

Research Article

Effects of Preoperative Non-Steroidal Anti-Inflammatory Drugs on Pain Mitigation and Patients' Shoulder Performance Following Rotator Cuff Repair

Alireza Rouhani¹, Ali Tabrizi^{1*}, Asghar Elmi¹, Naghi Abedini¹, Fardin Mirza Tolouei²

¹ Shohada Educational Hospital, Tabriz University of Medical Sciences, Tabriz, Iran.

² Imam Khomeini Hospital, Urmia University of Medical Sciences, Urmia, Iran.

Article info

Article History:

Received: 9 December 2013

Revised: 2 February 2014

Accepted: 19 February 2014

ePublished: 10 August 2014

Keywords:

- Postoperative pain control
- Rotator cuff tear
- Non-steroidal anti-inflammatory drugs
- Celecoxib

Abstract

Purpose: Pain is one of the most important factors adversely affecting clinical outcomes of operated patients. The present study aims at evaluating effects of preoperative COX2 non-steroidal anti-inflammatory inhibitors on pain mitigation and performance of patients with shoulder rotator cuff tear.

Methods: This case-control study was conducted on 60 patients suffering from rotator cuff injury candidate for arthroscopic repair. The patients were classified in two parallel and matched groups. One group (case group) was treated using Celecoxib (200mg/12h) started 48 hours before surgery and continued for 10 days after operation. In the control group, the placebo was prescribed in the same way. Postoperative pain, side effects, sleep disturbance, and short-term outcomes were compared between two groups using DASH questionnaire.

Results: Postoperative pain in the Celecoxib group significantly decreased in comparison with the control one. The difference was statistically meaningful ($P < 0.001$). Well motion ability was seen in 80% of patients of the Celecoxib group. It was 26.6% in the placebo group since pain inhibited them from exercising more motions. In this regard, there was a statistically meaningful difference between these two groups ($P = 0.02$). Sleep disturbance was meaningfully at higher levels in the placebo group ($P = 0.001$). Following up the patients for three months, it was made clear that performance of the Celecoxib group was better than that of the placebo one.

Conclusion: COX2 inhibitors are well efficient in patients' pain management after arthroscopic rotator cuff repair surgery. It results in less life complications, less sleep disturbances, improvement of patients' short-term clinical outcome, and more quick recovery.

Introduction

Postoperative pain affects patients' physiological performance and may adversely affect their surgery results. Evidently, postoperative acute pains management may improve patients' clinical performance.¹ Surgery-resulted traumas lead to different inflammatory modalities, {(Cyclooxygenase 2) Cox2} synthesis, and subsets such as Prostaglandins.^{2,3}

Non-steroidal anti-inflammatory drugs (NSAID) are of the most common non-opioid analgesic techniques used to control postoperative pain. Clinical trials have extensively referred to efficiency of non-steroidal anti-inflammatory drugs in postoperative pains management. On the other hand, non-steroidal anti-inflammatory drugs reduce postoperative consumption of narcotics, decrease narcotics-resulted complications, and accelerate recovery.¹⁻³

Additionally, non-steroidal anti-inflammatory drugs reduce surgery-related inflammatory responses. According to evidences, prostaglandins play a significant

role in developing of postoperative orthopedic pains. Lack of postoperative pain control was associated with low recovery and weak performance of the patients. Appropriate control of postoperative shoulder pain results in strengthening of postoperative rehabilitation, early mobilization, ideal performance recovery, improvement of range of shoulder motion, and muscular power.^{4,5} Less hospitalization period and quick rehabilitation are regarded as economical advantages of pain management in patients.⁶ The present study aims at evaluating effects of preoperative non-steroidal anti-inflammatory COX2 inhibitors on pain mitigation and performance of patients with shoulder rotator cuff tear underwent arthroscopic repair.

Materials and Methods

This case-control study was conducted on patients with rotator cuff injury candidate for arthroscopic repair in our center from 2009 to 2012. The qualified patients

*Corresponding author: Ali Tabrizi, Tel: (+98) 9148883851, Email: Ali.Tab.ms@gmail.com

©2014 The Authors. This is an Open Access article distributed under the terms of the Creative Commons Attribution (CC BY), which permits unrestricted use, distribution, and reproduction in any medium, as long as the original authors and source are cited. No permission is required from the authors or the publishers.

were invited to participate in the study while submitting informed satisfaction letter. The subjects' satisfaction to participate the study, non-consumption of non-steroidal anti-inflammatory drugs within the last 14 days, being 20-70 years old, and lack of extensive rotator cuff injury were regarded as the inclusion criteria of the study. Patients with history of allergy to non-steroidal anti-inflammatory drugs, history of gastric disease and peptic ulcer, renal insufficiency in the form of creatinine level >1.5 mg/dl and BUN >22 mg/dl, known coagulation disorder, and addiction to narcotics and alcohol were excluded from the study.

