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Comparative assessment of analgesic efficacy of intravenous paracetamol and intravenous tramadol in cases of cesarean section

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Abstract
Postoperative pain relief reduces the incidence of chest infection, deep vein thrombosis, stress response and sympathetic activity. Inspite of growing advances in the pharmacological approach of pain relief during surgery, relief of pain in the postoperative period continues to remain a challenge. Adverse effects of postoperative pain are many but they can be minimized by pain therapy. Patients with significant postoperative pain may show insomnia, restlessness, anxiety and helplessness. Further this will cause respiratory, cardiovascular, gastrointestinal, urinary and metabolic complications. Hence based on above findings the present study was planned for Comparative Assessment of Analgesic Efficacy of Intravenous Paracetamol and Intravenous Tramadol in Cases of Cesarean Section.
The present study was planned in Department of Anesthesia, Patna Medical College and Hospital, Patna, Bihar. The study was conducted from October 2016 to January 2017. The 40 cases of the cesarean delivery under spinal anesthesia were included in the present study. The 40 cases were divided equally in two study groups. Group I includes the 20 cases administered with the IV Paracetamol 1000 mg in 100 ml of normal saline over 15 minutes. The Group II includes the 20 cases IV Tramadol 50 mg.
The data generated from the present study concludes that intravenous paracetamol with better analgesic efficacy; shorter duration of labour and fewer maternal side-effects is a better labour analgesic than tramadol. Also complicated rules and restrictions on the use of opioids and the high rate of side effects related to opioids, prescribing paracetamol in the form of intravenous infusion could be recommended as a good alternative for relieving opioid after the operation.

Keywords: paracetamol, tramadol, cesarean section, postoperative pain, etc

Introduction
Caesarean section, also known as C-section, or caesarean delivery, is the use of surgery to deliver babies. A caesarean section is often necessary when a vaginal delivery would put the baby or mother at risk. This may include obstructed labor, twin pregnancy, high blood pressure in the mother, breech birth, or problems with the placenta or umbilical cord. A caesarean delivery may be performed based upon the shape of the mother's pelvis or history of a previous C-section. A trial of vaginal birth after C-section may be possible. The World Health Organization recommends that caesarean section be performed only when medically necessary. Some C-sections are performed without a medical reason, upon request by someone, usually the mother.
A C-section typically takes 45 minutes to an hour. It may be done with a spinal block, where the woman is awake, or under general anesthesia. A urinary catheter is used to drain the bladder, and the skin of the abdomen is then cleaned with an antiseptic. An incision of about 15 cm (6 inches) is then typically made through the mother's lower abdomen. The uterus is then opened with a second incision and the baby delivered. The incisions are then stitched closed. A woman can typically begin breastfeeding as soon as she is out of the operating room and awake. Often, several days are required in the hospital to recover sufficiently to return home [1].
C-sections result in a small overall increase in poor outcomes in low-risk pregnancies. They also typically take longer to heal from, about six weeks, than vaginal birth. The increased risks include breathing problems in the baby and amniotic fluid embolism and postpartum bleeding in the mother. Established guidelines recommend that caesarean sections not be used before 39 weeks of pregnancy without a medical reason. The method of delivery does not appear to have an effect on subsequent sexual function [2].
In 2012, about 23 million C-sections were done globally [8]. The international healthcare community has previously considered the rate of 10% and 15% to be ideal for caesarean sections. Some evidence finds a higher rate of 19% may result in better outcomes. More than 45 countries globally have C-section rates less than 7.5%, while more than 50 have rates greater than 27%. Efforts are being made to both improve access to and reduce the use of C-section. In the United States as of 2017, about 32% of deliveries are by C-section. The surgery has been performed at least as far back as 715 BC following the death of the mother, with the baby occasionally surviving. Descriptions of mothers surviving date back to 1500. With the introduction of antiseptics and anesthetics in the 19th century, survival of both the mother and baby became common [3].
Conventionally, caesarean sections are classified as being either an elective surgery or an emergency operation. Classification is used to help communication between the obstetric, midwifery and anaesthetic team for discussion of the most appropriate method of anaesthesia. The decision whether to perform general anesthesia or regional anesthesia (spinal or epidural anaesthetic) is important and is based on many indications, including how urgent the delivery needs to be as well as the medical and obstetric history of the

woman [4]. Regional anaesthetic is almost always safer for the woman and the baby but sometimes general anaesthetic is safer for one or both, and the classification of urgency of the delivery is an important issue affecting this decision.

