Effect of Diclofenac Sodium 1.5% Topical Solution on Coagulation Parameters in Patients With Knee Osteoarthritis Taking Anticoagulant and Antithrombotic Medications

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Introduction
- Although nonsteroidal anti-inflammatory drugs (NSAIDs) are effective for managing mild to moderately severe pain, they are also associated with adverse events (AEs) including the cardiovascular (CV) and gastrointestinal (GI) systems.
- These effects are related to the primary mechanism of action of NSAIDs (ie, cyclooxygenase [COX] enzyme inhibition).

Additional Information
- NSAIDs have been shown to significantly decrease platelet aggregation and to increase coagulation time.
- This effect has been observed in both noncirrhotic and cirrhotic patients.
- Using NSAIDs in patients who are also being treated with anticoagulants may further increase the risk for bleeding.

Objectives
- To determine whether diclofenac sodium 1.5% topical solution increases the anticoagulant and antithrombotic effects of warfarin, dabigatran, and aspirin and inpatients with osteoarthritis (OA) of the knee.

Methods

Study Design
- Single-center, phase-3, open-label, 4-week study.

Study Drugs
- Diclofenac sodium 1.5% topical solution was applied to the knee 4 times daily.

Inclusion Criteria
- Patients
- Patients were permitted to use acetaminophen (maximum dose, 1500 mg/day).
- Patients were permitted to use oral NSAIDs (maximum dose, 100 mg ibuprofen, 75 mg diclofenac, or 500 mg naproxen) but not concurrently with topical NSAIDs, which demonstrated little to no effect on platelet aggregation.
- Patients were primarily receiving warfarin 2 mg to 10 mg, clopidogrel 75 mg, aspirin 81 mg, and/or dabigatran 150 mg.

Exclusion Criteria
- Patients who were receiving anticoagulants and topiramate.
- Patients with use of corticosteroids within the previous 2 years.

Results

Baseline Characteristics
- Data were available for 21 patients aged 65 to 92 years (mean age, 70 years; female patients [n=14] outnumbered male patients [n=7]).
- Patients were primarily receiving warfarin 2 mg to 15 mg, clopidogrel 75 mg, aspirin 81 mg, and/or dabigatran 150 mg.

Coagulation Parameters
- Comparison was observed in median INR (baseline, 1.5; final evaluation, 1.9; P=.05), PT (10.8 seconds; final evaluation, 23.0 seconds; P=.001), and platelet aggregation time (103 seconds) for the control group were lower than that of the active treatment group.

Other exclusion criteria included:
- Abnormal coagulation test results that would require an alteration in anticoagulant dose
- Skin breakdown or rash at the application site

Outcome Measures
- The primary outcomes were international normalized ratio (INR), prothrombin time (PT), partial thromboplastin time, activated partial thromboplastin time (aPTT), and platelet aggregation time measured weekly during the 4-week study period.
- Timeliness was assessed by the proportion of AEs defined as an untreated medical condition occurring temporarily associated with the use of study drug.
- Intensity (ie, mild, moderate, or severe) and relationship to study drug (ie, not related, possibly related, probably related, or definitely related) were also assessed.

Statistics
- Because of the exploratory nature of this study, the sample size was determined based on clinical considerations; therefore, no formal statistical analysis was used.

Safety
- Data were summarized descriptively.

Discussion
- In a large-scale analysis of hospital admissions, topical NSAIDs were not associated with a significant risk of upper GI bleeding and perforation, whereas oral NSAIDs were associated with significant risk for developing these events.
- However, there are more studies needed specifically exploring the effect of topical NSAIDs on patients being treated with anticoagulant and antithrombotic medications to confirm the results of this and other previously conducted studies.

Conclusions
- Topical diclofenac sodium 1.5% topical solution did not interfere with coagulation parameters to a clinically significant degree compared with positive controls of warfarin or OA of the knee receiving concomitant anticoagulant therapy.

References