



Tramadol Versus Diclofenac in Pain Management after Cesarean Section: A Cost Analysis Study

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ABSTRACT

Introduction: Postoperative pain is considered frequently as one of the major problems in subjects after cesarean delivery. Meanwhile, the main analgesic drugs are opioids and non-steroidal anti-inflammatory drugs, side-effects such as nausea, vomiting, and sedation have been reported by opioids. Economic evaluation of analgesics is an important criterion in clinical practice and efficiency of the health system services. The aim of this study was to compare the efficacy and cost analysis of diclofenac versus tramadol for post-cesarean pain in postpartum women.

Patients and Methods: This study has been undertaken based on a randomized clinical trial that has evaluated postoperative pain in a double-blinded, randomized, single-dose comparison of tramadol intramuscular injection, 100 mg (group T) and diclofenac suppository, 100 mg (group D) given alone-single dose in 200 patients who had elective cesarean delivery. All patients were assessed at 0, 6, 12, and 24 h post-operation for pain degree (by Visual Analog Score: 1-10), nausea and vomiting incidence. Our outcomes assessment was based on the reduction in pain degree. For cost estimating of therapeutic schemes, we computed the direct costs of the analgesics (unitary cost) and disposable materials such as needles, syringes, and alcoholic pads (Padcols®). Average cost-effectiveness ratio (ACER) calculated for comparison.

Results and Discussion: The efficacy of tramadol and diclofenac were not different significantly ($P = 0.06$). Nausea and vomiting were minimal with all treatments. Total costs in T group were 43.35 USA Dollar (USD) and in D group were 12.1 USD. ACER for tramadol was 9.14 USD and 2.85 USD for diclofenac per one degree reduction in pain. Thus, ACER indicated that the cost of tramadol in this study was 3.21 times more than diclofenac resulted with the same effectiveness.

Conclusions: It has been concluded that diclofenac is a more cost-effective choice of treatment in comparison with tramadol for post-cesarean pain management.

Keywords: Cost analysis, average cost-effectiveness ratio, tramadol, diclofenac, caesarean section, postoperative pain

1. Introduction

Nowadays, analgesic therapy has been dominated by two major classes of analgesic drugs; which are opioids and non-steroidal anti-inflammatory drugs (NSAIDs) [1]. NSAIDs are comparable with opioids in postoperative pain [2,3]. In pain control, μ -opioidergic, monoaminergic (noradrenalin and 5-hydroxytryptamine) and prostaglandin-dependent mechanisms have a prominent role [4]. NSAIDs are choices with low nausea, vomiting and respiratory depression, in comparison with side-effects of opioids. Moreover, a decrease in opioid requirement may cause a decline in hospitalization and increase patient's chance to give analgesia [5]. NSAIDs effectively reduce patient's uterine contraction in the post-cesarean period and inflammatory substances by inhibiting the cyclooxygenase enzyme and preventing the central and peripheral synthesis of prostaglandins [6]. This process may cause a reduction in both pains including wound pain and uterine cramp pain [7,8]. Diclofenac is a derivative of phenyl acetic acid, which is used as antipyretic, anti-inflammatory, and analgesic agent [9]. Tramadol is a synthetic analog of codeine and is μ -opioid receptor agonist, which acts centrally [10-12]. Therapeutic effects of tramadol include pain relieving in both acute and chronic pain [12,13]. It is an effective postoperative analgesic, which has advantageous versus using morphine in the long term [10]. Common adverse effects of tramadol contain nausea, vomiting, dizziness, dry mouth, sedation, and headache [10]. One of the most accessible NSAIDs in Iran for postoperative pain is diclofenac suppository [1]. NSAIDs are drugs with diverse classes and routes of administration, among them, an intramuscular (IM) administration has been considered as rectal route, yet rectal route is not popular among postpartum women [1]. Furthermore, oral route of administration may not be an appropriate choice for early postoperative period [1]. Postoperative pain and cost-effectiveness analysis (CEA) of analgesics are two topics which are most important in worldwide literature in controlling pain [14]. Postoperative pain is

prominent because of its epidemiological relevance. CEA is important for cost issues in clinical practice and health systems questions about efficiency [14]. Furthermore, cost-effectiveness studies are essential in rational decisions such as allocating health care resources [15,16]. This study has been undertaken to be based on a randomized clinical trial that evaluated postoperative pain in a double-blinded, single-dose comparison of tramadol IM injection and diclofenac suppository in patients who had elective cesarean delivery. Another goal of this study was comparing costs of these analgesic therapies with calculating average cost-effectiveness ratio (ACER) for these medications.

