

Efficacy and Safety of Promethazine Hydrochloride as a Local Analgesia in Comparison with Bupivacaine Hydrochloride, in Various Peripheral Nerve Blocks

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Abstract

Abolishing the pain conduction in sensory nerves – this idea would have definitely come from progressive physicians. Various local anesthetic agents since 1860 have been isolated and synthesized till dates which have their action mediated through nerve conduction blockade. But there are other agents who can inhibit conduction to varying degrees, in a nerve and other excitable tissues – like H1 – blockers, Antihistaminics, Anti convulsants, opioids, Marine Biotoxins. Phenothiazine derivative of H1 – blocking agents viz. Promethazine and Diphenhydramine have potent local anesthetic activity as compared to procaine (a amide local anesthetic) when injected locally. Promethazine is widely used as anti emetic, anti histaminic and hypnotic agent by oral, intra muscular, intra venous and trans rectal route but its local anesthetic property has not been fully utilized and advocated in clinical practice. A careful search to literature was done and this study was undertaken to study the use of promethazine in aspect to onset of action, intra operative analgesia, post operative analgesia, sedation along with other complications as compared to Bupivacaine. Sixty patients of ASA status I & II, undergoing elective surgery like Hydrocelectomy, circumcision and others to be operated under regional blocks were randomly divided in two groups: Group I to receive Inj. Promethazine hydrochloride (2 mg/kg) diluted to make a volume of 15 ml, Group II to receive Inj. Bupivacaine 0.25% (2 mg/kg) to a maximum of 15 ml and patients were observed for onset of analgesia, duration, requirement of rescue analgesic using 4 point pain score and post operative sedation using Cook's Sedation Score along with hemodynamic stability and any other known complications. It was found that there was good analgesia in both the groups per operatively with good hemodynamic stability all throughout the surgery and surgery accomplished satisfactorily with no side effects except drowsiness seen in Group I specially of age > 45 years. Hence, promethazine can be considered as a safe alternative to standard local anesthetics for superficial surface surgeries where sensitivity to local anesthetics is a problem.

Keyword: Promethazine; Bupivacaine; Cook's Sedation Score; 4 Point Analgesia Score.

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Introduction

“The thought of producing anaesthesia by abolishing conduction in sensory nerves, by suitable means, should have arisen in the minds of progressive physicians” [6].

Local anesthetic agents reversibly depress the nerve conduction beyond the point of application. It was first demonstrated by Karl Kollar in 1860 by use of Cocaine in practice of regional anesthesia. There are diverse group of drugs other than local anesthetic drugs having the ability of inhibit nerve conduction in varying degrees in nerves and other excitable tissues. Of which H1 blockers are 2-4 times potent to few local anesthetic agents.

Phenothiazine derivative of H1 blockers like promethazine and diphenhydramine have potent local anaesthetic activity.

Fitzpatrick and Stabbart (1950) [2] used promethazine hydrochloride solution for urethral dilatation but patients had lot of local irritation

Dundee and Moore (1951) [5] used Promethazine as local infiltration and found it to be potent but the dose required was associated with deep sedation.

S. Kumar (1997) [4] did study promethazine as local infiltration for hernia repair and found its local anesthetic property as comparable to lignocaine.

Not much is known about the dose and action of Promethazine used as local analgesic.

A thorough search in the literature and to explore the unusual action of promethazine we undertook this study to compare the efficacy of Promethazine as local infiltration for superficial surface surgeries as compared to Bupivacaine in aspect to onset of analgesia, quality of analgesia, duration of analgesia and degree of sedation with optimally minimum dose of Promethazine.

Methodology

This prospective randomized study was conducted after approval from institution and written informed consent from the patients. For the study 60 patients posted for elective surgeries of ASA grade I & II, aged 5 to 55 years of either sex were selected. After thorough preoperative check up, fitness sought after the necessary systemic examination and relevant blood investigations, they were randomly divided in two groups (n=30): Group I to receive regional nerve block with Inj. Promethazine hydrochloride (maximum 2 mg/kg of body weight) diluted in saline up to 15 ml. Group II

to receive Inj. Bupivacaine (maximum 2 mg/kg body weight) 0.25% to a volume of 15 ml. All regional blocks were performed after informed consent obtained from patients. The patients were fasted for sufficient time and subjected to Inj. Glycopyrrolate 0.01 mg/kg body weight intramuscularly.

The surgery was allowed only after there was loss of pin prick sensation of the particular dermatome infiltrated with the drug. Fasting period and preoperatively intravenous fluids were administered to cover the deficit. Patients were observed for hemodynamic changes, respiration, other vital parameters and analgesia using Four point Pain Score (Melzeck and Wall, 1983) (Table 1).

In the post operative period the duration of analgesia was noted from the time of infiltration of regional block to the demand of first rescue analgesic. Patients were also observed for the sedation post operatively using Cook's Sedation Score (Table 2).

The result of both group were tabulated and mean and standard deviation value were taken out. Statistical analysis was done using chi-square test and t - test. $p < 0.05$ was regarded as statistically significant.

Results

The two groups were comparable in age, sex, type of surgery, type of anesthesia and duration of surgery as showed in table 4, 5, 6 & 8 respectively.

