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PRE-EMPTIVE ANALGESIA USING INTRAVENOUS PARACETAMOL IN PATIENTS UNDERGOING CAESAREAN SECTION UNDER SUBARACHNOID BLOCK: A RANDOMIZED CONTROL STUDY

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ABSTRACT **Objectives:** Cesarean section is one of the most common surgical procedure in women and is becoming more frequent. High quality postoperative analgesia is important for mother's recovery and for her to take care of new born baby. This study evaluated analgesic effect of one gram paracetamol given pre-emptively ,on postoperative pain scores and analgesic consumption during 24 hours after caesarean section. **Material And Methods:** A total of 80 pregnant women between age 18-39 years, height 155-165 cm and with ASA II grade, undergoing elective caesarian section under subarachnoid block were randomly enrolled. Patients were either given 1 gram IV paracetamol (study group,n=40) or 100ml normal saline (control group, n=40), 20 mins before the incision. **Results:** There was no significant difference between two groups regarding age, weight and height. Time of request for first analgesia was statistically higher in paracetamol/study group (P value of <0.001). Total number of requests for analgesic was statistically lower in paracetamol/study group (P value of < 0.001). VAS scores at 0 hours, 4 hours, 8 hours, 12 hours and 24 hours after shifting the patient to postoperative care unit were compared between study and control group, the difference in VAS scores at 8, 12 and 24 hours were statistically lower in paracetamol/study group. **Conclusion:** Preemptive administration with one gram intravenous paracetamol prolongs the time of request for first analgesia, reduces pain scores 24 hours postoperatively and also reduces total number of requests of analgesic in postoperative period in patients undergoing caesarean section under subarachnoid block.

KEYWORDS : Pre-emptive analgesia, Pain, caesarean section, Paracetamol

INTRODUCTION :

Cesarean section is one of the most common surgical procedure in women and is becoming more frequent. (1) (2). High quality postoperative analgesia is important as mother has to recover from major intra-abdominal surgery and also has to take care for her new born baby(3) Patients undergoing cesarean section may experience significant post-operative pain(4)which may impair mother's ability to feed her child, delay the development of mother-infant bonding (5) and delay ambulation & discharge. Significant pain in immediate post-operative period can contribute to post-partum depression and chronic pain , thus severely affecting the quality of life of the mother(5) (6) Preemptive analgesia is aimed to inhibit pain due to surgical incision and also pain due to re-initiation of CNS sensitization by surgical injury after block of nociceptive afferents diminishes (7) (8) (9).

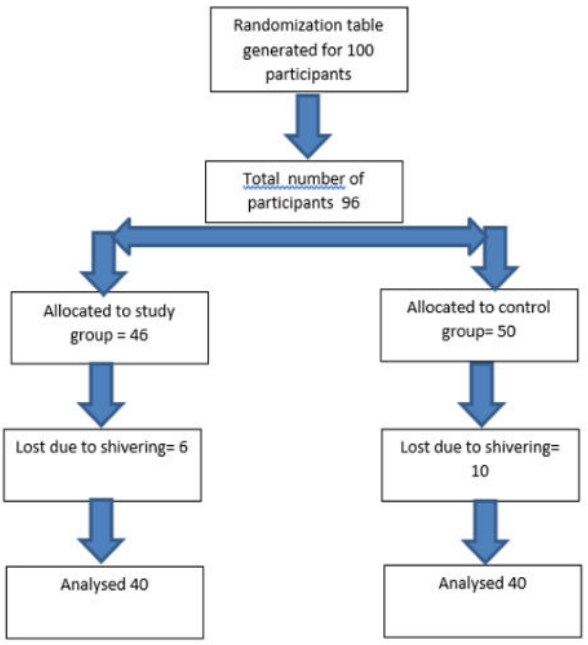
Commonly used post-operative analgesics following cesarean section are opioids, NSAIDS and paracetamol. (10) *Paracetamol* has high safety profile in recommended during labor,(2) and is also not contraindicated in peptic ulcer diseases, hemostatic disorders or pulmonary dysfunction. Since, pain relief is important in post cesarean delivery, we used paracetamol, a drug with safer profile for both mother and baby, (11) as preemptive analgesic in patients undergoing elective cesarean section under subarachnoid block .

The preemptive effect of intravenous paracetamol has been studied in various surgical procedures but , there are not many studies on the use of intravenous paracetamol as preemptive analgesic for patients undergoing cesarean section under subarachnoid block. Hence, present study was conducted to analyze the preemptive effect of IV paracetamol on post cesarean patients.