A planned caesarean (or elective/scheduled caesarean), arranged ahead of time, is most commonly arranged for medical indications which have developed before or during the pregnancy, and ideally after 39 weeks of gestation. In the UK, this is classified as a 'grade 4' section (delivery timed to suit the mother or hospital staff) or as a 'grade 3' section (no maternal or fetal compromise but early delivery needed). Emergency caesarean sections are performed in pregnancies in which a vaginal delivery was planned initially, but an indication for caesarean delivery has since developed. In the UK they are further classified as grade 2 (delivery required within 90 minutes of the decision but no immediate threat to the life of the woman or the fetus) or grade 1 (delivery required within 30 minutes of the decision: immediate threat to the life of the mother or the baby or both) [5].

Elective caesarean sections may be performed on the basis of an obstetrical or medical indication, or because of a medically non-indicated maternal request. Among women in the United Kingdom, Sweden and Australia, about 7% preferred caesarean section as a method of delivery. In cases without medical indications the American Congress of Obstetricians and Gynecologists and the UK Royal College of Obstetricians and Gynaecologists recommend a planned vaginal delivery. The National Institute for Health and Care Excellence recommends that if after a woman has been provided information on the risk of a planned caesarean section and she still insists on the procedure it should be provided. If provided this should be done at 39 weeks of gestation or later. There is no evidence that ECS can reduce mother-to-child hepatitis B and hepatitis C virus transmission [6].

Both general and regional anaesthesia (spinal, epidural or combined spinal and epidural anaesthesia) are acceptable for use during caesarean section. Evidence does not show a difference between regional anaesthesia and general anaesthesia with respect to major outcomes in the mother or baby. Regional anaesthesia may be preferred as it allows the mother to be awake and interact immediately with her baby. Compared to general anaesthesia, regional anaesthesia is better at preventing persistent postoperative pain 3 to 8 months after caesarean section. Other advantages of regional anesthesia may include the absence of typical risks of general anesthesia: pulmonary aspiration (which has a relatively high incidence in patients undergoing anesthesia in late pregnancy) of gastric contents and esophageal intubation. One trial found no difference in satisfaction when general anaesthesia was compared with either spinal anaesthesia [7].

Regional anaesthesia is used in 95% of deliveries, with spinal and combined spinal and epidural anaesthesia being the most commonly used regional techniques in scheduled caesarean section. Regional anaesthesia during caesarean section is different from the analgesia (pain relief) used in labor and vaginal delivery. The pain that is experienced because of surgery is greater than that of labor and therefore requires a more intense nerve block.

Antibiotic prophylaxis is used before an incision. The uterus is incised, and this incision is extended with blunt pressure along a cephalad-caudad axis. The infant is delivered, and the placenta is then removed. The surgeon then makes a decision about uterine exteriorization. Single-layer uterine closure is used when the mother does not want a future pregnancy. When subcutaneous tissue is 2 cm thick or more, surgical suture is used. Discouraged practices include manual cervical dilation, any subcutaneous drain, or supplemental oxygen therapy with intent to prevent infection [8].

Caesarean section can be performed with single or double layer suturing of the uterine incision. Single layer closure compared with double layer closure has been observed to result in reduced blood loss during the surgery. It is uncertain whether this is the direct effect of the suturing technique or if other factors such as the type and site of abdominal incision contribute to reduced blood loss.[66] Standard procedure includes the closure of the peritoneum. Research questions whether this is needed, with some studies indicating peritoneal closure is associated with longer operative time and hospital stay. The Misgave Ladach method is a surgery technical that may have fewer secondary complications and faster healing, due to the insertion into the muscle [9].

General anesthesia may be necessary because of specific risks to mother or child. Patients with heavy, uncontrolled bleeding may not tolerate the hemodynamic effects of regional anesthesia. General anesthesia is also preferred in very urgent cases, such as severe fetal distress, when there is no time to perform a regional anesthesia.

