

ORIGINAL ARTICLE

Comparison of outcome in patients undergoing elective cesarean delivery with intravenous acetaminophen versus placebo.

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ABSTRACT... Objective: To see effect of intravenous acetaminophen in post caesarean delivery to control pain in cases with general anesthesia. **Study Design:** Randomized Controlled Trail. **Setting:** Department of Obstetrics and Gynecology, University Teaching Hospital, Gujranwala. **Period:** Aug 31, 2019 till April 30, 2020. **Methods:** All cases meeting inclusion criteria was enrolled and underwent elective cesarean section. Then they were randomly divided to receive either 15 mg/kg intravenous acetaminophen (n = 146) or normal saline (n = 146) fifteen minutes before endotracheal intubation. Pain was measured after 6 hours of C-section. SPSS version 22 was used to analyze the data. **Results:** The mean age of cases in group-A was 26.59 \pm 4.95 years and in group-B was 26.44 \pm 4.72 years. The mean gestational age in group-A and group-B was 39.54 \pm 1.19 weeks and 39.38 \pm 1.08 weeks. The mean pain in group-A was 4.98 \pm 1.01 and in group-B was the mean pain was 6.18 \pm 1.30. The mean pain in group-A (acetaminophen group) was statistically lower than group-B (placebo), p-value < 0.001. **Conclusion:** It is concluded that IV acetaminophen is effective in controlling the pain in cases with general anesthesia after caesarean delivery. Hence in future this non-opioid analgesic without potential adverse effects can be used. This will surely reduce the analgesia requirement and hospital stay.

Key words: Analgesia Requirement, Caesarean Delivery Pain, IV Acetaminophen, Pain Control.

INTRODUCTION

Surgical procedures known as cesarean sections, or C-sections, are done all over the world to save the lives of mothers and fetuses and to avoid difficulties during childbirth.¹ In Pakistan, the percentage of C-sections performed has skyrocketed from 28.8% to 44% during the last 10 years.² A woman's quality of life may be significantly impacted by childbirth, and having a caesarean section during childbirth may result in long-term health issues. Acute postoperative pain is experienced by the majority of surgical patients; yet, data indicates that fewer than half of them report sufficient pain alleviation after their surgeries.^{3,4} One of the most worrying problems after a cesarean surgery is pain, which may vary from 4 to 9%.5

For the purpose of minimizing and controlling postoperative pain, several preoperative,

intraoperative, and postoperative treatments and management techniques are available.³ For the management of postoperative pain, different drugs (opioid vs. non-opioid), routes (oral, intravenous, neuraxial, regional), and modes (patient controlled vs. "as needed") are being employed.⁶ To avoid hemodynamic stress from tracheal intubation, there are several factors to take into account when choosing anaesthetic medications for a C-section.⁷ Additionally, there are major physiological advantages to postoperative pain reduction, making its efficient management among the most crucial. Thus, tracking pain alleviation is turning into a crucial postoperative quality indicator.⁶ Acetaminophen is a cyclooxygenase inhibitor that functions as a non-opioid analgesic via the central nervous system and the serotonergic system.8 It works without causing the side effects that opioids might have, such nausea, vomiting, and

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respiratory depression. It has been effectively used to the treatment of postoperative pain after a variety of surgical procedures.⁹ The effects of intravenous acetaminophen after a C-section were investigated in a research. In the recovery room, patients in the saline group reported higher mean pain (7.0 \pm 1.24 VAS) compared to 6.15 \pm 2.27 in the acetaminophen group (p-value = 0.041).¹⁰

The purpose of this research is to determine the impact of intravenous acetaminophen on postcesarean delivery outcomes in our community's general anesthesia patients. Data on other populations is similarly not readily accessible, and no local studies have been conducted too far. The aim of postoperative pain management after a C-section is to minimize adverse consequences while reducing or eliminating pain and suffering. Pain management is crucial for patients who have had cesarean sections because it helps the mother relax and improve her capacity for self-care. This leads to an earlier release, which lowers the risk of nosocomial infections and hospital stays. So, this study can help us to see the role of acetaminophen in controlling the pain, if find lower mean pain then in future this nonopioid analgesic without potential adverse effects can be used to minimize the pain.

To see effect of IV acetaminophen in post caesarean delivery to control pain in cases with general anesthesia

METHODS

This Randomized Controlled Trail was done at Obstetrics and Gynecology department, university teaching hospital Gujranwala for 8 months Aug 31, 2019 till April 30, 2020. A total of 292 cases (146 cases in each group) are estimated using mean pain in saline group as 7.0 \pm 1.24 and in Intravenous Acetaminophen group as 6.15 \pm 2.27.(10) We used 80% power of study, 95% confidence interval.

