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Research Article

Effect of Paracetamol Intravenous Infusion on Duration and Quality of Spinal Blockade in Patients Undergoing Major Gynaecological Surgeries: A Prospective, Randomised, Double-Blinded, Placebo-Controlled Study

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Abstract

Background: Effective pain management is an important component of post-surgical care. For pain relief after major gynecological surgeries, particular attention has been paid to NSAIDs and paracetamol. Paracetamol (acetaminophen) is one of the most commonly used antipyretic analgesics for the symptomatic treatment of acute pain and fever. This study was conducted with the primary aim of evaluating the effect of intravenous paracetamol infusion on the onset and duration of sensory-motor blockade in patients undergoing elective major gynecological surgeries under spinal anesthesia.

Methods: In this double-blind clinical trial study, 100 patients with ASA class I or II, aged 35 to 70 years who were scheduled to undergo elective major gynecological surgeries under spinal anesthesia were randomly allocated into either of two groups. An intravenous infusion of either paracetamol 1g/100ml (group P) or normal saline 100ml (group C) was administered over 20 minutes before performing subarachnoid block at L3-L4 intervertebral space with 3.5 ml of 0.5% hyperbaric bupivacaine. Apart from sensory block and motor block, the severity of pain was recorded on the basis of Visual Analog Scale (VAS) every 4 hours during the first 12 postoperative hours, and if severe pain (VAS > 3) was observed, 100 mg tramadol was administered by IV infusion over 15 minutes, to a maximum of three times a day (8 hourly). All data were analyzed statistically by VASSAR STATS online statistical calculator using Student's independent t-test and Fisher's exact test. P < 0.05 was considered statistically significant.

Results: Each group included 50 subjects. Duration of sensory blockade was significantly longer in group P (5.78 ± 0.536 h) compared to group C (4.19 ± 0.473 h, P<0.001). Mean VAS scores at baseline as well as after 4, 8 and 12 hours were significantly lower in group P (P<0.001). There was a significantly higher level of sensory block in group P at 1 (P=0.002), 2 (P<0.001), and 3 (P<0.001) hours. The time of first requirement of rescue analgesic was 4.27 ± 0.394 h in group C compared to 8.144 ± 0.487 h in group P (P<0.001). Consumption of rescue analgesic in first 12 post-operative hours was also significantly less in group P (P=0.011).

Conclusion: The use of IV paracetamol significantly prolongs the duration of sensory block following spinal anesthesia, reduces pain intensity at different hours after surgery, and decreases the use of rescue analgesic after surgery.

Keywords: Paracetamol; Tramadol; Spinal anesthesia

Introduction

Pain is an unpleasant emotional and sensory experience associated with active or potential tissue damage. Acute postoperative sequelae, such as pain, nausea, and drowsiness, tend to produce an unfavorable effect on patients' general well-being and increase perioperative morbidity as well as the length of hospital stay. 40 to 70% of patients report moderate to severe pain after surgery hampering ambulation, discharge and satisfaction [1]. Preventing and/or treating this pain can minimize these consequences. So, effective pain management is an important component of post-surgical care.

For pain relief after major gynecological surgeries, various drugs such as opioids and non-steroidal anti-inflammatory drugs (NSAIDs) are used. Due to complications of opioids, particular attention has been paid to NSAIDs and paracetamol.

Paracetamol (acetaminophen) is one of the most commonly used antipyretic analgesics for the symptomatic treatment of acute pain and fever. Oral paracetamol in adequate doses is effective alone for the treatment of mild and moderate pain. But in an acute situation, the intravenous preparation is more convenient and may perform better. With intravenous administration, the onset of its analgesic and antipyretic action is rapid, with the analgesic action occurring within 15 minutes and reduction of fever occurring within 30 minutes [2].

The mechanism of action of paracetamol has not been fully established. Its analgesic action has been attributed to inhibition of prostaglandin synthesis in the central nervous system (CNS) and in peripheral tissues. It is likely to be linked also with the serotonergic system. To have effects within the CNS, paracetamol must penetrate the blood-brain barrier (BBB). The penetration of intravenous paracetamol into cerebrospinal fluid (CSF) has been evaluated, and studies have demonstrated that this drug permeates readily into the CSF [2].

But in literature no data are available which have documented the influence of intravenous preparation of paracetamol on spinal anesthesia. This study was conducted with the primary aim of evaluating the effect of intravenous paracetamol infusion on the onset and duration of sensory-motor blockade in patients undergoing elective major gynecological surgeries under spinal anesthesia. Secondary aim was to investigate analgesia, rescue analgesic consumption, adverse events and satisfaction scores.