It is common for women who undergo caesarean section to have reduced or absent bowel movements for hours to days. During this time, women may experience abdominal cramps, nausea and vomiting. This usually resolves without treatment. Poorly controlled pain following non-emergent caesarean section occurs in between 13% to 78% of women. Abdominal, wound and back pain can continue for months after a caesarean section. Non-steroidal anti-inflammatory drugs can be helpful. For the first couple of weeks after a cesarean, women should avoid lifting anything heavier than their baby. To minimize pain during breastfeeding, women should experiment with different breastfeeding holds including the football hold and side-lying hold.[80] Women who have had a caesarean are more likely to experience pain that interferes with their usual activities than women who have vaginal births, although by six months there is generally no longer a difference. Pain during sexual intercourse is less likely than after vaginal birth; by six months there is no difference [10].

There may be a somewhat higher incidence of postnatal depression in the first weeks after childbirth for women who have caesarean sections, but this difference does not persist [28]. Some women who have had caesarean sections, especially emergency caesareans, experience post-traumatic stress disorder.

Pain is an unpleasant, subjective feeling registered in the post central gyrus of the cerebral cortex as a response to tissue damage in the organism or functional changes in some part of CNS. Also pain is one of the most common subjective symptoms and the patient’s statement is only proof to the doctor that the patient is experiencing pain [11].

Postoperative pain, which leads to severe patient discomfort, is common problem in anaesthesia practice and can be associated with increased respiratory complications and length of the hospital stay. Therefore, anaesthetic strategies which reduce the postoperative pain, if used routinely could

enhance overall patient cure [12]. Surprisingly, there is little published data about how much pain to expect after common operations. Management of post-operative pain is complicated and challenging because of large variations in the pain experience and analgesic requirements. Non-steroidal anti-inflammatory drugs (NSAID) are widely used although clinical response is variable [13].

Postoperative pain relief reduces the incidence of chest infection, deep vein thrombosis, stress response and sympathetic activity. Inspite of growing advances in the pharmacological approach of pain relief during surgery, relief of pain in the postoperative period continues to remain a challenge. Adverse effects of postoperative pain are many but they can be minimized by pain therapy. Patients with significant postoperative pain may show insomnia, restlessness, anxiety and helplessness. Further this will cause respiratory, cardiovascular, gastrointestinal, urinary and metabolic complications [14]. Hence based on above findings the present study was planned for Comparative Assessment of Analgesic Efficacy of Intravenous Paracetamol and Intravenous Tramadol in Cases of Cesarean Section.

Methodology

The present study was planned in Department of Anesthesia, Patna Medical College and Hospital, Patna, Bihar. The study was conducted from October 2016 to January 2017. The 40 cases of the cesarean delivery under spinal anesthesia were included in the present study. The 40 cases were divided equally in two study groups. Group I includes the 20 cases administered with the IV Paracetamol 1000 mg in 100 ml of normal saline over 15 minutes. The Group II includes the 20 cases IV Tramadol 50 mg.

On arrival of patients to the operation theatre, intravenous line was initiated with 18G cannula. Preoperative recording of Heart Rate (HR), non-invasive blood pressure (SBP, DBP, MAP) and arterial oxygen saturation (SpO2) was carried out. All patients were premedicated with inj. Metoclopromide 10 mg and inj. Fentanyl (2 µg/kg) intravenously. All the patients were preoxygenated with 100% oxygen for 3 minutes. Induction of anaesthesia was carried out with inj. Propofol 2 mg/kg intravenously. Endotracheal intubation was facilitated with a paralyzing dose of inj Atracurium 0.5 mg/kg intravenously. Anaesthesia was maintained with oxygen-40%, nitrous oxide- 60% delivered through Bain's circuit using IPPV and a continuous infusion of inj Propofol (150 mcg/kg/min).

Here pain is described in terms of numbers. VAS is a visual scale that allows the patient in pain to visually select a point on a 10cm scale. The point selected would correspond to their personal experience of pain. This scale has two anchoring points in the 10cm scales: at the left side 0 represent "no pain" and at the right side 10 represent worst pain.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.

Following was the inclusion and exclusion criteria for the present study.

Inclusion Criteria: Parturient who were undergoing cesarean delivery under spinal anesthesia.

