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The efficacy of celecoxib in preventing heterotopic ossification recurrence after open arthrolysis for post-traumatic elbow stiffness in adults



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Background: Heterotopic ossification (HO) recurrence after joint surgery is always a disturbing problem for patients and surgeons. Our study was performed to assess the efficacy and safety of celecoxib in preventing the recurrence of HO after open arthrolysis for post-traumatic elbow stiffness.

Methods: We retrospectively studied 152 patients with stiff elbows caused by post-traumatic HO. After surgery, 77 patients received celecoxib (200 mg once daily) for 28 days, whereas 75 did not. Radiographic evaluation was performed at 3, 6, and 9 months postoperatively. Univariate and multivariate analyses were performed to determine which factors affected HO recurrence.

Results: HO was both more common and more severe in the no-celecoxib group than in the celecoxib group at 3, 6, and 9 months after surgery. A significant difference was observed between the 2 groups in terms of postoperative extension (P = .030), flexion (P = .008), and pronation (P = .005); however, no significant difference in postoperative supination was noted (P = .622). Logistic regression analysis showed that taking celecoxib was the protective factor for HO recurrence, whereas overweight (body mass index > 25) and male gender were the risk factors.

Conclusions: A short course of celecoxib aids in the prevention of HO recurrence after open arthrolysis for elbow stiffness in adults and could be an effective and safe option.

Level of evidence: Level III, Retrospective Cohort Design, Treatment Study.

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Keywords: Heterotopic ossification; celecoxib; elbow stiffness; open arthrolysis; risk factor; trauma

The study protocol was approved by the Ethical Committee of Shanghai Jiao Tong University Affiliated Sixth People's Hospital East Campus: No. DYLL-201502.

As a common complication after trauma, elbow stiffness is defined as a flexion-extension arc of $<100^{\circ}$ or flexion contracture of $>30^{\circ}$. When nonoperative management fails after more than 6 months, patients whose lifestyle or vocation is greatly affected often request open arthrolysis to restore elbow function. However, because of the clinical recurrence of heterotopic ossification (HO) postoperatively, some patients may suffer from repeated elbow stiffness and

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have to undergo repetitive surgical interventions to excise new bone formation. A systematic review of published clinical results of surgeries for HO around the elbow found a clinical recurrence rate of HO of 13.7% after excision in post-traumatic elbows (with recurrence being defined as loss of motion or a reoperation due to HO).¹¹

Clinicians have been searching for ways to prevent the occurrence of HO since the 1970s. Nonsteroidal antiinflammatory drugs (NSAIDs)3,4,10 and radiation therapy^{15,17} are the 2 major measures reported to be effective in the prophylaxis of HO. Compared with radiation therapy, the use of NSAIDs, which inhibit the cyclooxygenase enzymes (COX-1 and COX-2), is regarded as an easier and more cost-effective method and is recommended as a general prophylactic in most hospitals, although it has side effects that must be taken into account.¹⁹ Celecoxib, a selective COX-2 inhibitor, retains anti-inflammatory action but reduces the occurrence of side effects caused by other NSAIDs, especially on gastrointestinal toxicity¹ and hemostasis. 12 The majority of studies involving celecoxib have reported that it is effective in preventing ectopic bone formation after total hip arthroplasty with fewer side effects than with other NSAIDs. 10,20,23 However, to our knowledge, the independent effect of celecoxib in preventing HO recurrence after open arthrolysis for elbow stiffness has not yet been reported in the English-language literature. This study aimed to address this issue as well as to evaluate the impact of age, sex, body mass index (BMI), and preoperative Hastings and Graham classification on the development of HO after open elbow arthrolysis.

