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Efficacy of Diclofenac Rectal Suppository in Patients with Laparoscopic Cholecystectomy: A Prospective Randomized Double Blinded Clinical Trial

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Background: Post laparoscopic cholecystectomy pain management can reduce recovery and discharge time. Non-steroidal anti-inflammatory drugs and opioids are used for this purpose.
Objectives: This randomized clinical trial evaluates the efficacy of diclofenac rectal suppository for the management of postoperative pain.
Patients and Methods: Forty four patients were randomized to receive either 100 mg diclofenac rectal suppository or placebo at the time of recovery and three hours later after laparoscopic cholecystectomy. Postoperative visual analogue pain scale (VAS, ranges 0 to 10 cm) and adverse reactions were recorded over a 24-hour period. If VAS score was ≥ 7, 25mg, pethedin was given intravenously as a rescue analgesic.
Results: In both groups, VAS score was reduced in 24 hours. It was statistically lower in diclofenac group rather than placebo group in all intervals except at the time of recovery. Moreover, the mean pethedin consumption dose and the incidence of administration of postoperative rescue analgesic were statistically lower in diclofenac group. Postoperative bleeding was not statistically different between two groups.
Conclusions: Diclofenac rectal suppository provided simple and safe pain relief in laparoscopic cholecystectomy.

Keywords: Cholecystectomy, Laparoscopic; Diclofenac; Analgesics, Opioid

1. Background

Although minimally invasive surgeries have reduced the postoperative pain, most of the patients still require opioids after surgery. Opioids have important side effects including respiratory depression, drowsiness, apnea, nausea, vomiting, and ileus (1, 2). Non-steroidal Anti-inflammatory Drugs (NSAIDs) are safer than opioids with the similar effect on postoperative pain (2). It has been shown that using intramuscular or intravenous diclofenac and ketrolac in upper abdominal and gynecologic surgeries could decrease the need for opioids. Muscle and kidney damage and increasing the risk of bleeding are important side effects of intramuscular administration of diclofenac (3).

2. Objectives

This study was doneto evaluate the effect of rectal suppository diclofenac on post laparoscopic cholecystectomy pain.

3. Patients and Methods

The protocol of this prospective randomized double-blinded, controlled clinical trial was approved by the local ethical committee of the medical faculty, Tehran University of Medical Sciences. Forty four patients candidate for laparoscopic cholecystectomy of gallbladder stone enrolled in this study from January 2011 to January 2013 at Rasool Akram and Firouzgar hospital, Tehran, Iran., . Exclusion criteria were acute cholecystitis, patient refusal to enter or continue the study, morbid obesity (body mass index ≥ 30), chemical substance abuse, chronic or recent use of analgesics, chronic pain, a history of significant cardiopulmonary, hepatic or renal disease, hypersensitivity to the medications, any contraindication of non-opioid analgesics, asthma, peptic ulcer, upper or lower gastrointestinal bleeding, pregnancy, and breastfeeding. The patients who required analgesic the night before surgery were also excluded from this study. A written informed consent was obtained from all patients and

Implication for health policy/practice/research/medical education:
Post laparoscopic cholecystectomy pain management can reduce recovery and discharge time. Non-steroidal anti-inflammatory drugs and opioids are used for this purpose. This randomized clinical trial evaluates the efficacy of diclofenac rectal suppository in the management of postoperative pain.

they were randomly assigned into either treatment (100 mg diclofenac rectal suppository at recovery time and 3 hours later) or placebo group (using placebo at recovery time and 3 hours later) using computer table of random numbers. All patients underwent pain assessment with Visual Analogue Scale (VAS, ranges 0 – 10 cm) at the time of recovery, and 3, 6, 12, and 24 hours after operation. Patients were given 25 mg Pethedin intravenously if their VAS score was ≥ 7. Pain scores, total Pethedin consumption, patients requests for administration of postoperative analgesics, and also intraoperative and postoperative complications including bleeding, visceral injury, nausea, vomiting, and headache were recorded.

3.1. Statistical Analysis

Continuous variables are summarized by mean ± standard deviation and categorical variables are expressed as percentage (%). Univariate analyses were performed by Chi square, student T-test, Mann-Whitney U test using SPSS software (version 17; SPSS Inc, Chicago, IL). Results were considered significant if P values were less than 0.05.