Exclusion Criteria: Patients with known contraindication/allergic to Paracetamol or Tramadol. Pregnancy with medical disorders (hepatic, renal, diabetes, cardiovascular and pulmonary disease) preeclampsia/ eclampsia cases and chorioamnionitis. Women taking monoamine oxidase inhibitors and those who received any analgesics till four hours before surgery

Results & Discussion

Although pain is a predictable component of the postoperative experience, inadequate management of pain is very common. Inadequately treated post-operative pain may result in altered physiological and psychological changes that increase morbidity and mortality in patients. In our randomized study, we tried to demonstrate the comparative analgesic efficacy and safety profile of paracetamol vis-à-vis the commonly used drug tramadol, both administered intravenously. Most of the opioid agonists are suitable to treat acute pain. However their use is not always without side effects commonly nausea, vomiting, pruritis, excessive sedation and respiratory depression that limit their generous use in treating patients with acute post-operative pain. Also, opioid agonists are limited by their availability in recent days.

Paracetamol is the most commonly prescribed analgesic for the treatment of acute pain. Its major advantages over NSAIDs are its lack of interference with platelet function and safe administration in patients with a history of peptic ulcers or asthma [15]. The main mechanism of action of Paracetamol is considered to be the inhibition of cyclooxygenase (COX) and recent findings suggest that it is highly selective for COX-2. Paracetamol is metabolised primarily in the liver into non-toxic products.

Researches have shown that besides its effective analgesic properties, paracetamol administered during perioperative period supports effective and speedy recovery in patients undergoing laparoscopic cholecystectomy [16, 17].

Tramadol is a synthetic opioid which belongs to aminocylohexanol group, is an analgesic with central effect and weak opioid agonistic properties. Tramadol possesses weak agonist actions at the µ-opioid receptor with additional monoaminergic activity. This drug is also effective on noradrenergic and serotonergic neurotransmission. However, tramadol has shown to be failing in ensuring optimal analgesia in moderate to severe pain [18].

Table 1: Basic Details

Parameters	Group I	Group II
Administration of	**Paracetamol 1000 mg**	**Tramadol 50 mg**
No. of Cases	**20**	**20**
Age	21 – 26 years	19 – 28 years
Null Parity	9	10
Multi Parity	11	10
Elective Cesarean	6	5
Emergency Cesarean	14	15
Duration of Surgery	35 – 60 mins	38 – 63 mins

Table 2: Pain Assessment by VAS Scoring

Parameters	Group I	Group II
Administration of	**Paracetamol 1000 mg**	**Tramadol 50 mg**
No. of Cases	**20**	**20**
VAS after		
30 mins	2.5 ± 0.05	4.4 ± 0.04
1 hr	4.1 ± 0.02	6.5 ± 0.04
2 hrs	5.3 ± 0.04	6.6 ± 0.05
4 hrs	5.1 ± 0.04	6.9 ± 0.04
6 hrs	6.1 ± 0.03	7.5 ± 0.03
8 hrs	6.2 ± 0.04	7.8 ± 0.03
12 hrs	6.4 ± 0.04	8.2 ± 0.04
24 hrs	7.5 ± 0.04	8.5 ± 0.03

The intravenous route is especially advantageous in postsurgical situations when oral (e.g. infections with severe fever or vomiting or post-operative period where nil- per-oral is maintained) or rectal (e.g. high variability in uptake and bioavailability) routes are not suitable or effective. Has been found to be a useful antipyretic and moderately potent analgesic across various conditions, patient populations and circumstances. The remarkable tolerability and lack of serious side effects at clinical doses explain its popularity. However variable bioavailability of oral formulations and inability to use it in „nil per oral" patients limited its use in perioperative conditions. With the introduction of a stable intravenous (IV) formulation of Paracetamol, it is now possible to use its analgesic effect in perioperative patients. The study was designed to evaluate the analgesic effect of infusion Paracetamol for post-operative analgesia. It was compared with the commonly used drug IV Tramadol.

A study conducted by Bhandari *et al*. in 2015 concluded that time to first rescue analgesia was significantly longer in children receiving rectal acetaminophen (8.96 ± 3.46 h) compared with those receiving IV acetaminophen (6.00 ± 1.63 h) [19].

Capici *et al*. in 2008 conducted a randomized controlled trial for comparing the duration of analgesia following IV versus rectal acetaminophen after adenotonsillectomy in children concluded that rectal acetaminophen provides longer analgesia as compared to IV route [20].