Patients requiring rotator cuff repair are admitted in the hospital 48 hours before surgery. In this study, 60 adult patients candidate for elective arthroscopic repair were alternately matched in two parallel groups (30 patients in each group). The matched patients were classified considering age, gender, and type of injury. One group was treated using Celecoxib and the other with placebo. In the Celecoxib group, it was prescribed as 200 mg/12h and 400mg in the operation day. Then, it was continued as 200 mg/12h for 10 days after surgery. In the control group, the placebo was used as similar capsules considering size, form, and color and prescribed in the same order. In the control group, acetaminophen 500mg/hydrocodone 5mg tablets were used to manage the patients' pain. Intravenous petedin (25mg) was prescribed for severe pains.

All patients were qualified according to American Society of Anesthesiologists Criteria of Physical Status 1&2. General anesthesia was used for the patients. Anesthesia was induced using propofol 1.5-2 mg/kg, rocuronium 0.6-1 mg/kg, and fentanyl 1-2 mg/kg, sevofluran (2-5%) and N₂O (66%) while in-oxygen was applied in general anesthesia.

Subacromial decompression arthroscopy and acromioplasty were conducted and suture anchors were used in arthroscopic rotator cuff repair. The patients' pain was measured based on pain score of Visual Analogue Scale (VAS). The scale ranges from zero (painless) to 10 (the worst imaginable pain). Also, 10-point scale (0=no sleep disturbance, 10=greatest sleep disturbance) was used to measure sleep disturbance within the last 24 hours and every hospitalization days. Pain was measured and recorded one hour after surgery and, then, every 4-48 hours, based on VAS. Following surgery, all patients were given abduction brace. Passive mobilization and assisted active exercise were started during first four weeks of operation and one day after surgery, respectively. Patients' ability in exercising of the trained motions was recorded and they were followed up at least for three months. Recovery and performance process was measured using DASH questionnaire where the scores range from zero (no disability) to 100 (maximum disability). The study was supervised by Ethics Committee of University of Medical Sciences and the required conditions were obtained.

Statistical methods

Descriptive statistical methods (frequency, percentage, mean \pm standard deviation) were used to statistically analyze data. Chi-square or Exact Fisher Test was used to qualitatively compare the groups. Once normality of data distribution between two groups was evaluated, Independent T-test was applied to quantitatively compare the groups. The quantitative data was repeatedly measured using Repeat Measure Test. Additionally, SPSS-17 software was used and $P < 0.05$ was considered meaningful.

Results

In this study, 60 patients with one-lateral shoulder rotator cuff injury candidate for arthroscopic repair were participated and classified in two groups, i.e. one group was treated using pre- and postoperative prescription of Celecoxib, and the other group received placebo. Considering demographic findings (Table 1), there is not any statistically meaningful difference between two groups and both groups were matched. Measuring patients' pain using VAS score every 4-48 hours after surgery indicate to statistically meaningful difference between Celecoxib and placebo groups considering pain severity ($P < 0.001$). According to Diagram 1, pain peak of both groups was at higher levels within 8-20 hours after surgery. However, it was less severe in the Celecoxib group. Among patients received placebo, 12 cases (40%) required petedin to mitigate pain. It was not used in any of patients of the Celecoxib group. In placebo groups acetaminophen 500mg/hydrocodone 5mg tablets were used every 12 hours to pain control, if patients had severe and uncontrolled pain narcotic prescribed. In the intervention group was not taking acetaminophen.

Table 1. Comparing demographic findings of two Celecoxib and placebo groups.

Variable	Celecoxib group N=30	Placebo group N=30	P value
Sex (Male/Female)	24:6	22:8	0.3
Age(year)	48.4 \pm 11.6	47.2 \pm 12	0.1
Size of tear (cm)	2.4 \pm 0.3	2.5 \pm 0.7	0.2
Preoperative pain(VAS)	6.5 \pm 2	6.4 \pm 1.9	0.1
Operative time(min)	91 \pm 25	90 \pm 32	0.6

Statistically meaningful difference was observed between two understudy groups considering patients' ability in starting postoperative passive and active motions of shoulder ($P=0.02$) such that 24 (80%) patients of the Celecoxib group completely exercised the motions but only 8 (26.6%) subjects of the placebo group was completely successful in exercising the motions and the rest avoided from starting or continuing of exercise due to pain intensification during motions.