The Sampling Technique used was Non-probability consecutive sampling.

Inclusion Criteria

Females of age 18-35 years of age, parity<4, undergoing Elective cesarean section due to previous 1 and previous 2 section at term (> 37 weeks on LMP) under general anesthesia were enrolled in the study.

Exclusion Criteria

Predicted difficult airway, known allergies to study drug and history of medical disorder i.e. hypertensive and diabetics were excluded from the study.

All cases meeting inclusion criteria was taken in this study after approval from the ethics committee and obtaining an informed consent from participants and the study was started. After taking age, name, and contact details they was counseled about the procedure. All patients who had elective cesarean delivery under general anesthesia were randomly assigned to either 15 mg/kg intravenous acetaminophen (n= 146) or normal saline (15 minutes before endotracheal intubation). All individuals received 5ml/kg intravenous crystalloid fluids at baseline. Patients received the same general anaesthetic procedure and medication. All procedures were done by a single consultant to avoid any related baise. Pain was measured after 6 hours of C-section as per operational definition. This study is ethically approved from the Institutional review board (IRB) of university teaching hospital Gujranwala with IRB number 1149 dated 07-10-2019.

All data was entered and analyzed using SPSS version 22. Independent sample t-test evaluated pain in both groups, with p-value< 0.05 considered significant.

RESULTS

The mean age of cases in group-A was 26.59 \pm 4.95 years and in group-B was 26.44 \pm 4.72 years. The mean weight of cases in group-A was 75.86 \pm 8.73 kg and in group-B was 73.21 \pm 8.97 kg. The mean height in group-A and group-B was 1.64 \pm 0.11 m and in group-B was 1.65 \pm 0.12m. The mean BMI in group-A was 28.25 \pm 3.31 and in group-B was27.11 \pm 4.43. The mean gestational age in group-A and group-B was

39.54 \pm 1.19 weeks and 39.38 \pm 1.08 weeks. In group-A there were 57(39.04%) females who had para 1, 38(26.03%) females had para 2 and 51(34.93%) females had para 3 while in group-B there were 59(40.41%) females who had para 1, and 44(30.14%) females who had para 2 and 43(29.45%) females had para 3. Table-I

	Acetaminophen	Placebo		
n	146	146		
Age (in years)	26.59 ± 4.95	26.44 ± 4.72		
Height	75.86 ± 8.73	73.21 ± 8.97		
Weight	1.64 ± 0.11	1.65 ± 0.12		
BMI	28.25 ± 3.31	27.11 ± 4.43		
Gestational age (weeks)	39.54 ± 1.19	39.38 ± 1.08		
Parity				
Primiparous	57 (39%)	59 (40%)		
Para 2	38 (26%)	44 (30%)		
Para 3	51 (35%)	43 (30%)		
Table-I. Basic information of enrolled females in bothstudy groups				

The mean pain in group-A was 4.98 ± 1.01 and in group-B was the mean pain was 6.18 ± 1.30 . The mean pain in group-A was statistically lower than group-B, p-value < 0.001. Table-II

In 18-29 years old females, the mean pain was statistically less in group-A (4.96 ± 1.05) when compared with group-B (6.27 \pm 1.25), p-< 0.05, while among 30-35 years old cases the mean pain was statistically less in group-A (5.02 ± 0.94) than in group-B (5.92 ± 1.40), p-< 0.05. In obese females, the mean pain was statistically less in group-A (5.03 \pm 0.95) when compared with group-B (6.34 \pm 1.37), p-value < 0.05, while among non-back old cases the mean pain was statistically less in group-A (4.97 \pm 1.03) than in group-B (6.13 ± 1.27), p-value < 0.05. Among 30-39 weeks of gestation, the mean pain was statistically less in group-A (4.91 \pm 1.09) when compared with group-B (5.87 \pm 1.26), p-value < 0.05, while among females with gestational age 40- 41 week, the mean pain was statistically less in group-A (5.04 \pm 0.94) than in group-B (6.54 ± 1.25), p-value < 0.05. Among 30-39 weeks of gestation, the mean pain was statistically less in group-A (4.47 \pm 1.07) when compared with group-B (6.08 \pm 1.30), p-value < 0.05, while among females having para 2, the mean pain was statistically less in group-A (4.95 \pm 1.04) than ingroup-B (6.41 \pm 1.42), p-value < 0.05 and among females with para 3, the mean pain was also statistically less in group-A (5.24 \pm 0.89) than in group-B (6.07 \pm 1.14), p-value < 0.05. Table-III

	Acetaminophen	Placebo		
n	146	146		
Pain (VAS)	4.98 ± 1.01	6.18 ± 1.30		
Table-II. Comparison of pain (VAS) in both study groups				

t-test= -8.805.