Methods

This prospective, randomized, double blinded, placebo-controlled study was carried out following approval of the Institutional Ethics Committee. The study population included patients undergoing elective major gynecological surgeries under spinal anesthesia, after obtaining informed written consent.

Inclusion criteria for patients were ASA class I or II, aged 35 to 70 years, and exclusion criteria included unwillingness to give consent, sensory blockade inadequate for surgery, any contraindication to spinal anesthesia or paracetamol, history of alcoholism, drug abuse, and psychiatric disorders, history of allergy to any of the study drugs, hepatic disease, renal disease, cardiopulmonary disease, hypertension, diabetes, central or peripheral nervous system disorders, emergency laparotomy, chronic abdominal pain undergoing treatment with opioid analgesic.

After routine pre-anesthetic check-up, 111 patients were enrolled into the study. Among them, six patients refused to participate, four patients did not meet the inclusion criteria, and one patient had neurologic disorder (traumatic paraparesis). One hundred patients were randomly allocated into either of two groups using a computer generated randomization chart, to achieve 50 patients each in groups P and C.

Following preoperative routine check of equipments, machine, and resuscitative drugs, standard ASA monitoring aids were attached to the patients. Monitoring was conducted in terms of heart rate and arterial oxygen saturation continuously as well as the systolic and diastolic blood pressure once every 5 minutes. Peripheral intravenous access was achieved, and an intravenous infusion of either paracetamol 1g/100ml (group P) or normal saline 100ml (group C) was started to run over 20 minutes. This infusion was administered by an anesthesiologist who was not involved in monitoring or data collection, and the infusion bottles were covered to conceal their identity.

At the completion of infusion, spinal anesthesia was administered at L3-L4 intervertebral space with 3.5 ml of 0.5% hyperbaric bupivacaine by a particular anesthesiologist blinded to the study drugs. All surgeries were performed by one gynecologist who was also blinded. None of the patients was administered opioid or sedative drug during the operation.

Sensory block was assessed by pinprick and cold sensation in the mid-axillary line, and motor block was evaluated with the Bromage Scale. In both groups, Visual Analogue Scale (VAS) score was assessed using a continuous 0-10 cm scale every 4 hours during the first 12 postoperative hours, beginning at the end of the operative procedure (VAS-0). When it exceeded a score of 3 cm, postoperative rescue dose for both groups consisted of 100 mg tramadol by IV infusion over 15 minutes, to a maximum of three times a day (8 hourly). Total rescue analgesic consumption was noted over first 12 hours along with dermatomal regression of sensory block at 10 minutes, 30 minutes,1 hour, 2 hour and 3 hour by an independent anesthesiologist. Adverse effects were noted and satisfaction scores of patient, gynecologist and anesthesiologist were recorded by 3 point satisfaction scales.

It was calculated that to detect a difference of 60 minutes between the two groups in duration of analgesia (defined as the time period from the onset of spinal anesthesia till the time of demand for first rescue analgesia) with a standard deviation (SD) of 90 minutes with a power of 90%, 49 patients in each group would be required (accepting a two-tailed alpha error of 0.05). All data were analyzed statistically by VASSAR STATS online statistical calculator. Student's independent t-test and Fisher's exact test were used for data analysis in the study. $P < 0.05$ was considered statistically significant.

Results

There was no difference between the study and control groups in age, height, weight, ASA physical status and duration and types of surgery (Table 1,2). Onset of sensory and motor block were similar. Though the duration of motor blockade showed no significant difference, duration of sensory blockade was significantly longer in group P (5.78 ± 0.536 h) compared to group C (4.19 ± 0.473 h, $P<0.001$) (Table 3). Mean VAS scores at baseline as well as after 4, 8 and 12 hours were significantly lower in group P ($P<0.001$) (Table 4). Comparison of dermatomal regression of sensory block between the groups showed no difference at 10 and 30 minutes, but significantly higher level of block in group P at 1 ($P=0.002$), 2 ($P<0.001$), and 3 ($P<0.001$) hours(Table 5). The time of first requirement of rescue analgesic was 4.27 ± 0.394 hours in group C compared to 8.144 ± 0.487 hours in group P ($P<0.001$). Consumption of rescue analgesic in first 12 post-operative hours was also significantly less in group P ($P=0.011$) (Table 6). Incidence of various adverse effects was found to be comparable between the two groups.

