Original Research Article

Study of intravenous paracetamol and intravenous tramadol for post operative analgesia in infra umbilical surgery

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Abstract

Background: Relief of postoperative pain is a major concern for patients and anaesthesiologists. Postoperative analgesia has traditionally been provided by opioid analgesics. However, recent trend is to use opioid free analgesia since opioids exhibit a variety of side effects like respiratory depression, nausea, vomiting, urinary retention. Nonsteroidal anti inflammatory drugs (NSAIDs) like ibuprofane, diclofenac also are used but they have damaging effect on kidneys. With the introduction of intravenous Acetaminophen (Paracetamol) a quest for analgesic which is truly devoid of side effects has come to reality. In a dose of 1 gm, its damaging effects on kidney are negligible. In the present study we wish to assess and compare analgesic efficacy and safety of a mild opioid Tramadol with Paracetamol for postoperative analgesia. **Aim and Objectives:** To evaluate and compare the efficacy and safety of a single dose of intravenous Paracetamol and intravenous Tramadol for post operative analgesia in infra umbilical surgery. **Material and Method:** This study was done in a tertiary care hospital during the period August 2017 to March 2018. ASA-I or II patients from both the sexes, age group between 18-60 years, scheduled for infra umbilical surgery under spinal anaesthesia were randomly divided in two groups of 36 each. The patients receiving IV infusion of Paracetamol 15 mg/kg (maximum 1g in 100 ml infusion) were included in Group A while patients receiving IV infusion of Tramadol 2 mg/kg (maximum150 mg in 100 ml NS infusion) were included in Group B for the study purpose. The infusions were given over 15 minutes, 20 minutes prior to the end of surgery. Parameters recorded were Visual Analogue Scale (VAS), Sedation score, Pulse rate, Mean arterial pressure, Spo2, duration of analgesia and complications like nausea and vomiting, hypotension, bradycardia and respiratory depression. **Observation and Results:** Data so collected was statistically analysed. Paracetamol and Tramadol both produced statistically significant reduction in mean VAS scores in early postoperative period. In intergroup comparison, Paracetamol showed significantly lower VAS scores as compared to tramadol at 4 hour and 6 hour follow-up intervals during postoperative period. Subjects from tramadol group were more sedated compared to the paracetamol group. Complications like nausea and vomiting were more evident in tramadol group than paracetamol group. **Conclusion:** Though both the study drugs produce adequate postoperative analgesia, Paracetamol is safer and more effective analgesic than Tramadol when given intravenously in patient undergoing infra umbilical surgeries.

Key Words: Paracetamol, Postoperative pain, Tramadol, VAS score.

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Pain is an inevitable component of any surgical procedure, and postsurgical pain is often treated inadequately. Pain and suffering in the postoperative period, has multiple physiological and psychological consequences (e.g. splinting of diaphragm, impaired gastrointestinal motility, impaired wound healing and anxiety) which may adversely affect perioperative outcome and contribute to increased length of stay. For decades now, opioids and NSAIDs have been used which can produce undesirable effects like postoperative nausea and vomiting (PONV), respiratory depression, sedation,

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gastrointestinal bleeding and renal injury. With the advent of intravenous (IV) paracetamol interest is now being shown as to its efficacy in mitigating pain especially against the backdrop of commonly used analgesics. Paracetamol is an analgesic and antipyretic agent, recommended worldwide as a first-line agent for the treatment of mild to moderate pain and fever in adults and children. Paracetamol is not an NSAID and interferes neither with platelet nor kidney function. *Paracetamol* is a metabolite of phenacetin with similar analgesic and antipyretic effects. It affords a central analgesic action secondary to a raised pain threshold and can be administered orally, rectally, intramuscularly and IV. Excretion occurs following conjugation in the liver. Action tends to peak by 1 h and lasts till 4–6 h. Hepatic toxicity can occur only if therapeutic doses are exceeded. (for patients weighing 50 kg or more, the total daily dose of paracetamol should not exceed 4 g). Paracetamol, a centrally acting inhibitor of cyclooxygenases, has weak peripheral effects. Adverse reaction emerging from the use of IV formulation of paracetamol are extremely rare (<1/10,000). Tramadol, a synthetic opioid of the aminocyclohexanol group, is a centrally acting analgesic with weak opioid agonist properties, and effects on noradrenergic and serotonergic neurotransmission. In the present study, we have compared paracetamol and tramadol given intravenously, for their efficacy safety as postoperative analgesics in the patients undergoing infra umbilical surgeries under spinal anaesthesia.