Following arthroscopic rotator cuff repair, mean score of sleep disturbance was 2.4 \pm 0.5 in Celecoxib patients within the first day of surgery. However, it was 5.6 \pm 1.6

in the placebo group and there was statistically meaningful difference between two groups in this regard ($P=0.001$). During the second day, the calculated score was showed a meaningful difference between two groups according to Table 2.

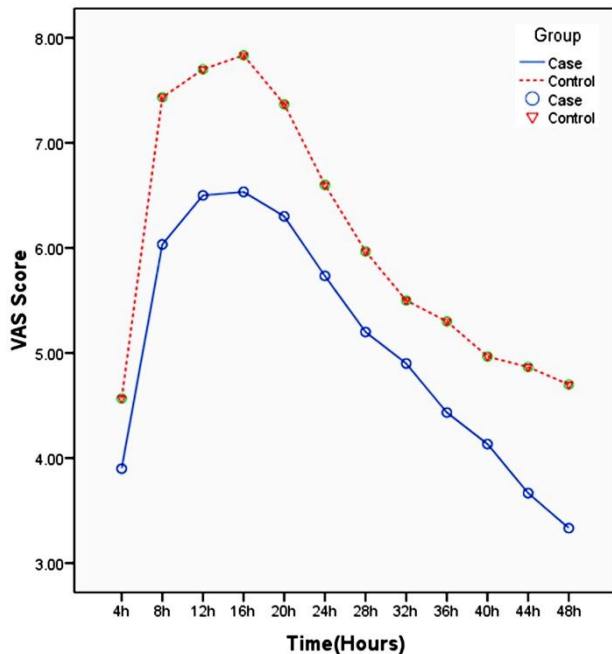


Diagram 1. Comparing pain of both Celecoxib and placebo patients every 4 hours after surgery.

Table 2. comparing pain, sleep disturbance and other symptoms of two Celecoxib and placebo groups.

Variable	Celecoxib group N=30	Placebo group N=30	P value
Pain after 2days	3.6±0.8	5.2±1.4	0.001*
Sleep disturbance	1.5±0.4	4.7±1.2	0.03*
Vomit and Nausea	6(20%)	19(63.3%)	0.02*
Narcotic Using	-	18(60%)	<0.001*
Function recovery by DASH score	36.7±4.8	42.8±5.6	0.02*
Abdominal Distention	-	10(33.3%)	0.01*

*Meaningfully difference.

There was significant difference ($P=0.03$) between the groups considering postoperative complications, i.e. vomit and nausea (Table 2). To control vomit and nausea, Metoclopramide was used in 2 (6.6%) and 15 (50%) cases of the Celecoxib and placebo groups, respectively. The difference is statistically meaningful ($P=0.02$). Distention and flatulence were seen in the placebo group and narcotics were used to control their pain. They were not seen in any cases of the Celecoxib group. Patients of both groups were discharged 72 hours after surgery. The patients were followed up for three months and the performance capabilities were measured using DASH questionnaire. The scores were 36.7±4.8 and 42.8±5.6 for the Celecoxib and placebo groups, respectively. In this regard, there was statistically meaningful difference between two groups and

Celecoxib-receiving patients demonstrated better performance.

Discussion

Non-steroidal anti-inflammatory drugs mitigate pain, reduce consumption of opioids, and increase postoperative recovery.¹ However, using NSAIDs to inhibit prostaglandin synthesis may lead to some complications including renal injury, gastric ulcer, and hemorrhage. Therefore, special Cyclooxygenase 2 (COX2) inhibitors were considered.¹ Out of 19 clinical trials conducted about rofecoxib, 17 studies indicated to its significant effect in comparison with placebo used in the control group. Some studies compared COX2 inhibitor and other NSAIDs and indicated to more effects and less complications of COX2. In comparison with the postoperative non-steroidal anti-inflammatory drugs, preoperative ones were more efficient in postoperative pain control.^{1,7-9}