Parameters	Group P	Group C	*p*
Age (years)	47.24 ± 4.762	49.56 ± 7.226	0.060
Height (cm)	157.42 ± 4.131	157.92 ± 4.309	0.557
Weight (kg)	57 ± 4.6	56.92 ± 5.005	0.936
ASA Physical Status (I:II)	41:9	40:10	0.060
Duration of surgery (minutes)	108.62 ± 13.144	112.16 ± 14.745	0.207

Table 1: Comparison of demographic, anthropometric and clinical parameters

Type of surgery	Group P	Group C	*p*
TAH + BSO	28	27	0.5
VH with PFR	3	3	
VH	0	3	
Ward Mayo	19	17	

TAH + BSO-Total abdominal hysterectomy with Bilateral saphingo-oophorectomy
VH - Vaginal hysterectomy
PFR - Pelvic floor repair

Table 2: Comparison of types of surgery performed

Parameters	Group P	Group C	*p*
Onset of sensory loss (minutes)	2.256 ± 0.512	2.266 ± 0.522	0.921
Onset of motor block (minutes)	3.26 ± 0.443	3.27 ± 0.454	0.913

Duration of sensory loss (hours)	5.78 ± 0.536	4.19 ± 0.473	<0.001
Duration of motor block (hours)	2.96 ± 0.333	3.04 ± 0.333	0.233

Table 3: Comparison of sensory-motor blockade onset and duration

VAS_time	Group P	Group C	*p*
VAS_0	0.1 ± 0.364	1.7 ± 0.463	<0.001
VAS_4	2.36 ± 0.485	3.7 ± 0.463	<0.001
VAS_8	3.86 ± 0.495	1.76 ± 0.625	<0.001
VAS_12	2.54 ± 0.503	2.94 ± 0.550	<0.001

Table 4: Comparison of VAS scores at a particular point of time

Time (T2-T4 : T5-T7 : T8-T10 : T11-T12)	Group P	Group C	*p*
10 minutes	14:36:0:0	13:37:0:0	0.99
30 minutes	26:24:0:0	18:32:0:0	0.114
1 hour	13:37:0:0	2:46:2:0	0.002
2 hours	5:39:6:0	0:13:37:0	<0.001
3 hours	1:27:22:0	0:6:35:9	<0.001
T2,T4, T5, T7, T8, T10, T11, T12 - Respective thoracic vertebrae level			

Table 5: Comparison of dermatomal regression at specified times

Parameters	Group P	Group C	*p*
Time of first dose (hour)	8.114 ± 0.487	4.27 ± 0.394	<0.001
Consumption of dose in first 12 hours	1.0 ± 0.0	1.12 ± 0.328	0.011

Table 6: Comparison of rescue analgesic requirement

Discussion

According to this study results, IV paracetamol infusion significantly increases the duration of sensory loss without affecting motor blockade [3]. It provides better analgesia as evident by VAS scores. Paracetamol also reduces post-operative tramadol consumption, increases the time to first dose of tramadol and delays dermatomal regression of sensory block. The drug has a good margin of safety and satisfies the entire operating team as well as the patient.

Till date, no study could be found in literature review that highlighted the effect of IV paracetamol on spinal anesthesia.

Caliskan E et al. showed in a study in 2013 that after lower abdominal surgery conducted under spinal anesthesia in children, intravenous paracetamol appears to have good analgesic properties to intravenous dipyrone, suggesting that it can be used as an alternative in the early postoperative period [4]. In this study paracetamol infusion was given after spinal anesthesia.

The present study analysed the clinical effects of intravenous paracetamol on subarachnoid block using hyperbaric bupivacaine. Intrathecal fentanyl was avoided because its confounding effect could have been a limited factor in analysis. Therefore, inability to perform surgery because of inadequate blockade was considered an exclusion criterion.

The exact mechanism by which paracetamol exerts this effect is not known. The relatively fast and extensive CNS permeation of this drug after IV administration probably plays a role [2]. Other postulated mechanisms are N-arachidonylphenolamine (AM404) mediated inhibition of uptake of anandamide, an endocannabinoid from synaptic cleft and vanilloid receptor agonist [5], cannabinoid receptor type 1(CB1) agonistic activity [6], reinforcement of descending serotonergic inhibitory pain pathways, prostaglandin synthesis inhibition, 5-HT3 receptor agonistic activity and COX-3 inhibition [7].

Conclusions

This study indicates that the use of IV paracetamol significantly prolongs the duration of sensory block following spinal anesthesia, reduces pain intensity at different hours after surgery, and decreases the use of rescue analgesic after surgery. That is what the rationality of multimodal analgesia is which emphasizes targeting pain management at different sites.

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