MATERIAL AND METHODS

After getting approval of institutional ethical committee and written informed consent from all study participants, the study was undertaken in a tertiary care hospital during the period August 2017 to March 2018. Total 72 patients from both the sexes aged between 18-60 years of ASA grade I and II scheduled for elective infra umbilical surgery under spinal anaesthesia were included in the study. The patients were randomly divided into two equal groups by sealed envelope method. The infusion bottles were prepared and handed over to a blinded observer in a covered manner masking the contents of the bottle. The patients of ASA grade III/IV, patients undergoing laparoscopic surgeries, surgeries on upper abdomen, chest, limb, supramajor surgeries of duration more than 3 hours, surgeries under general anesthesia, epidural anesthesia or blocks were excluded from the study. Patients with renal, hepatic, cardiac, major respiratory disease, those receiving anti diabetic, anti hypertensive medications, anticoagulants were excluded from the study. Pregnant patients, those with body mass index greater than 35 kg/m2 were also excluded from the study.

Group A: IV Paracetamol 15 mg/kg (maximum 1 g in 100 ml infusion) over 15 minutes, 20 minutes prior to the end of surgery.

Group B: IV Tramadol 2 mg/kg (maximum150 mg in 100 ml NS infusion) over 15 minutes, 20 minutes prior to the end of surgery. In the preanaesthesia room baseline parameters to be studied were noted. All the patients received premedications and spinal anaesthesia as per standard protocol of the institution. Intraoperative monitoring was done as per standard protocols. 20 minutes prior to the end of surgery, the study drugs were given. All **t**he patients were observed in post anaesthesia recovery room and later in high dependency ward as per institutional protocol. To assess effects of study drugs on postoperative analgesia in patients undergoing infra-umbilical surgeries, the 10cm standard Visual Analogue Scale (VAS) was used; where '0' indicated 'no pain' and '10' indicated 'worst imaginable pain'. VAS scores were assessed at an interval of 0, 1, 2, 4 and 6 hours in the postoperative period and rescue analgesic inj. Diclofenac sodium 75 mg IM was given when VAS was more than 3. Heart rate, Mean arterial pressure, respiratory rate and adverse effects like nausea, vomiting, sedation were noted. Sedation was assessed by using the University of Michigan Sedation Scale, where 0= awake and alert, 1= minimally sedated, 2= moderately sedated, 3= deeply sedated, 4= unarousable.

Statistical Analysis: Minimum sample size was calculated by statistical formula $n=\frac{2(Z_\alpha+Z_\beta)^2 \cdot \sigma^2}{\delta^2} = 35$ taking α as 5% and power of study as 80%. The data was collected and compiled in excel sheet. Continuous variables were presented as mean +SD; Ordinal and Nominal data were presented as number or percentage of incidents. Comparison between the groups was made using student's t test for quantitative data and chi-square test for qualitative data. Hemodynamic parameters were analyzed using one-way ANOVA to find statistical difference within and between the groups. P value <0.05 was considered statistically significant. Statistical analysis was done using SPSS version 22.0.

OBSERVATIONS AND RESULTS

Table 1: Demographic data

Variables	Group-A N-36	Group-B N-36	P value	Significance
Age (year)	45.4±8.3	48.2 ±6.4	0.1137	Not significant
Weight (kg)	57.5±4.8	56.38±4.6	0.3156	Not significant
ASA I/II	28/8	24/12	0.1012	Not significant
Sex (Male/Female)	26/10	22/14	0.1679	Not significant
Duration of surgery (min)	71.32±9.2	68.63±6.52	0.1573	Not significant

Demographic data was comparable with respect to age, weight, ASA physical status, gender status and duration of surgery in both the groups.

Table 2: Comparison of mean VAS scores between two groups at different time intervals

Sr. No	Duration	Group-A Mean±SD	Group-B Mean±SD	P Value	Significance
1	0 hr	1.12±0.32	1.03±0.43	0.3175	Not significant
2	1 hr	1.18±0.43	1.3±0.56	0.3116	Not significant
3	2 hr	1.68±0.54	1.93±0.62	0.07242	Not significant
4	4 hr	2.6±0.57	3.12±0.54	0.00016	Significant
5	6 hr	2.83±0.88	3.36±0.65	0.005	Significant

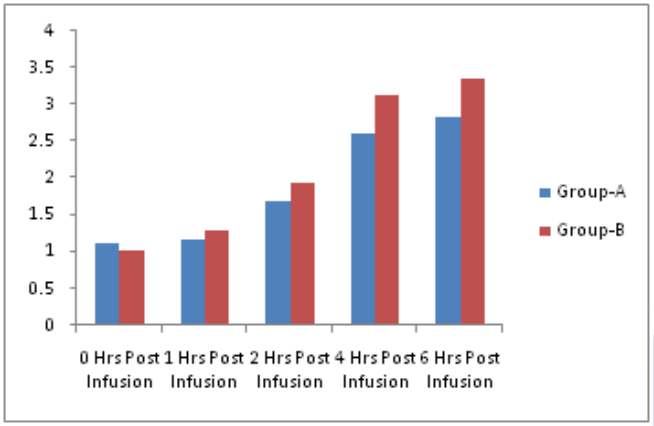

Figure 1: Comparison of mean VAS scores between two groups at different time intervals