SUBJECTS AND METHODS

This randomized control study was conducted after obtaining approval from research and ethical committees .This study included 80 American Society of Anesthesiologist grade II pregnant women between age 18-39 years, height 155-165 cm ,undergoing elective caesarian section under subarachnoid block. Exclusion criteria was patient's refusal for study, any associated comorbidity. known allergy to Paracetamol and patients who received tramadol for perioperative or postoperative shivering.

Computer generated randomization was done for 100 patients and were allocated in study group or control group accordingly. Patients inclusion in respective group was continued until each group had total 40 participants. In total,96 patients participated in this study, out of which total 16 patients (6 in study group and 10 in control group) were excluded as they had received intravenous tramadol for perioperative/ postoperative shivering. 80 patients completed the study (n = 40 in each group).



All patients underwent elective cesarean section under subarachnoid block. Pre- anesthetic evaluation was done for all the patients and patients were fasted as per standard protocol. On the day of surgery after securing intravenous access, patients were premedicated with Inj. Emeset(Ondansetron) 4mg IV and Inj. Rantac(Ranitidine) 50mg iv, as per departmental protocol . Each patient was pre-loaded with 500ml of Ringer lactate solution. Patients in study group received 1 gram IV paracetamol 20 minutes before incision. Patients in control group received placebo (100ml normal saline) 20 mins before the incision. All routine standard monitors were attactched on taking patient to operating room and baseline vitals(HR,NIBP,SPO2,RR) were noted 5 minutes before the spinal anesthesia . With patient in sitting position and taking all aseptic precautions , lumbar puncture was performed at L3-L4 or L4-L5 interspaces using 26 gauze Quincke's type spinal needle. Subarachnoid block was given using 2.2ml of 0.5% bupivacaine (heavy) to all patients in study and control group . Vitals

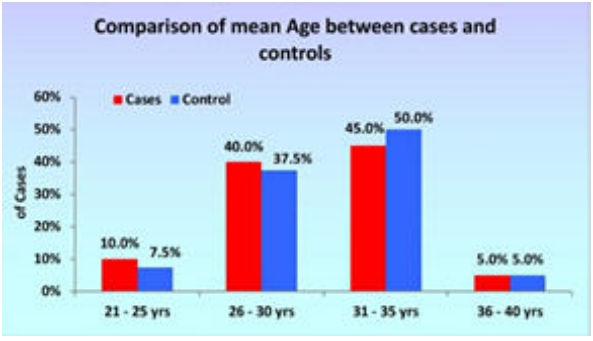
parameters (Heart rate, Blood pressure, Mean arterial pressure, respiratory rate) were noted at 3mins after spinal anesthesia and at interval of 5 minutes thereafter throughout the procedure. Patients having perioperative or post-operative shivering were given injection Tramadol 50mg IV slowly and these patients were excluded from the study. Time of first request for analgesic was noted and patient was given injection Diclofenac 75mg IV as rescue analgesic. Total number of analgesic requests in post operative period was compared in paracetamol group and control group. In the post anesthesia care unit and during 24 hours post operatively, the pain score was noted using Visual analogue scale (VAS 0 to 10) at 1 hour , 4 hours, 8 hours, 12 hours and 24 hours postoperatively.VAS score is simple verbal scale to assess pain in range where 0 signifies no pain through 10 which signifies excruciating pain.

Statistical Analysis:

Statistical testing was conducted with the statistical package for the social science system version SPSS 17.0. Continuous variables were presented as meanSD or median if the data is unevenly distributed. Categorical variables were expressed as frequencies and percentages. The comparison of continuous variables between the groups was performed using Student's t test. Nominal categorical data between the groups was compared using Chi-square test or Fisher's exact test as appropriate. Non-normal distribution continuous variables was compared using Mann Whitney U test. For all statistical tests, a p value less than 0.05 was taken to indicate a significant difference.