A similar study by Moller *et al*. in 2005 compared IV with oral route of paracetamol showed that oral paracetamol is similar to IV for postoperative analgesia after the third molar extraction in adults. This is due to the fact that plasma concentrations became very similar following both oral and IV from 1 to 24 h postadministration. [21].

A prospective, randomized double blinded study conducted by Uysal HY, Takmaz SA, Yaman F, Baltaci B, Basar H. among 64 patients between age group of 6-16 years done to compare the efficacy IV Paracetamol and IV Tramadol for postoperative analgesia showed that IV Paracetamol and IV Tramadol are associated with similar analgesic properties and early recovery with IV Paracetamol to that of IV Tramadol after adenotonsillectomy in children [22].

In a single centre, Ioltercattabriga, Davidepacini conducted placebo controlled, double blind, randomized trial done on 113 patients to study the efficacy of IV Paracetamol as a adjunctive analgesic to a Tramadol based background analgesia after cardiac surgery, it showed that in patients undergoing cardiac surgery IV Paracetamol in combination with Tramadol provides effective pain control. [23].

Wei-wu Pang, Shyuan Huang, Chien- Chiung Tung, Min-Ho Huang, conducted a study on 50 patients who had undergone major orthopedic surgeries were enrolled in to a prospective, randomized, and double blinded study under General Anaesthesia. At the beginning of wound closure, an equal volume dose of either Tramadol 2.5 mg/Kg or Tramadol 1.25 mg/Kg + Lysine acetyl salicylate 12.5 mg/Kg mixture was administered slowly intravenous, and it was concluded that aspirin can be used as an effective and safe adjuvant to Tramadol after Orthopedic surgeries and the adverse effects associated with Tramadol such as nausea and vomiting were reduced [24].

A Placebo controlled, double blinded, randomized trial was conducted on 113 patients by IolterCattabriga, DavidePacini, Gaia Lamazza, Francesco Talarico, Roberto Di Bartolomeo, Giovanni Grillone, 56 were given Intravenous study drug (1g) 15 minutes before the end of the surgery and postoperative pain was evaluated by visual analog scale and it was measured at rest and during deep breath. 2-5 mg of intravenous Morphine was used as a rescue drug. At 12, 18, 24hrs patients who received Paracetamol had less pain at rest. Paracetamol group required less cumulative Morphine than placebo group [25].

This study conducted by Cliff Ong KS, Philip Lirk, Juliana Tan MH in the year 2005 for 72 patients, undergoing elective third molar surgery, divided in two groups, i.e. oral group & intravenous group. The intravenous group received an oral Placebo capsule followed by intravenous Tramadol 50 mg pre operatively. In both the groups, a standard intravenous sedation technique was administered and the impacted third molar was removed under local anesthesia. In this study they compared duration of analgesia, pain intensity, and time to rescue analgesic. They concluded that preoperative intravenous Tramadol is superior to oral Tramadol for preventing postoperative pain following third molar surgery [26].

Increasing rates of caesarean sections are a continuing concern for the obstetric and public health communites. Fears of maternal and neonatal morbidity from vaginal delivery (VD) may be encouraging this trend [27]. Nonsteroidal anti-inflammatory drugs, ketamine, acetaminophen, and local anesthetics have all been reported to reduce postoperative opioid consumption [28, 29]. Pain management can take many forms. Although systemic opioid analgesics and patientcontrolled analgesia remain at the forefront of pain management. This class of medications is associated with multiple common adverse reactions [30]. Due to complications of opioids, particular attention has been paid to other strategies, and the physicians use these drugs as useful analgesics in controlling different types of pain. [31-322 All opioids could cause common side effects that include depression of respiratory center in the

brainstem, hypotension and vomiting. Morphine often causes histamine release and may cause flashing, tachycardia, hypotension, itch, and bronchospasm. Long-term administration of opioids slows gastrointestinal transit and causes ileus and constipation in many patients [33].

Conclusion

The data generated from the present study concludes that intravenous paracetamol with better analgesic efficacy; shorter duration of labour and fewer maternal side-effects is a better labour analgesic than tramadol. Also complicated rules and restrictions on the use of opioids and the high rate of side effects related to opioids, prescribing paracetamol in the form of intravenous infusion could be recommended as a good alternative for relieving opioid after the operation.

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