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Oral gabapentin (600mg) versus oral pregabalin (75mg) for orthopedic surgery under spinal anesthesia: Hemodynamic changes

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Abstract

The myelinated A δ (sharp pain, first pain) peripheral nociceptors and unmyelinated C nociceptors (delayed pain, second pain) respond to strong mechanical, thermal, chemical stimuli that act as transducers, converting chemical, mechanical or thermal energy at the site of stimulus to electrical activity, which are conducted to the dorsal horn of CNS. Based on previous study by Usha Bafna *et al*., sample size was calculated to be 30 patients, to be randomly included in each group to demonstrate a 40% difference in duration of analgesia with a power of 0.8 and type-1 error of 0.05. To allow for study error and attrition, 35 patients were included in each group. In Group A, 3 (8.57%) patients and in Group B, 4 (11.42%) showed hypotension that is mean SBP was less than 20% of the base line, were as none of patients in either group showed hypertension that is more than 20% of the baseline SBP (intraop and postop). There was no statistically significant difference between two groups P value (0.6903).

Keywords: Gabapentin, pregabalin, hemodynamic changes

Introduction

Preemptive analgesia, a preventive or pre incisional analgesia is an antinociceptive treatment, prevents central hyperexcitability, central sensitization, central neuroplasticity evoked by the incisional and inflammatory injuries occurring during surgery and early postoperative period via altering the afferent input involved in pain.

George Washington Crile-postulated the concept of preemptive analgesia in 1913 further developed by Wall and Woolf who suggested that simple changes in the timing of treatment can have profound effect on postoperative pain.

Central neuroplasticity or changes in CNS processing (hyperexcitability) due to surgical nociception can amplify postoperative pain. As a result hyperalgesic state called `wind up´ can occur in postoperative patients [1].

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stimuli that act as transducers, converting chemical, mechanical or thermal energy at the site of stimulus to electrical activity, which are conducted to the dorsal horn of CNS [2].
In the dorsal horn, the pain signals are transmitted to secondary nociceptive neurons known as specific neurons (NS neurons) and the wide-dynamic range neurons (WDR neurons) that are involved in response to and further signaling of pain sensation.
Substances involved in the transmission of nociceptive signals are aspartate, glutamate, Substance P, calcitonin, gene related peptide, prostaglandins, histamine, bradykinin, serotonin etc. which acts on N-methyl-D-aspartate (NMDA) and 2-amino-3-hydroxy-5-methyl-4-isoxazole-propionic acid (AMPA) receptors.
Pain or stimulus without accompanying tissue damage generally results in a proportionate relationship between the stimulus and the response.
In contrast, stimuli associated with actual tissue damage initiate a number of modulations, of both peripheral and central pain pathways. At the periphery, tissue damage results in a local inflammatory response with release of pain promoting (algogenic) substances from peripheral nerve endings and extraneural sources [3].
These mediators lead to peripheral sensitization of the nociceptors, resulting in altered transduction and increased conduction of nociceptive impulses towards the CNS.
In addition, the barrage of pain signals from the nociceptors onto the NS and WDR neurons in the dorsal horn leads to prolonged alterations in the responsiveness of these neurons. Signals from Aδ and C fibers will be amplified (hyperalgesia) and activity in Aβ fibers will be interpreted not as touch but as pain signals by the WDR neurons (allodynia) and become a pain memory.
Gabapentin and Pregabalin binds potently to the $\alpha_2\delta$ subunit and modulates calcium influx at nerve terminals, there by reduces the release of several neurotransmitters, including glutamate, noradrenaline, serotonin, dopamine, and substance P. These neurotransmitter involved in the pain, transmission, transduction, modulation, cental sensitization, central neuroplasticity and central hyperexcitability are responsible for development acute and acute-chronic pain postoperatively [4].

Methodology

Based on previous study by Usha Bafna *et al*., sample size was calculated to be 30 patients, to be randomly included in each group to demonstrate a 40% difference in duration of analgesia with a power of 0.8 and type-1 error of 0.05. To allow for study error and attrition, 35 patients were included in each group. Standard qualitative and quantitative tests were used to compare the data. (E.g. unpaired student-t-test, Chi-Square).