There was statistically significant reduction in mean VAS scores (<2) in both the groups in the early postoperative period. From 0 hour (at the end of surgery), till 2 hours postop, there was no significant difference in mean VAS scores between the two groups. However, at 4 hours and 6 hours postop, mean VAS score in Group-A (2.6±0.57and 2.83±0.88 respectively) was significantly lower as compared to that in Group-B (3.12±0.54 and 3.36±0.65 respectively). Only one patient from group B had VAS score > 3, needing a rescue analgesic Inj. Diclofenac sodium 75 mg I.M. to alleviate the pain.

Table 3: Comparison of mean Sedation scores between two groups at different time intervals

Time	Group-A Mean ± SD	Group-B Mean ± SD	P Value	Significance
0 Hrs Post Infusion	0.62 ± 0.53	0.70 ± 0.59	0.547	Not significant
1 Hrs Post Infusion	0.46 ± 0.60	1.16 ± 0.60	<0.0001	Significant
2 Hrs Post Infusion	0.18 ± 0.38	1.07 ± 0.60	<0.0001	Significant
4Hrs Post Infusion	0.12 ± 0.27	0.92 ± 0.60	<0.0001	Significant
6Hrs Post Infusion	0.08 ± 0.44	0.40 ± 0.50	<0.0001	Significant

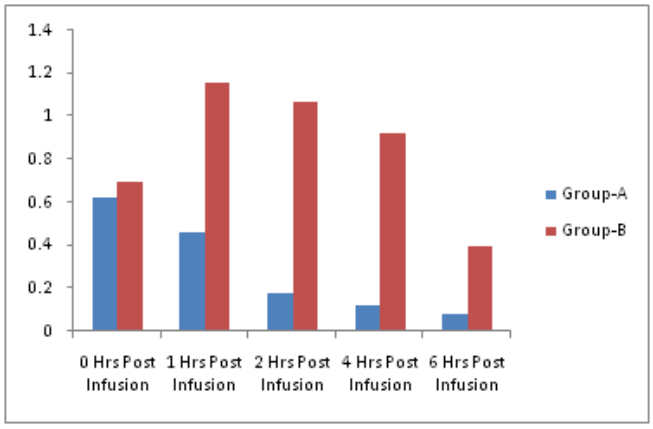

Figure 2: Comparison of mean sedation scores between two groups at different time intervals

At 1 hour, 2 hour, 4 hour and 6 hour, mean sedation scores in Group-A (0.46±0.60, 0.18±0.38, 0.12±0.27 and 0.08±0.44 respectively) was significantly lower as compared to that in Group-B (1.16±0.60, 1.07±0.60, 0.92±0.60 and 0.40±0.50 respectively).

Table 4: Comparison of adverse effects between two groups

Sr. No.	Parameter	Group-A (N-36)	Group-B (N-36)	P – value	Significance
1	Nausea and Vomiting	3	12	0.001	significant
2	Bradycardia	0	0	-	-
3	Hypotension	0	0	-	-
4	Respiratory depression	0	0	-	-

More number of patients from group B developed nausea and vomiting and the intergroup difference was statistically highly significant. There was no statistically significant variation noted in mean heart rates, mean blood pressures (mmHg), and mean respiratory rates at various postoperative time intervals till 6 hrs in both the study groups. In intergroup comparison, the difference between mean heart rates, mean blood pressures(mmHg), and mean respiratory rates was also statistically not significant. (p>0.05).

DISCUSSION

Post operative pain management is one of the most important and often inadequately managed aspect leading to morbidity and poor postoperative outcome. In a quest to find out an ideal non opioid analgesic for postoperative pain relief, we compared the analgesic efficacy and safety of Paracetamol with a commonly used mild opioid derivative Tramadol, both administered intravenously. Acetaminophen (paracetamol) a cyclooxygenase inhibitor, is a widely prescribed analgesic devoid of clinically significant antiinflammatory effects. It can be