RESULTS:

In present study there was no statistical significant difference between two groups with respect to age and height.(Graph 1, table 1)

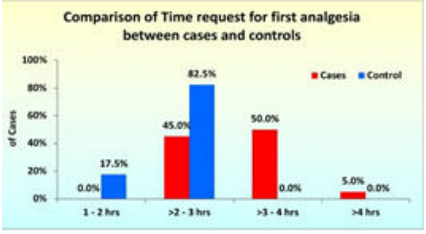


Graph 1

Table 1

	Paracetamol Group	Control group	P-value
AGE	30.35± 3.70	30.78± 2.89	0.569
HEIGHT	160.55±3.5	159.95±3.31	0.433

Time of request for first analgesia was noted and compared between study and control group. Mean time of first request of analgesia after incision by study group was 3.28±0.45 hours compared to 2.30 ± 0.24 hours after incision for control group. T test showed a P value of <0.001 ,indicating that time of request for first analgesia was statistically significant and higher in study group. (GRAPH 2, TABLE 2)



Graph 2

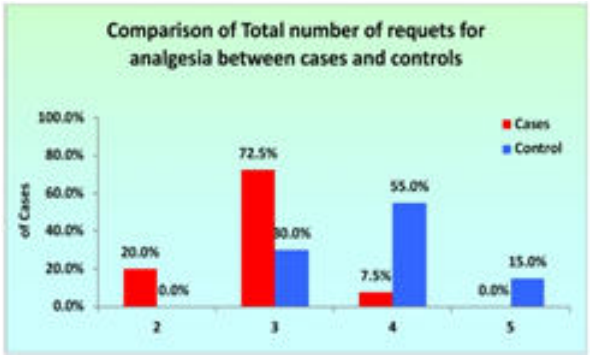
Table 2

Time request for first analgesia	Cases		Control		p value
	Frequency	%	Frequency	%	
1 - 2 hrs	0	0.0%	7	17.5%	<0.001
>2 - 3 hrs	18	45.0%	33	82.5%	
>3 - 4 hrs	20	50.0%	0	0.0%	
>4 hrs	2	5.0%	0	0.0%	
Total	40	100%	40	100%	
Mean ± SD	3.28 ± 0.45		2.30 ± 0.24		<0.001

Total number of requests for analgesic was compared. The mean requirement was 2.88±0.52 times for study group compared to 3.8885±0.66 times for control group. T test showed a P value of < 0.001, indicating that total number of requests for analgesic was statistically significant and higher in control group.(TABLE 3, GRAPH 3, TABLE 4)

Table 3

	Paracetamol group (mean+SD)	Control group (mean +SD)	P-value
Time request for first analgesia	3.28+0.45	2.30+0.24	<0.001
Total number of requests for analgesics	2.88+0.52	3.85+0.66	<0.001



Graph 3

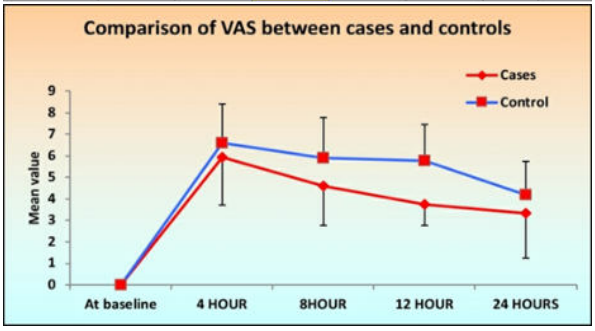
Table 4

Total number of requets for analgesia	Cases		Control		p value
	Frequency	%	Frequency	%	
2	8	20.0%	0	0.0%	<0.001
3	29	72.5%	12	30.0%	
4	3	7.5%	22	55.0%	
5	0	0.0%	6	15.0%	
Total	40	100%	40	100%	
Mean ± SD	2.88 ± 0.52		3.85 ± 0.66		<0.001

VAS scores at 0 hours, 4 hours, 8 hours, 12 hours and 24 hours after shifting the patient to postoperative care unit were compared between study and control group. The average VAS score in study group was 0, 5.92, 4.6, 3.75, 3.32 and in control group was 0, 6.6, 5.9, 5.78, 4.2 at 0, 4, 8,12, 24 hours respectively. T test showed p values of 0, 0.142, 0.002, <0.001, 0.036 respectively for these differences. Hence the difference in VAS scores at 8, 12 and 24 hours were statistically significant. The VAS scores were lower in study group.(GRAPH 4,TABLE 5)

Table 5

VAS	Cases	Control	p value	Mean Difference	SE	95% CI	
	Mean ± SD	Mean ± SD				Lower	Upper
At baseline	0.00 ± 0.00	0.00 ± 0.00	–				
4 HOUR	5.92 ± 2.22	6.6 ± 1.82	0.142	-0.675	0.455	-1.581	0.231
8HOUR	4.6 ± 1.82	5.9 ± 1.89	0.002	-1.3	0.415	-2.127	-0.473
12 HOUR	3.75 ± 0.98	5.78 ± 1.69	<0.001	-2.025	0.412	-2.845	-1.205
24 HOURS	3.32 ± 2.08	4.2 ± 1.56	0.036	-0.875	0.411	-1.694	-0.056