In their randomized clinical trial, Riest *et al*¹⁰ suggested that prescription of pre- and postoperative parecoxib (40mg) meaningfully affect postoperative pain mitigation in comparison with placebo. They indicated to significant decrease of side effects of narcotics.¹⁰ Reuben *et al* used preoperative Celecoxib (200mg) in 200 patients underwent total knee arthroplasty and concluded that it accelerates range of knee motion and the patients reach maximum range of knee motion in a shorter time.¹¹ Pre- and postoperative Celecoxib lead to improvement of clinical outcome of patients underwent knee arthroscopy even one year after surgery.¹¹ Reuben *et al* studied knee arthroplasty in 50 patients and suggested that use of rofecoxib within 10 days before surgery meaningfully affected decrease of preoperative pain score of the patients. It did not affect hemorrhage rate and no important side effects were seen.¹² There is not any study evaluating effects of non-steroidal anti-inflammatory drugs on rotator cuff repairs. This is the first study in this regard and studies conducted in other surgical cases were used to compare the findings. The idea of using non-steroidal anti-inflammatory drugs was inspired by observation of those studies conducted on other surgical cases. Considering less complications of COX2 inhibitors, it was decided to prescribe pre- and postoperative Celecoxib in arthroscopic rotator cuff repair cases and compare the results with that of placebo-receiving group. According to Chen *et al*, short-term use of COX2 inhibitors to control pain has generally less side effects than other non-selective non-steroidal anti-inflammatory drugs. In this systematic review, there was not any significant difference between COX2 oral inhibitors.¹³

Less prostaglandin E2 leads to improvement of postoperative joint performance and, probably, ideal performance of patients and acceleration of their discharge process. According to studies, use of Celecoxib before knee arthroplasty significantly improves range of knee motions one month after surgery. It also has useful economical advantages and

meaningfully decreases the costs. Rehabilitation plan of the patients is accelerated and the patients recover more quickly.¹⁴

Once effects of anesthetic drugs disappear, the patients' pain is intensified about 8-24 hours after surgery (known as rebound pain).⁶ In our study, Celecoxib mitigated postoperative pain of the patients 8-24 hours after surgery. The placebo-receiving patients suffered from more severe pain and even, in some cases, their VAS was over than 7 and 8. Postoperative pain management is of high importance. Oh Hun *et al*⁶ studied arthroscopic rotator cuff repair cases and concluded that interscalene block better controls postoperative pain and its severity. On the other hand, pain severity was less than 6, based on VAS. In our study, the placebo group experienced more severe pain and required narcotics in some cases. Similar to previous studies, pain mitigation is seen in our patients received Celecoxib before surgery. There was statistically meaningful difference between two groups considering pain severity. Celecoxib group did not require narcotics and their pain was controlled equally. Vomiting and nausea were the most important postoperative complications. According to Reuben *et al*,¹¹ vomiting and nausea in the placebo group were more than the Celecoxib one. In this regard, the difference was statistically meaningful and anti-vomiting drugs were required at higher levels.¹¹ Similar findings of our study indicate to meaningful effect of Celecoxib in reducing vomiting and nausea in those patients underwent arthroscopic rotator cuff repair.

Bekker *et al*⁷ demonstrated that rofecoxib significantly decreases use of narcotics in lumbar laminectomy patients. However, it was not so effective in patients' discharge time.

In our study, Celecoxib resulted in better control of the patients' pain such that narcotics were not required. But, opioids were used in some cases in placebo-receiving patients and some complications such as distension and flatulence were observed. Similar to the previous study, it did not affect the discharge time.

Following up the patients and evaluating their performance for three months after arthroscopic rotator cuff repair was one of power points of our study. Comparing patients' performance three months after surgery using DASH questionnaire indicate to significant improvement of Celecoxib patients' performance. They experienced the minimum level of disability which can be attributed to better performing of rehabilitation program (due to pain control) and acceleration of return of range of shoulder motions, as seen in knee arthroplasty cases. Placebo group obtained higher DASH score and faced with more performance disability three months after surgery. This is while the same treatment and rehabilitation plan was used for both groups. Following surgery, total sleep time and rapid eye movement in sleep decreased typically.¹⁵ In their study, Buvanendran *et al* suggested that rofecoxib controls and meaningfully mitigates patients' pain following total knee arthroplasty. Also, decrease of sleep disturbance

was seen in the operated patients. In our study, there was different rate of sleep disturbance between two groups within the first and second days. The Celecoxib patients experienced less sleep disturbance.¹⁴

Conclusion

According to findings of the present study, COX2 inhibitors effectively control postoperative pain of patients with arthroscopic rotator cuff repair, reduce side effects, decrease sleep disturbances, and, finally, improve short-term clinical outcome of the patients and accelerate their recovery.