Inclusion criteria

- Patient age between 18-60 years.
- ASA physical status 1 and 2.
- Patient undergoing lower limb surgery under spinal anaesthesia.

Exclusion criteria

- Age < 18 and > 60 years.
- ASA physical status 3 and above.
- Patients not giving consent.
- History of psychiatric illness, pregnancy, anticipated difficult intubation.
- Patient on drugs that affect central nervous system.
- Patient receiving any type of analgesia 8 to 10 hr prior to procedure.
- Patient on chronic pain treatment.

- Patient sensitive/allergic to local anaesthetic agents.
- Patients with peripheral sensorineural deficit.
- Patients with altered coagulation profile or having bleeding disorder.
- Signs of infection at puncture site for spinal anaesthesia.

Materials required

1. All equipments needed for resuscitation of the patient were kept ready before the institution of the spinal block including appropriate size endotracheal tubes, laryngoscopes, resuscitation bag, oxygen source, suction machine, suction catheter.
2. Autoclaved spinal tray including povidone iodine, spirit, gauge pieces and a skin towel.
3. Disposable syringes 2, 5, 10 cc.
4. 25G Quincke spinal needle.

The study population was randomly divided into two groups of 35 patients each with the help of a computer-generated table of random numbers into
Group A: Oral Gabapentin 600 mg.
Group B: Oral Pregabalin 75 mg.

Results

In Group A, percentage of patients who were operated at hip, femur, knee, tibia, ankle, miscellaneous were 22.85%, 17.145%, 17.14%, 17.14%, 11.42% respectively. In Group B, percentage of patients who were operated at hip, femur, knee, tibia, ankle, miscellaneous were 20%, 11.42%, 11.42%, 22.85%, 17.14%, 17.14% respectively. There was no statistically significant difference between two groups (P = 0.8960).

Table 1: Site of Surgery

Site	Group A (n=35)		Group B (n=35)		
	No. of patients	Percent	No. of patients	Percent	
Hip	8	22.85	7	20	
Femur	6	17.14	4	11.42	
Knee	6	17.14	4	11.42	*P* value 0.8960
Tibia	6	17.14	8	22.85	
Ankle	4	11.42	6	17.14	
Miscellaneous	5	14.28	6	17.14	
Chi-square test was used for statistical analysis					

Perioperative pulse rate

None of the patients in either group Group A or Group B showed bradycardia or tachycardia. Mean pulse rate remained within 20% of the baseline throughout the period of the study (intraop and postop).

Perioperative systolic blood pressure

In Group A, 3 (8.57%) patients and in Group B, 4 (11.42%) showed hypotension that is mean SBP was less than 20% of the base line, were as none of patients in either group showed hypertension that is more than 20% of the baseline SBP (intraop and postop). There was no statistically significant difference between two groups P value (0.6903).

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Perioperative diastolic blood pressure

None of the patients in either group Group A or Group B showed Hypotension or Hypertension. Mean DBP remained within 20% of the baseline throughout the period of the study (intraop and postop).

Table 2: Hemodynamic parameters: Mean pulse rate, systolic blood pressure, diastolic blood pressure throughout the period of study

Time (min)	Group A (n=35) Mean			Group A (n=35) Mean			*P* value
Intraop (min)	**Pulse**	**SBP**	**DBP**	**Pulse**	**SBP**	**DBP**	
0	76.23	120.94	74.97	76.57	120.91	75.29	
5	85.46	118.57	78.31	84.31	120.17	76.40	
10	81.89	114.86	76.14	80.80	117.66	76.86	
15	78.20	115.69	74.94	77.06	115.69	74.94	
20	77.21	114.85	72.03	75.26	117.31	75.37	
25	76.97	115.97	76.43	76.12	116.18	77.24	Pulse: 0.1995
30	79.17	115.50	79.27	78.03	115.93	77.21	SBP: 0.1980
45	78.90	123.38	74.65	79.74	121.57	77.87	DBP: 0.2094
60	76.76	126.65	74.71	77.67	116.75	76.17	
70	77.79	126.07	75.14	78.82	117.55	75.45	
90	74.86	126.71	71.25	79.40	118.67	77.17	
100	79.50	125.00	78.00	81.00	119.00	88.00	
120	80.50	134.00	68.00	81.00	123.00	78.00	
140	87.00	134.00	74.20	73.00	129.46	67.00	
Post op (hr)							
2	75.54	130.60	72.66	76.69	128.91	75.94	
4	83.09	127.74	69.51	76.71	128.20	75.89	
6	79.49	127.71	69.40	76.74	128.63	76.17	
8	75.77	132.06	69.51	76.94	128.09	75.97	
10	75.54	127.71	70.91	76.97	129.29	75.29	
12	75.54	131.03	69.40	76.37	129.06	76.60	
16	79.49	132.06	70.63	76.83	128.63	77.46	
20	79.37	131.03	70.49	76.43	129.29	76.49	
24	76.77	129.37	74.20	73.00	128.09	77.03	