Materials and methods

This is a retrospective cohort study of 307 patients who suffered from elbow stiffness with HO and were then treated with open arthrolysis combined with a hinged external fixator by a single surgeon (C.F.) at our institution from January 2010 to April 2013. Patients were eligible for inclusion if (1) they were aged ≥18 years, (2) they suffered from post-traumatic elbow stiffness, or (3) they had a diagnosis of mature HO based on confirmation of cortical boundaries observed on serial radiographs. Patients were excluded if (1) their HO was the result of trauma caused by burns, central nervous system injury, or genetic disease; (2) they had a history of peptic ulceration, gastrointestinal bleeding, coagulation defects, cerebral or myocardial infarction, allergy to NSAIDs or sulfonamides, renal or hepatic insufficiency, or mental disorder; or (3) they failed to complete routine radiographic evaluation at 3, 6, and 9 months.

According to the inclusion and exclusion criteria, a total of 152 patients were included in our study. Specifically, 45 patients were excluded because of incomplete radiographic evaluation at 3, 6, and 9 months. The patients included were 69 men and 83 women, with an average age of 43.9 (18-82) years. Open elbow arthrolysis was performed >6 months after trauma or last surgery. The surgical approaches were based on the location of the HO and previous scars from past operations. The surgical techniques were similar to those

described in previous studies. ^{13,21} A hinged external fixator was applied for 6 to 8 weeks in most cases to provide sufficient stability and to allow immediate postoperative rehabilitation. After surgery, the patients were divided into 2 groups: 77 patients who received celecoxib 200 mg once daily for 4 weeks for acute pain relief according to the physician's suggestions (celecoxib group) and 75 patients who were not willing to take celecoxib just for acute pain relief (no-celecoxib group). All patients were standardized to a rehabilitation program from the first postoperative day. A cycle of exercises including flexion, extension, and rotation were devised to guide all patients, gradually including active and passive exercises, which should be performed at least 4 times a day for 30 minutes each time. This progressive exercise program continued for at least 2 months after discharge.

Range of motion (ROM) of the elbow was measured with a hand-held goniometer. Radiographic follow-up consisted of anteroposterior and lateral radiographs obtained preoperatively and at 3, 6, and 9 months postoperatively. The presence of HO was assessed on these radiographs by 2 radiologists according to the classification system devised by Hastings and Graham. Class I includes radiographically evident HO but without functional limitation. Class II includes limited yet functional range of elbow motion but radiographically demonstrable HO with functional limitation in 1 or more planes of motion, subdivided into IIA, IIB, and IIC. Limitation of flexion-extension constitutes subclass IIA, limitation of pronation-supination constitutes subclass IIB, and limitation in both planes forms subclass IIC. Class III includes complete ankylosis of the particular articulation. The 2 radiologists were blinded to each patient's treatment regimen. Any disagreement was resolved on the basis of the opinion of a third radiologist.

The Fisher exact test was used to evaluate the association between treatment with celecoxib and recurrence of HO at 3, 6, and 9 months. A rank sum test was used to assess the association between taking celecoxib at 3, 6, and 9 months and the severity of the disease based on the Hastings and Graham classification. ROM was analyzed by the unpaired Student t test. The association of age and BMI with HO was tested by unpaired Student t test, and the association of sex and preoperative Hastings and Graham classification with HO was tested by χ^2 analysis. Considering the interactions between the variables, a nonconditional logistic regression analysis was performed to analyze the relationship between and among variables at 9 months. A P value <.05 was considered to be statistically significant. All statistical analyses were performed with SPSS 19.0 statistical software (SPSS Inc., Chicago, IL, USA).

Results

As shown in Table I, there were no significant differences between the 2 groups with regard to sex, age, BMI, or Hastings and Graham classification preoperatively. Overall, the number of patients with HO recurrence (including class I, class II, and class III) was 63 (41.4%), among whom severe HO (class III) was found in 12 patients (7.9%) at 9 months after open arthrolysis.

HO recurrence was more common in the no-celecoxib group than in the celecoxib group at 3 months (30.7% vs. 10.4%; P = .002), 6 months (50.7% vs. 18.2%; P < .001),

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