2. Patients and Methods

This clinical, randomized, and double-blinded study has been undertaken for 200 patients from 18 to 40 who chose elective low-risk cesarean. All of the patients have been entered into the study with their own consent. Exclusion criteria for this research has contained history of an allergic reaction to tramadol or diclofenac, background of gastrointestinal bleeding or peptic ulcer disease, use of opioid during the last month, preeclampsia or eclampsia, significant pulmonary disease, intra-operative complications, changed operative procedure, inability or reluctance to give written consent or share their information in spite of obeying the ethical rules, or deviation from the standardized anesthetic regimen. Patients were separated by computerized randomization in two groups before operation: D group taking alone-single dose of diclofenac 100 mg suppository (Diclogin®; Aburaihan Pharmaceutical Company, Tehran, Iran) and T group taking alone-single dose of tramadol 100 mg injection (Tramexir®; Exir Pharmaceutical Company, Boroojerd, Iran). Anesthetic and preoperative procedures have been standardized. Any opioid or NSAID has not given to patients as premedication. After cesarean, patients have been received diclofenac via rectal or tramadol in buttock. Pain

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degree, nausea, and vomiting have been examined 0, 6, 12, and 24 h after cesarean. Pain degree has been assessed by Visual Analog Score (VAS): 1-10. Four categories have been scheduled for pain intensity contained: painless: 0, mild: 1-4, moderate: 5-8, severe: 9-10. T-test analysis has been conducted for statistical calculations [1]. Direct costs of the analgesics and disposable material (needles, syringes, and alcoholic pads [Padcols[®]]) were calculated for the cost estimates of therapeutic schemes. Costs have been converted from Iranian Rials (IRR) into USA dollar (USD) at an official exchange rate of 9920 IRR/1 USD 2010 to have an international comparison. ACER has been calculated for tramadol and diclofenac and has been compared with each other. Results have been expressed as mean \pm standard error of the mean. In order to analyze the data, ANOVA test has been conducted by using the Statistical Package for Social Sciences (SPSS) for Windows 14.0 (Chicago, IL, USA). The critical criterion for statistical significance has been $P < 0.05$.

3. Results

A total of 200 consecutive patients have been screened for inclusion of 150 patients in this study. Basic characteristics of patients are presented in table 1. Mean pain degrees have been $T = 8.1 \pm 0.7$, $D = 7.9 \pm 0.6$ after 0 h, $T = 6.3 \pm 0.6$, $D = 5.7 \pm 0.6$ after 6 h, $T = 3.5 \pm 0.7$, $D = 3.3 \pm 0.3$ after 12 h, and $T = 1.5 \pm 0.6$, $D = 1.2 \pm 0.5$ after 24 h (Figure 1). Effectiveness of these drugs has been extracted from our clinical trial and results have been showed that diclofenac and tramadol were efficient ($P < 0.01$). In addition, there were no significant differences between diclofenac and tramadol in efficiency ($P > 0.05$). Nausea and vomiting rates have been assessed in all treatment groups at each time point over the 24-h period. Mild nausea has been reported in three patients with tramadol and one patient with diclofenac. Vomiting has occurred four patients with tramadol and one patient with diclofenac. There were no significant differences in the incidences of nausea and vomiting ($P > 0.05$). Sleepiness and drowsiness in the 24 postoperative hours have been reported by tramadol in 30 patients and 21 patients by diclofenac. There were no serious side-effects throughout the study. Direct cost of medications and equipment calculated, and the results for each of the two treatment groups have been reported. Nursing and hospitalization cost have been similar with both groups. They have been ignored in our calculation. According to VAS, tramadol efficiency has been 4.74 and diclofenac efficiency has been 4.25 degree. D group with diclofenac 100 mg suppository has cost 12.1 USD and T group with tramadol 100 mg injection cost 43.35 USD. The ACER has been computed 9.14 for tramadol and 2.56 for diclofenac, respectively. Overall, cost of treatment with tramadol is 3.21 times more than diclofenac with the same analgesic effect (Table 2).

