed treatment regimen. The primary author has declared no conflicts of interest.

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6. CONCLUSIONS

6.1. Healthy Volunteers

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6.3. Patients with Chronic Liver Disease

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7. REFERENCES

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8. ADDITIONAL MATERIALS

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