Discussion

Hemodynamic changes were recorded to observe the effect of gabapentin or pregabalin on pulse rate and blood pressure both intraoperatively and post operatively for 24hr.

All the patients of either group remained hemodynamically stable postoperatively, except that 3 patient of group A and 4 patients of group B were found to be hypotensive immediately after spinal block, which was comparable with both the group. This was in accordance with other studies Usha Bafna *et al*., Pragati Arora *et al*., were in the patients remained hemodynamically stable [5, 6]. Both drugs Gabapentin or Pregabalin have got no drug interaction and there is no evidence available in direct correlation of hypotension to these drugs as observed by other studies so hypotension observed in our study was because of spinal blockade.

Usha Bafna *et al*. [5] compared the efficacy of gabapentin (600 mg) versus pregabalin (150 mg) and placebo capsule. One hour before entering into the operation theatre the blinded drug selected for the study was given with a sip of water. Group A-received identical placebo capsule, Group B-received 600mg of Gabapentin capsule and Group C-received 150 mg of Pregabalin capsule. Spinal anaesthesia was performed using 3.5 ml of 0.5% bupivacaine heavy. VAS score at first rescue analgesia, mean time of onset of analgesia, level of sensory

block at 5 and 10 min interval, onset of motor block, total duration of analgesia and total requirement of rescue analgesia were observed as primary outcome. Hemodynamics and side effects were recorded as secondary outcome in all patients. A significantly longer mean duration of effective analgesia in group C was observed compared with other groups (P<0.001). The mean duration of effective analgesia in group C was 535.16 ± 32.86 min versus 151.83 ± 16.21 min in group A and 302.00 ± 24.26 min in group B. The mean numbers of doses of rescue analgesia in the first 24 hours in group A, B and C was 4.7 ± 0.65, 4.1±0.66 and 3.9±0.614 (P value <0.001) respectively, and they concluded that preemptive use of gabapentin 600mg and pregabalin 150mg orally significantly reduces the postoperative rescue analgesic requirement and increases the duration of postoperative analgesia in patients undergoing elective gynaecological surgeries under spinal anaesthesia.

V Saraswat *et al*. [7] the study was made to compare the efficacy of Gabapentin (1200 mg) versus Pregabalin (300mg) with respect to increase in duration of analgesia, reduction in total postoperative requirements of analgesics and study side effects and complications [8].

Sixty patients of ASA grade I and II were randomly allocated to one of the two groups of thirty each. Patients in Group G were given single dose of Gabapentin 1200mg, whereas in Group P were administered Pregabalin 300mg one hour prior to administration of spinal anaesthesia. 0.5% heavy bupivacaine 15mg was standardised dose used in spinal anaesthesia for all patient. The total postoperative analgesic time was 8.98h in Group G whereas 14.17h in Group P (HS, P< 0.001). Total dose of analgesics in first 24h was 62.5mg Diclofenac in Group P and 72.5mg Diclofenac in Group G and was not significant (P > 0.05). Dizziness and somnolence were the only side effects noticed in both groups. Gabapentin and Pregabalin, both were found to be effective in prolongation of post-spinal analgesia, Pregabalin more than Gabapentin and either can be used as part of multimodal therapy if not as sole analgesic.

Conclusion

None of the patients in either group Group A or Group B showed Hypotension or Hypertension. Mean DBP remained within 20% of the baseline throughout the period of the study (intraop and postop).

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