P-value = < 0.001 (Highly Significant)

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	Acetaminophen	Placebo	P-Value	
Age 18-29 years	4.96 ± 1.05	6.27 ± 1.25	< 0.001	
Age 30-35 years	5.02 ± 0.94	5.92 ± 1.40	0.001	
BMI				
Obese	5.03 ± 0.95	6.34 ± 1.37	< 0.001	
Non-obese	4.97 ± 1.03	6.13 ± 1.27	< 0.001	
Gestational age				
38-39 weeks	4.91 ± 1.09	5.87 ± 1.26	< 0.001	
40-41 weeks	5.04 ± 0.94	6.54 ± 1.25	< 0.001	
Parity				
Primiparous	4.77 ± 1.07	6.08 ± 1.30	< 0.001	
Parity 2	4.95 ± 1.04	6.41 ± 1.42	< 0.001	
Parity 3	5.24 ± 0.89	6.07 ± 1.14	< 0.001	
Table-III. Comparison of Pain (VAS) in both study				

groups with respect to effect modifiers

DISCUSSION

Although the World Health Organization (WHO) recommends that the optimal rate of cesarean sections be fewer than 15%, the incidence of these procedures has been rising lately and is now the most common abdominal surgery done in the US. The percentage of C-sections in the US surpassed 32% in 2008, while in Colombia, the rate rose from 24.9% in 1988 to 45.7% in 2013.^{11,12}

The rates rose significantly across Latin America and the Caribbean between 1990 and 2014, staying higher than those seen in any other area.¹³ In Brazilian private clinics, 80–90% of births may occur by cesarean section. In order to maximize mother and newborn welfare after a cesarean section, postoperative pain management is crucial.^{14,15}

In addition to reducing suffering, managing postoperative pain results in faster mobility, shorter hospital stays, lower medical expenses, and more patient satisfaction. Opioid analgesics have historically been used to provide perioperative analgesia. Excessive opioid usage. however, is linked to a number of perioperative adverse effects that might postpone hospital including respiratory depression, release. sleepiness and sedation, postoperative nausea and vomiting, pruritus, urine retention, ileus, and constipation.¹⁶ Perfalgan is a unit-dose injectable version of paracetamol (1g/100ml) that is ready for infusion. Numerous scientific investigations demonstrate that paracetamol is a useful analgesic medication for managing pain after surgery, with few contraindications and negligible drug interactions. Although its exact mode of action is not entirely known, following infusion, it is present in the cerebrospinal fluid (CSF) in substantial concentration.17 The descending serotonergic pathway may be activated and prostaglandin E2 synthesis in the central nervous system reduced as a result of central cyclooxygenase (COX2) inhibition. According to a plasma half-life of 2.7 hours, the analgesic action of intravenous (IV) paracetamol begins in 5 minutes, peaks at 1 hour, and lasts for 4-6 hours.¹⁸

In the present research, the mean pain was 4.98 \pm 1.01 in group A and 6.18 \pm 1.30 in group B. Group A had significantly less mean pain than group B, with a p-value of less than 0.001. According to a different research, patients in the saline group had mean pain in the recovery room that was higher (7.0 ± 1.24 VAS compared to 6.15 ± 2.27 in the acetaminophen group; p-value = 0.041).¹⁰ In 2016, another research examined whether IV acetaminophen lowers opioid use for elective cesareans with neuraxial anesthesia. Postoperative opioid needs, pain management satisfaction, and visual analogue scores were measured. Two fentanyl and one morphine trials. All articles indicated IV acetaminophen improved results, however 3 suggested it worked better with a nonsteroidal anti-inflammatory medication. Multimodal treatment with IV acetaminophen reduces post-c-section opioid use, according to research. The present research suggests IV acetaminophen for elective cesarean deliveries under neuraxial anesthesia.¹⁹