Graph 4

DISCUSSION

Pain relief is important to reduce immediate postoperative discomfort and to avoid long term adverse effects. The strategies to decrease pain in postoperative period has changed considerably overtime with focus now moving to pre-emptive analgesia in which analgesic is given before incision. The major role of pre-emptive analgesia is reducing postoperative pain and post operative requirement of analgesics, thereby reducing their side effects and also to prevent chronic pain due to central sensitization.

Patients undergoing caesarean section done under subarachnoid block experience moderate to severe postoperative pain. Therefore postoperative pain relief is important for mother's well being and her ability to feed, care , bond with the baby and also for her early discharge.

Many drugs and multimodal analgesic regimen have been tried for pre-emptive analgesia .We used intravenous paracetamol in our study. The safety of paracetamol in mother and baby has been clearly established by various studies done over last many years. In a study done by C. Rebordosa et al in 2008, no association was found between congenital abnormalities and paracetamol exposure.(2) Similarly ,in a study done by Baghianimoghadam B et al in 2014, IV paracetamol was concluded to be efficacious for post-operative pain and patients receiving IV paracetamol did not have any considerable neonatal complications. (12)

We used one gram intravenous paracetamol for pre-emptive analgesia as efficacy of this dose is well proven by various studies. (13)(14)(15). We gave IV paracetamol 20mins before incision as it achieves therapeutic plasma concentration within 20 minutes of an initial dose. (16). Similar dose and time of administration of drug has been used in previous studies.(17) (18)(8).

The efficacy of pre-emptive paracetamol in patients undergoing surgery under general anaesthesia is well established and supported by various studies. But lately, many studies were undertaken to study the effect of IV paracetamol , given pre-emptively in surgeries done under subarachnoid block also (18)(15).

In our study, one group received one gram IV paracetamol and control group received 100ml normal saline. Mean time of first request for analgesia was found to be statistically significant higher in paracetamol group(mean 3.28$\pm$0.45 hours) compared to control group (mean 2.30 $\pm$ 0.24 hours) which is in line with previous studies. (19) (14).

In our study, total number of requests of analgesics was statistically higher in control group(3.8885$\pm$0.66 times) compared to paracetamol group (2.88$\pm$0.52 times) which is also in line with previous studies (15)(19)(17)(14). We observed the VAS scores at 0 hours, 4 hours, 8 hours, 12 hours and 24 hours in postoperative period in both the groups. The average VAS score in paracetamol group were 0, 5.92, 4.6, 3.75, 3.32 and in control group were 0, 6.6, 5.9, 5.78, 4.2 at 0, 4, 8,12, 24 hours respectively.

T test showed p-values of 0, 0.142 at 0 and 4 hours respectively which is not statistically significant. This initial non-significant difference in VAS scores may be attributed to effect of spinal anaesthesia which was common in both groups. At 8, 12 and 24 hours, p-value is 0.002, <0.001, 0.036 respectively which shows that there is statistically significant difference in VAS score at 8, 12 and 24 hours and implies that pre-emptive paracetamol is effective in decreasing postoperative pain scores. This finding has been reported in previous studies as well studies(19) (13).

The main limitation of our study was that it required more systemic reviews of high-quality randomized control trials (RCTs) to be conducted regarding the use of pre-emptive i.v. paracetamol in case of caesarean section under subarachnoid block to provide us with level I evidence for evidence-based study.

Taken all together ,after our study we recommend use od one gram intravenous paracetamol pre-emptively in patients undergoing caesarean section under subarachnoid block as we found that pre-emptive analgesia using intravenous paracetamol delays time of first request for analgesia after surgery, decreases postoperative analgesia requirement and statistically decreases VAS scores over 24 hours postoperatively

CONCLUSION:

In conclusion, our findings indicate that intravenous Paracetamol given 20 mins before incision (pre-emptive) delays the time of first request for analgesia postoperatively compared to control group. Pre-emptive intravenous paracetamol also decreases total number of analgesia requests during surgery thereby decreases postoperative analgesia consumption and eventually their side effects . Pre-emptive paracetamol also decreases postoperative pain over 24 hours post operatively in patients undergoing caesarean section under subarachnoid block.

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