4. Results

Baseline characteristics of patients were not statistically different between two groups (Table 1). One patient (4.5%) in diclofenac group and another one (4.5%) in placebo group underwent Magnetic Resonant Cholangiopancreaticography (MRCP). Moreover, six patients (27%) in diclofenac group and eight patients (36%) in placebo group underwent Endoscopic Retrograde Cholangiopancreaticography (ERCP) before laparascopic cholecystectomy. Intraoperative findings including gallbladder adhesion was detected in 17 patients (77.3%) of diclofenac group and 12 patients (54.5%) of placebo group which was not statistically different among them (P = 0.101). Moreover, three patients in diclofenac group (13.6%) and six patients (27.3%) in placebo group had intraoperative bleeding which was not statistically different, too (P = 0.228). Five patients (22.7%) of diclofenac group and 12 patients (54.5%) of placebo group required analgesic treatment for one day. Furthermore, one patient (4.5%) of diclofenac group and nine patients (40.9%) of placebo group required analgesic treatment for two days. Results showed that the incidence for administration of postoperative analgesic in diclofenac group was statistically lower than that in placebo group (P < 0.001). Similarly, the mean Pethedin consumption dose in diclofenac group (18.18 ± 15.77 mg) was statistically lower than that in placebo group (66.59 ± 18.80 mg) with P value < 0.001. Table 2 demonstrates the mean VAS score at the time of recovery, 3, 6, 12, and 24 hours after cholecystectomy. It has been shown that the pain reported by diclofenac group was statistically lower than that in placebo group in all intervals except at the time of recovery.

5. Discussion

It has been shown that NSAIDs reduce postoperative pain by blocking cyclo-oxigenase (COX) enzyme (2) and can be used as anesthetic drugs, solely or in combination with other opioids (4, 5). This randomized controlled clinical trial evaluated the efficacy of rectal diclofenac suppository in post laparoscopic cholecystectomy pain management. Preoperative characteristics of patients including age, sex, right upper quadrant and epigastric pain, and anorexia were not statistically different between treatment and placebo group. Moreover, intraoperative clinical findings including gall bladder adhesion and bleeding were not significantly different between them. Therefore, the results could be directly related to the effect of using diclofenac rectal suppository. In our study, the administration of postoperative opioid (pethedin) was limited to the patients whose VAS score was ≥ 7. The results showed that mean pethedin consumption dose and the incidence of its administration were significantly lower in diclofenac group than that in placebo group. Opioids have critical side effects including nausea, vomiting, drowsiness, and respiratory depression especially in higher doses (6). lack of need for opioids in diclofenac group would be able to decrease these side effects. This study demonstrated that the severity of post laparoscopic cholecystectomy pain was lower in the patients received 100 mg diclofenac rectal suppository than that in patients received placebo. This happened while the pain severity in placebo group might be masked by receiving higher dose of pethedin. Moreover, one of the side effects of using NSAIDs is increasing the risk of bleeding by inhibiting the effect of COX-1 in platelet aggregation and homeostasis (7). However, Intraoperative and postoperative bleeding was not statistically different between two groups. Most of the previous studies evaluated the efficacy of intramuscular diclofenac with regard to decreasing the post laparascopic cholecystectomy pain. Fredman et al. (8) compared diclofenac, Ketrolac, and placebo groups. They showed that pain severity and need for opioid is lower in diclofenac and ketrolac group rather than in placebo one. In another study, Wilson et al. demonstrated the same results in addition to this fact that diclofenac would not increase the postoperative complications (9). Muscle damage and increasing the risk of bleeding and kidney injury are the important reported side effects of intramuscular administration of diclofenac (3). Therefore, a great need exists for finding other roots of administration. Limited number of studies evaluated the effect of other types of diclofenac on postoperative pain. Alessandri et al. demonstrated that subcutaneous diclofenac is effective in reducing postoperative pain (10). Moreover, Ng et al. compared the effect of suppository diclofenac to Intravenous parecoxib on postoperative pain. They showed that there is not statistically significant difference between them (11). Our study confirmed previous results and showed that 100 mg diclofenac rectal suppository at the time of recovery and three hours

later could reduce post laparoscopic cholecystectomy pain and also the need for opioid consumption. Therefore, diclofenac rectal suppository would be a simple and effective alternative for this purpose.

Table 1 . Baseline Characteristics of Patients

Baseline Characteristics	Diclofenac Group	Placebo Group, No. (%)	P value
Sex, No. (%)			0.272
Male	8 (36.4)	11 (50)	
Female	14 (63.6)	11 (50)	
Age, Mean ±SD	47.05 ± 16.11	44.47 ± 17.72	0.658
Preoperative findings, No. (%)			
Epigastric pain	2 (9.1)	6 (27.3)	0.120
RUQ[a]pain	17 (77.3)	13 (59.1)	0.166
Anorexia	4 (18.2)	9 (40.9)	0.093
Intraoperative findings, No. (%)			
Gall bladder adhesion	17 (77.3)	12 (54.5)	0.101
Bleeding	3 (13.6)	6 (27.3)	0.228

[a] Right Upper Quadrant

Table 2. Mean Visual Analogue Scale

	Diclofenac Group, Mean ± SD	Placebo Group, Mean ± SD	P value
VAS[a](Recovery time)	7.95 ± 0.899	8.32 ± 0.477	0.101
VAS (After 3 hours)	6.59 ± 1.046	7.64 ± 0.685	0.013
VAS (After 6 hours)	5.82 ± 1.468	7 ± 0.69	0.001
VAS (After 12 hours)	4.05 ± 1.588	5.91 ± 0.921	< 0.001
VAS (After 24 hours)	2.41 ± 1.501	4.59 ± 1.141	< 0.001

[a] Visual Analogue Scale

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Authors' Contribution

The first author and corresponding author contributed 80% and the others 50%.

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