Another research examined how intravenous reduced acetaminophen (paracetamol) hemodynamic responses to endotracheal intubation and postoperative pain in general anesthesia cesarean section patients. Patients were compared for postoperative pain severity and analgesic need. The saline group had higher recovery room pain (VAS 7.0 ± 1.24 vs. 6.15 ± 2.27; P value = 0.041), required more fentanyl $(150 \mu g vs. 87.7 \pm 75; P value < 0.01)$, and needed more meperidine (12.88 ± 20.84 mg vs. 1.35 \pm 5.73; P value = 0.002) than the paracetamol group. Mean arterial pressure (MAP) variations were comparable after intubation in both groups (P = 0.71), while pulse rates changed more in the saline group (P = 0.01). Thus, intravenous acetaminophen before caesarean section lowered tachycardia after intubation, narcotics during and after surgery, and PACU pain.¹⁰

As another research the first 40 patients got 1g/100ml intravenous paracetamol at the conclusion of surgery and every 6 hours for 24 hours, whereas the second 40 received 100ml normal saline as a placebo. The research found that no patients in group I needed rescue drugs, but 25% in group II did (P< 0.0001). Group satisfaction was similar. Thus, intravenous paracetamol may lessen the need for rescue opioids for pain relief following cesarean section.²⁰

Another experiment examined IV and oral acetaminophen postoperative pain on management and morphine requirements in Caesarean patients receiving PCIA. In a study of 45 term Caesarean patients, group A got acetaminophen 1 gm every six hours with oral placebo and group I received ibuprofen 400 mgpo with oral placebo. First dose 30 min preop. VAS (0-10) at rest and morphine requirements were recorded every hour for four hours and then every four hours for 48 hours postoperatively. Patient satisfaction 48 hours after surgery was rated 1-10. While both groups' visual analogue scale scores decreased similarly with time, no significant changes were seen (estimated marginal means: $1.4 \pm \text{SEM } 0.2$ against $1.9 \pm \text{SEM } 0.2$ for groups A and I, respectively, P = 0.124). While Group A had a total postoperative morphine intake of 98 \pm 37 mg, Group I had 93 \pm 33 mg (P = 0.628). Both groups had high patient satisfaction with analgesia (9 \pm 1 vs 9 \pm 1, P = 0.93). Hence, intravenous acetaminophen may replace oral ibuprofen for morphine patient-controlled analgesia after Caesarean birth.²¹

In another study, Group A received 650mg oral paracetamol tablet 20 minutes before surgery, Group B received 35-45 mg/kg rectal suppository after spinal anesthesia, and Group C received 10-15mg/kg i.v. paracetamol infusion 20 minutes before surgery. Analgesia duration was the main outcome while other characteristics were secondary. No significant haemodynamic abnormalities or deleterious effects were seen in the three groups. Thus, rectally administered paracetamol improves postoperative analgesic quality and duration more than oral and intravenous paracetamol without adverse effects.²²

CONCLUSION

It is concluded that IV acetaminophen is effective in controlling the pain in cases with general anesthesia after caesarean delivery. Hence in future this non-opioid analgesic without potential adverse effects can be used. This will surely reduce the analgesia requirement and hospital stay.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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REFERENCES

1. Un Nisa Q, Raza F, Shams R, Gul R. Frequency and indications of cesarean section in a Tertiary Care Hospital of Peshawar, Khyber Pakhtunkhwa, Pakistan. Journal of Rehman Medical Institute. 2016; 2(1):27-34.

- Khatoon A, Karim SA, Hussain S. Changing prevalence of cesarean section, repeated cesarean section and indications for repeated cesarean section over 10 year period at a tertiary care center, Karachi. Annals Abbasi Shaheed Hospital & Karachi Medical & Dental College. 2016; 21(2):82-7.
- Chou R, Gordon DB, de Leon-Casasola OA, Rosenberg JM, Bickler S, Brennan T, et al. Management of Postoperative Pain: A clinical practice guideline from the American pain society, the American Society of Regional Anesthesia and Pain Medicine, and the American Society of Anesthesiologists' committee on regional anesthesia, executive committee, and administrative council. The Journal of Pain. 2016; 17(2):131-57.
- Gordon DB, de Leon-Casasola OA, Wu CL, Sluka KA, Brennan TJ, Chou R. Research gaps in practice guidelines for acute postoperative pain management in adults: Findings from a review of the evidence for an American Pain Society Clinical Practice Guideline. The Journal of Pain. 2016; 17(2):158-66.
- Lavand'homme P. Long-term problems and chronic pain after Caesarean section. Anesthesia for Cesarean Section. 2017; 169-82.
- Garimella V, Cellini C. Postoperative pain control. Clinics in Colon and Rectal Surgery. 2013; 26(03):191-6.
- Ayatollahi V, Faghihi S, Behdad S, Heiranizadeh N, Baghianimoghadam B. Effect of preoperative administration of intravenous paracetamol during cesarean surgery on hemodynamic variables relative to intubation, postoperative pain and neonatal apgar. Acta Clinica Croatica. 2014; 53(3):272-8.
- Majumdar S, Das A, Kundu R, Mukherjee D, Hazra B, Mitra T. Intravenous paracetamol infusion: Superior pain management and earlier discharge from hospital in patients undergoing palliative head-neck cancer surgery. Perspectives in Clinical Research. 2014; 5(4):172-7.
- Sener M, Kocum A, Caliskan E, Yilmaz I, Caylakli F, Aribogan A. Administration of paracetamol versus dipyrone by intravenous patient-controlled analgesia for postoperative pain relief in children after tonsillectomy. Revista Brasileira de Anestesiologia. 2015; 65:476-82.
- Soltani G, Molkizadeh A, Amini S. Effect of intravenous acetaminophen (paracetamol) on hemodynamic parameters following endotracheal tube intubation and postoperative pain in caesarian section surgeries. Anesthesiology and Pain Medicine. 2015; 5(6):e30062.