administered orally, rectally, intramuscularly and as intravenous infusion. Peak action is seen at 1 hr and lasts 4-6 hours. Intravenous administration of pacetamol avoids variabilities associated with gastric absorption and first-pass hepatic metabolism, resulting in higher plasma concentrations and greater analgesic efficacy than orally administered drug. Sinatra *et al*[1] found that the efficacy of IV paracetamol in orthopaedic surgeries to be superior to tramadol in terms of rapid onset of analgesia and significant reduction in morphine consumption over the 24 hour postoperative period and safety in terms of clinical and laboratory parameters. Intravenous acetaminophen was well tolerated in the elderly and high-risk (American Society of Anaesthesiologists physical status II and III) population. However, monotherapy with nonopioid analgesics would not be expected to eliminate opioid dosing in patients recovering from major orthopedic surgery. Opioid sparing would be expected to provide clinical advantages in patients who are sensitive to opioid-induced sedation, confusion, respiratory depression, and gastrointestinal complications. Optimal analgesia for moderate to severe post-operative pain cannot be achieved using a single agent alone, but a balanced approach in combination with non-steroidal agents can result in upto 40 to 50 percent reduction in opioid requirements. Paracetamol with its safety profile can prove to be an asset in managing perioperative pain, especially of mild to moderate severity. NSAIDs inhibit platelet function, increase perioperative bleeding, and have been shown to have nephrotoxic effects in patients with and without preexisting renal insufficiency. Selective COX-2 inhibitors have been associated with salt and water retention and hypertension, and inhibit bone remodeling in animal models. This latter observation has raised concerns of impaired healing and nonunion after various forms of orthopedic surgery.[2] Paracetamol offers a historically low incidence of adverse effects and untoward drug interactions. However, higher-than-recommended doses have been associated with hepatotoxicity and hepatic failure.[3] 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.[4] Tramadol, a centrally acting synthetic agonist at μ opioid receptor, acts by modifying the transmission of pain impulses via inhibition of noradrenaline and serotonin uptake. The relative lack of respiratory depression, major organ toxicity or abuse potential affords credence to use of the drug. Furthermore, tramadol does not cause the appearance of tolerance, so it is therefore unnecessary to increase the dosage to maintain the analgesic effect over time.[5] In terms of onset, depth, duration of analgesia, incidence of adverse reactions like PONV and sedation, the efficacy and safety of IV Paracetamol was found to be superior to IV Tramadol When Paracetamol and Tramadol were compared by various researchers,[5,6,7] they concluded that, IV Paracetamol can serve as a sole analgesic in moderate to severe post-operative pain scenarios. Our study results are similar to previous studies done by various researchers. Uysal *et al*[6] concluded that compared with IV Tramadol, IV Paracetamol provided adequate analgesia, less sedation and earlier readiness for recovery room discharge among paediatric patients undergoing tonsillectomy. One major concern regarding the use of tramadol which is a synthetic opioid analogue is respiratory depression. But its safety and respiratory depressant activity is less when compared to other strong opioids. However, Paracetamol does not affect respiration. In a study done by Hoogewij *et al*,[7] patients had considerably higher PaCO2 in the tramadol group (48±6 mmHg) compared to the paracetamol group (42.2±3.4mmHg). Dejonckheere *et al*[8] compared IV tramadol to propacetamol for postoperative analgesia following thyroidectomy. They found more patients complained of nausea and vomiting (P = 0.01) in the tramadol group during first 2 h of the study. According to them, Paracetamol is a viable alternative to opioids and nonsteroidal anti-inflammatory agents, because of its less adverse effects. Gynecological operation involving lower abdominal surgery is always associated with more incidence of nausea and vomiting and use of intravenous Tramadol aggravates the incidence of postoperative nausea and vomiting. Similarly, post-cesarean pain is typically treated with opioids or non-steroidal anti-inflammatory drugs (NSAIDs), however, opioids carry the risk of respiratory depression and sedation and NSAIDs are not desirable in lactating mothers. In contrast, intravenous paracetamol is a non-opioid analgesic that is devoid of these adverse effects. J. Alhashemi *et al*[9] in their study concluded that IV paracetamol is an effective alternative to oral ibuprofen for post-cesarean section analgesia. Pendeville PE *et al*.[10] compared the post-operative analgesia between tramadol versus paracetamol in children who had undergone tonsillectomy. Surprisingly, they found that, the side effects of nausea and vomiting were comparable between the two groups, pain relief was higher and need for rescue medication was less in the Tramadol group. Hemodynamic parameters, blood pressure levels and heart rate, were observed after the administration of our study drugs at regular intervals postoperatively. Initial high scores as a result of post-surgical stress response and rise in blood pressure and heart rate after 6 and 8 hour

intervals could be attributed to return of pain as the plasma concentration of the drugs decline with time. Both drugs have been observed to show a similar pattern of rise and fall and no significant clinical impact on hemodynamics has been reported as demonstrated by previously done studies.

CONCLUSION

Paracetamol and Tramadol both produce adequate postoperative analgesia. However, intravenous paracetamol is a safer and more effective analgesic than intravenous Tramadol for the treatment of postoperative pain in patients undergoing infra umbilical surgeries.

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