Alternative Protocol for Heterotopic Ossification Prophylaxis in Posterior Approaches for Acetabulum Fractures

Deren T. Bagsby, MD
Karl Shively, MD
Brian H. Mullis, MD

Department of Orthopaedic Surgery,
Indiana University School of Medicine,
Indianapolis, IN

Introduction

Heterotopic ossification (HO) is a well-known potential complication that can adversely affect patient outcomes by decreasing functional range of motion.[1,2] There are multiple known patient and injury-related factors associated with HO formation, including male sex, hip dislocation, certain fracture patterns, head injury, extensive burns, and a delay in surgical fixation.[1-6] However, it has also been shown that certain exposure types, such as the Kocher-Langenbeck or extensile approaches, increase the risk of postoperative HO formation. Non-steroidal anti-inflammatory drugs (NSAIDs) have been shown to reduce the risk of HO, but these drugs carry potential risks, which include long bone nonunion, GI symptoms, and hemorrhage.[1,3] Additionally to date, NSAID prophylaxis has only been examined in the context of single agent therapy. The purpose of this retrospective pilot study was to evaluate a novel dual NSAID protocol to determine if this protocol was an acceptable alternative to the traditional use of indomethacin in preventing HO following open fixation of acetabulum fractures through a posterior approach, while minimizing complications traditionally associated with NSAID usage.

Methods

A retrospective review of patients treated by two fellowship-trained orthopaedic traumatologists (KS, BHM) at a Level One trauma center from September 2006, through July 2011, was performed, following IRB approval. Sixty-nine patients were identified with acetabulum fractures that were treated by internal fixation. This study included 44 of these patients who were done through a posterior approach and had a minimum of six months of follow-up. Thirty of these 44 patients received an NSAID protocol of ketorolac, 30mg intravenous every 6 hours for 3 days, followed by naproxen, 500mg twice a day for 6 weeks. The remaining patients received no prophylaxis. Given the retrospective nature of this study, the reason for this is unknown. HO severity was evaluated using the Brooker classification. Grading of the radiographs was done by an independent reviewer, who was not involved in the care of these patients and was blinded to the treatment groups. To ensure a homogenous study population, all patients were evaluated for other potential risk factors for HO formation, including age at the time of injury, time delay of operative intervention, head and burn injuries, and hip dislocation or other associated high-risk fractures. Statistical analysis was performed for comparison of treatment and no treatment groups. Wilcoxon rank sum tests, Pearson chi-square tests, and Mantel-Haenszel chi-square tests were used to compare the two groups for differences in continuous, non-ordered categorical and ordered categorical responses, respectively.

Results

There were no significant differences in operative side, gender, presence of head injuries, or presence of associated high-risk fractures between our two groups (Table 1). Additionally, there was no difference between age ($p=0.88$), follow-up time in months ($p=0.25$), operating surgeon ($p=0.39$), surgical approach ($p=0.25$), or fracture type ($p=0.11$) (Table 2). There was a statistically significant reduction in HO rates in the treatment group seen in the individual Brooker classes ($p=0.004$) and the absolute presence of HO ($p=0.0275$), shown in Table 3. Treatment was associated with an absolute risk reduction of 33.81% and a relative risk reduction of 60% compared with those who did not get prophylaxis. Importantly, no severe (Brooker grade 3 or 4) HO was seen in the treatment group. Post-hoc power analysis demonstrated power of 0.9 and effect size of 0.5 with 44 patients.There was no increased risk for complications such as renal failure ($p=0.49$), GI bleeding ($p=0.48$), nonunion ($p=0.48$), repeat operation ($p=0.16$), or nerve palsy ($p=0.39$).

Discussion

Debate continues over which method of HO prophylaxis is best or whether any should be given routinely. NSAIDS provide a cheap and convenient method of prophylaxis while avoiding potential risks of radiation. Treatment

Corresponding author:
Deren T. Bagsby, MD
Department of Orthopaedic Surgery
Indiana University School of Medicine
541 Clinical Drive, Suite 600
Indianapolis, IN 46202-5111
dbagsby@iupui.edu

Table 1. Data for treatment and control groups.

		Treatment	Control	p
Side	Left	15 (50%)	8 (57%)	0.66
	Right	15 (50%)	6 (43%)	
Gender	Male	8 (27%)	3 (21%)	0.71
	Female	22 (73%)	11 (79%)	
Head Injury	Present	3 (10%)	1 (7%)	0.76
	Absent	27 (90%)	13 (93%)	
Other Fractures	Present	13 (43%)	6 (43%)	0.98
	Absent	17 (57%)	8 (57%)	

Table 2. Acetabular fracture types in treatment and control groups.