Acknowledgments

This study was financially supported by Tabriz University of Medical sciences.

Conflict of Interest

There is no conflict of interest to be reported.

Ethical Issues

The study was confirmed by Ethics Committee of Tabriz University of Medical Sciences.

References

1. Gilron I, Milne B, Hong M. Cyclooxygenase-2 inhibitors in postoperative pain management: current evidence and future directions. *Anesthesiology* 2003;99(5):1198-208.
2. Woolf CJ, Chong MS. Preemptive analgesia--treating postoperative pain by preventing the establishment of central sensitization. *Anesth Analg* 1993;77(2):362-79.
3. Varrassi G, Marinangeli F, Agro F, Aloe L, De Cillis P, De Nicola A, et al. A double-blinded evaluation of propacetamol versus ketorolac in combination with patient-controlled analgesia morphine: analgesic efficacy and tolerability after gynecologic surgery. *Anesth Analg* 1999;88(3):611-6.
4. Gordon SM, Brahim JS, Rowan J, Kent A, Dionne RA. Peripheral prostanoid levels and nonsteroidal anti-inflammatory drug analgesia: replicate clinical trials in a tissue injury model. *Clin Pharmacol Ther* 2002;72(2):175-83.
5. Arroyo JL, Reiner RP, Dawson E, Iribarren MJ, Haro F, Carrascosa F, et al. The effects of epidural analgesia and conventional anaesthesia on renal excretion of PGE2 during orthopaedic surgery. *Eur J Anaesthesiol* 1985;2(4):401-6.
6. Oh JH, Rhee KY, Kim SH, Lee PB, Lee JW, Lee SJ. Comparison of analgesic efficacy between single interscalene block combined with a continuous intrabursal infusion of ropivacaine and continuous interscalene block after arthroscopic rotator cuff repair. *Clin Orthop Surg* 2009;1(1):48-53.
7. Bekker A, Cooper PR, Frempong-Boadu A, Babu R, Errico T, Lebovits A. Evaluation of preoperative administration of the cyclooxygenase-2 inhibitor rofecoxib for the treatment of postoperative pain after

- lumbar disc surgery. *Neurosurgery* 2002;50(5):1053-7; discussion 10577-8.
8. Chang DJ, Fricke JR, Bird SR, Bohidar NR, Dobbins TW, Geba GP. Rofecoxib versus codeine/acetaminophen in postoperative dental pain: a double-blind, randomized, placebo- and active comparator-controlled clinical trial. *Clin Ther* 2001;23(9):1446-55.
 9. Chang DJ, Desjardins PJ, Chen E, Polis AB, McAvoy M, Mockoviak SH, et al. Comparison of the analgesic efficacy of rofecoxib and enteric-coated diclofenac sodium in the treatment of postoperative dental pain: a randomized, placebo-controlled clinical trial. *Clin Ther* 2002;24(4):490-503.
 10. Riest G, Peters J, Weiss M, Dreyer S, Klassen PD, Stegen B, et al. Preventive effects of perioperative parecoxib on post-discectomy pain. *Br J Anaesth* 2008;100(2):256-62.
 11. Reuben SS, Buvenandran A, Katz B, Kroin JS. A prospective randomized trial on the role of perioperative celecoxib administration for total knee arthroplasty: improving clinical outcomes. *Anesth Analg* 2008;106(4):1258-64.
 12. Reuben SS, Fingerroth R, Krushell R, Maciolek H. Evaluation of the safety and efficacy of the perioperative administration of rofecoxib for total knee arthroplasty. *J Arthroplasty* 2002;17(1):26-31.
 13. Chen LC, Elliott RA, Ashcroft DM. Systematic review of the analgesic efficacy and tolerability of COX-2 inhibitors in post-operative pain control. *J Clin Pharm Ther* 2004;29(3):215-29.
 14. Buvenandran A, Kroin JS, Berger RA, Hallab NJ, Saha C, Negrescu C, et al. Upregulation of prostaglandin E2 and interleukins in the central nervous system and peripheral tissue during and after surgery in humans. *Anesthesiology* 2006;104(3):403-10.
 15. Rosenberg-Adamsen S, Kehlet H, Dodds C, Rosenberg J. Postoperative sleep disturbance: mechanisms and clinical implications. *Br J Anaesth* 1996;76(4):552-9.