Table 1. Basic characteristics of patients

Characteristics	Mean \pm SEM
Maternal age (year)	32.3 \pm 11.4
Gestational age (week)	36.2 \pm 5.9
Gravid	1.9 \pm 0.8
Abortion history (%)	
No	88.6 \pm 17.9
Yes	11.4 \pm 4.3

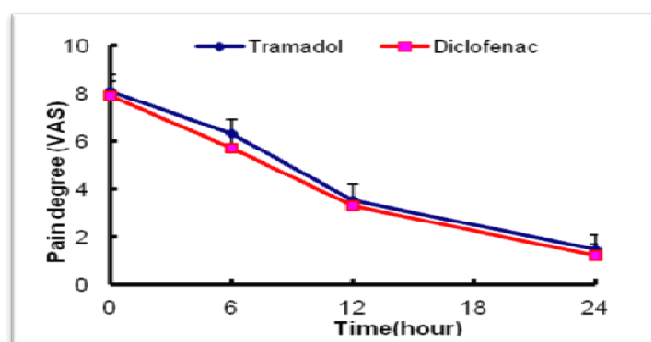


Figure 1. Pain degree in 200 patients after prescription of tramadol 100 mg or diclofenac 100 mg. Values are mean \pm standard error of mean

Table 2. Cost-effectiveness comparison of tramadol versus diclofenac

Drug	Effectiveness	Total cost (\$)	ACER	Ratio
Tramadol	4.74	43.35	9.14	3.21
Diclofenac	4.25	12.10	2.85	-

ACER: Average cost-effectiveness ratio

4. Discussion

The ACER of diclofenac has been compared with tramadol in this paper. After cesarean section as a major operation, distress and pain can predict postpartum women [1]. McDonnell et al. have reported that fewer inpatients, infant care (including breast feeding, maternal-infant bonding) and prevention of postoperative morbidity are important criteria for being effective post-cesarean analgesic [17]. Each analgesic regimen should be safe, effective with fewer adverse effects for the mother and her baby [17]. Since patients' pain is not objective, new methods for controlling the pain such as patient-controlled analgesia (PCA) and continuous epidural analgesia have partially substituted for older parenteral administration method of opioids [18,19]. Nonetheless, these new methods are not accessible for all patients; because of their high price and also requirement to well-trained personnel and special equipment [20,21]. Moreover, different side-effects of these methods such as respiratory depression have been revealed [19,22,23]. The most usual side-effects of opioids such as drowsiness, sleepiness, or restricted access to their infants due to equipment and they are not acceptable for postpartum women because they want to take care of their infants few hours after cesarean section [24]. In order to avoid adverse effects of opioids such as respiratory depression, many challenges have been done to ameliorate effectiveness of non-opioid drugs [25]. Patients benefit pre-, peri- and post-operative administration of NSAIDs like diclofenac and oxicams, which are widely used in out-patient surgeries, in pain management of mild to moderate postoperative pain [26-28]. According to related medical evidences, there is not any paper published which has evaluated cost-effectiveness ratio of NSAID versus opioid. Thus, this paper is the first. Previous researches demonstrated tramadol is an effective postoperative analgesic [11,12,28,30]. Secoli et al. in 2008 assessed cost-effectiveness of combination therapies for post-hemorrhoidectomy pain. The results have showed that acetaminophen 2000 mg plus codeine 120 mg have been more cost-effective than other schemes without breakthrough pain episodes as a scheme which contains opioid [14]. Chang et al. in 2004 measured efficacy and cost-effectiveness of morphine intravenous PCA against discontinuous morphine IM injection in Chinese women after elective gynecological operation. It has been concluded that intravenous PCA induces considerably better pain relieving effect on postoperative pain in comparison to discontinuous morphine IM injection [15]. Also, the cost-effectiveness study showed intravenous PCA is more costly than discontinuous IM injection [15]. Vercouteren et al. in 2002 compared cost-effectiveness of intrathecal morphine with epidural PCA. The research has demonstrated that epidural PCA has been better analgesic effect with less nausea and vomiting, it is more costly [31]. Contreras-Hernandez et al. in 2008 compared cost-effectiveness of NSAIDs to cyclooxygenase-2 selective inhibitors. It has been concluded that cyclooxygenase-2 inhibitors such celecoxib is the most cost-effective in the treatment of joint pain [32].

Current study has indicated that diclofenac is more cost-effective than tramadol. In other words, diclofenac is an affordable option for post-cesarean pain in elective cesarean sections in comparison to tramadol.

5. Conclusion

This study has demonstrated analgesic effect of diclofenac is 3.21 times more cost-effective than tramadol with the same efficiency and for post-cesarean pain. Therefore, a single dose therapy of diclofenac suppository can be a proper choice of pain management for postpartum women.

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