	Treatment	Control
Associated Both Column	2 (7%)	0 (0%)
Posterior T-type/Anterior Column	0 (0%)	1 (7%)
Posterior Column	1 (3%)	1 (7%)
Posterior Wall	12 (40%)	4 (29%)
Transverse/Posterior Wall	12 (40%)	3 (21%)
T-type	1 (3%)	4 (29%)
Transverse	0 (0%)	1 (7%)
Posterior Column/Posterior Wall	1 (3%)	0 (0%)
Posterior Wall/Posterior Column	1 (3%)	0 (0%)

Table 3. Brooker Classification of HO for patients in the treatment and control groups.

Class	Treatment	Control
0	23 (77%)	6 (43%)
1	4 (13%)	2 (14%)
2	3 (10%)	3 (21%)
3	0 (0%)	1 (7%)
4	0 (0%)	2 (14%)

as short as three weeks has been shown to be effective, but treatment beyond six weeks postoperatively has also been recommended in some studies.[7] Unfortunately NSAIDs carry multiple drawbacks, including reduced patient compliance and ulcer formation, possibly leading to GI bleeds.[8,9] This is particularly concerning in patients already on anticoagulation. Additionally, NSAIDs can increase the risk of bony nonunion after fixation. With our two agent combination protocol, we were able to show a reduction in the overall presence of ossification and reduced prevalence at each Brooker grade. Interestingly, there was no severe HO (grade 3 or 4) seen in our treatment group. Furthermore, our protocol was associated with no increased incidence of GI bleeding, renal failure, or fracture nonunion. The primary limitation of this study was its small sample size and retrospective design comparing our prophylactic regimen against no treatment. In addition, our control group averaged a two day delay before operative fixation, which can also be associated with HO.

Overall, our pilot study suggests that the use of intravenous NSAIDs (ketorolac) for 3 days postoperatively followed by 6 weeks of naproxen appears to be a safe and possibly efficacious method of preventing HO following posterior approaches for acetabulum fractures. This study serves to demonstrate the safety and potential efficacy of our protocol in HO prophylaxis. Further work will involve a prospective, randomized double-blind comparison of our protocol to standard indomethacin and radiation protocols.

References

Ghalambor N, Matta JM, Bernstein L. Heterotopic Ossification Following Operative Treatment of Acetabular Fracture: An Analysis of Risk Factors. *Clin Orthop* 1994; 305: 96-105.

McLaren AC. Prophylaxis with Indomethacin for Heterotopic Bone. An analysis of risk factors. *J Bone Joint Surg Am* 1990; 72: 245-247.

Giannoudis PV, Grotz MR, Papakostidis C, et al. Operative Treatment of Displaced Fractures of the Acetabulum. A Meta-Analysis. *J Bone Joint Surg* 2005; 87: 2-9.

Moed BR, Maxey J. The Effect of Indomethacin on Heterotopic Ossification Following Acetabular Fracture Surgery. *J Orthop Trauma* 1993; 7: 33-38.

McCarthy EF, Sundaram M. Heterotopic Ossification: A Review. *Skeletal Radiol* 2005; 34: 609-619.

Daum WJ, Scarborough MT, Gordon W, et al. Heterotopic Ossification and Other Perioperative Complications of Acetabular Fractures. *J Orthop Trauma* 1992; 6: 427-432.

Rout ML, Swiontkowski MF. Operative Treatment of Complex Acetabular Fractures. Combined Anterior and Posterior Exposure During the Same Procedure. *J Bone Joint Surg* 1990; 72: 897-902.

Wright R, Berret K, Christy MJ, et al. Acetabular Fractures: Long Term Follow-Up of Open Reduction Internal Fixation. *J Orthop Trauma* 1994; 8: 397-403.

Kjaergaard-Anderson P, Schmidt SA. Total Hip Arthroplasty: the Role of Anti-Inflammatory Medications in the Prevention of Heterotopic Ossification. *Clin Orthop* 1991; 263: 78-86.

Dahners LE, Mullis BH. Effects of Nonsteroidal Anti-Inflammatory Drugs on Bone Formation and Soft-Tissue Healing. *J Am Acad Orthop Surg* 2004; 12: 139-143.