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- 11. MacDorman M, Declercq E, Menacker F. Recent trends and patterns in cesarean and vaginal birth after cesarean (VBAC) deliveries in the United States. Clinics in Perinatology. 2011; 38(2):179-92.
- Rubio-Romero JA, Fonseca-Pérez JE, Molina S, Buitrago Leal M, Zuleta JJ, Ángel-Müller E. Racionalización del uso de la cesárea en Colombia. Consenso de la Federación Colombiana de Obstetricia y Ginecología (Fecolsog) y la Federación Colombiana de Perinatología (Fecopen). Bogotá, 2014. Revista Colombiana de Obstetricia y Ginecología. 2014; 65(2):139-51.
- Betrán AP, Ye J, Moller A-B, Zhang J, Gülmezoglu AM, Torloni MR. The increasing trend in caesarean section rates: Global, regional and national estimates: 1990-2014. PloS One. 2016; 11(2):e0148343.
- Jesus G, Jesus N, Peixoto-Filho FM, Lobato G. Caesarean rates in Brazil: what is involved? 2015; 122(5):606-9.
- Eisenach JC, Pan PH, Smiley R, Lavand'homme P, Landau R, Houle TT. Severity of acute pain after childbirth, but not type of delivery, predicts persistent pain and postpartum depression. Pain. 2008; 140(1):87-94.
- de Beer JdV, Winemaker MJ, Donnelly GA, Miceli PC, Reiz JL, Harsanyi Z, et al. Efficacy and safety of controlled-release oxycodone and standard therapies for postoperative pain after knee or hip replacement. Canadian Journal of Surgery. 2005; 48(4):277.

- Uysal HY, Takmaz SA, Yaman F, Baltaci B, Başar H. The efficacy of intravenous paracetamol versus tramadol for postoperative analgesia after adenotonsillectomy in children. Journal of Clinical Anesthesia. 2011; 23(1):53-7.
- Aronoff DM, Oates JA, Boutaud O. New insights into the mechanism of action of acetaminophen: Its clinical pharmacologic characteristics reflect its inhibition of the two prostaglandin H 2 synthases. 2006; 79(1):9-19.
- Pickering-Luttrell HM, Gayden J, Pellegrini J. Effectiveness of intravenous acetaminophen administration in the postoperative pain management of the cesarean section patient. Anesthesia eJournal. 2016; 4(1):43-49.
- Omar A, Issa K. Intravenous Paracetamol (Perfalgan) for analgesia after cesarean section: A double blind randomized controlled study. Rawal Medical Journal. 2011; 36(4):269-73.
- 21. Alhashemi J. Intravenous acetaminophen vs oral ibuprofen in combination with morphine PCIA after Cesarean delivery. Can J Anaesth. 2006; 53(12):1200-6.
- 22. Mahajan L, Mittal V, Gupta R, Chhabra H, Vidhan J, Kaur A. Study to compare the effect of oral, rectal, and intravenous infusion of paracetamol for postoperative analgesia in women undergoing cesarean section under spinal anesthesia. Anesthesia Essays and Researches. 2017; 11(3):594-8.

AUTHORSHIP AND CONTRIBUTION DECLARATION

- 1 **Ammara Shakeel:** Writing original draft, conceptualization.
- 2 Sadaf Aziz: Data analysis, interpretation.
- 3 Bushra Shakeel: Proof read, methodology.
- 4 Maryam Naeem: Formulation of results.
- 5 Wajiha Irfan: Collection of data.
- 6 **Rao Nouman Ali:** Supervision of work.