Table 1: Four Point Pain Score (Melzeck and Wall, 1983)

Score	Interpretation
0	No Pain
1	Wincing With/Or Facial Grimace
2	Verbalization
3	Withdrawal

Table 2: Cook's Sedation Score

Command	Response	Score
Eyes Open	Spontaneously	4
	To Speech	3
	To Pain	2
	None	1
Response to Nursing Procedure	Obeys Commands	5
	Purposeful Movements	4
	Non Purposeful Flexion	3
	Non Purposeful Extension	2
Cough	None	1
	Spontaneous Strong	4
	Spontaneous Weak	3
	On Suction Only	2
	None	1

The type of cases selected were those of superficial surgeries, Table 6 shows the types of surgeries considered for both the groups and the type of anesthesia given for them. Field blocks, local infiltration, regional blocks like wrist, ankle block, penile block were performed for the cases selected for the study.

The time duration of onset of effect was observed by the observer who was blind to the type of drug used. Table 7 shows that in majority of patients the onset was quick (within 3 minutes) in group I whereas the onset was bit delayed in Group II (from 4 minutes onwards) with a mean onset of 1.95 ± 0.70 minutes in Group I as compared to 3.35 ± 1.25 minutes in group II. This comparison was statistically significant.

The patients were observed for their compliance during surgery in terms of feeling of pain, discomfort or totally comfortable with no pain. These observations were made using the four point Pain Score (Melzeck and Walls). Table 8 shows that 18 patients were comfortable during the surgery in Group I with the score of '0' whereas 19 patients had score of '0' in group II. The score was 1 in 10 and 8 patients and it was 2 in one and two patients in Group I and Group II respectively. Patients with score of 3 were needed to be supplemented with either O_2+N_2O through mask ventilation or Inj. Ketamine but the proportion of such patients was very less in both the groups. When compared statistically there was not much difference as far as the pain relief and efficacy of both drugs were taken in consideration.

Table 3: Interpretation of Cook's Score

Score	Interpretation
11-13	Very Mild or No Sedation
8-10	Mild Sedation
6-7	Moderate Sedation
<6	Deep Sedation

Table 4: Distribution of Patients Age Wise

Age Group (Years)	Group I (N=30)	Group II (N=30)
15-25	16	14
26-35	07	07
36-45	04	04
46-55	03	05
Mean \pm Sd	28.4 ± 12.24	30.07 ± 12.54
p Value	>0.05	

Table 5: Distribution of Patients Sex Wise

Sex	Group I (N=30)	Group II (N=30)
Male	19 (63.3%)	21 (70%)
Female	11 (36.7%)	9 (30%)

Ratio	6.3:3.7	7:3
p Value	>0.05	

Table 6: Distribution of Patients as Per Type of Surgery and Anesthesia

Sr. No.	Type of Surgery	Group I (n=30)	Group II (n=30)
1	Skin Grafting (Local infiltration)	4	3
2	Gynecomastia (local infiltration)	5	5
3	Fibroadenoma breast excision (local infiltration)	8	7
4	Lord's Plication (Block for hydrocele)	5	6
5	Lipoma excision (local infiltration)	5	6
6	K wiring # metacarpal (wrist block)	1	2
7	Skin grafting (femoral nerve block)	2	1

Table 7: Time for Onset of Action

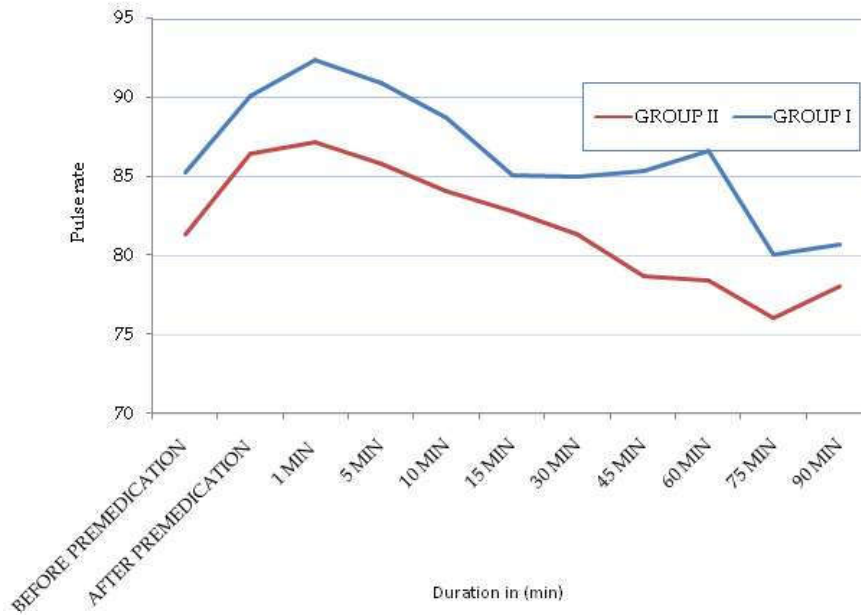
Duration (Min)	Group I (N=30)	Group II (N=30)
0.0-1.0	04	00
1.1-2.0	12	00
2.1-3.0	11	07
3.1-4.0	03	20
4.1-5.0	00	02
5.1-6.0	00	01
6.1-7.0	00	00
Mean \pm SD	1.95 ± 0.70	3.35 ± 1.25
t value	5.38	
p value	<0.05	

Table 8: Time for Surgery

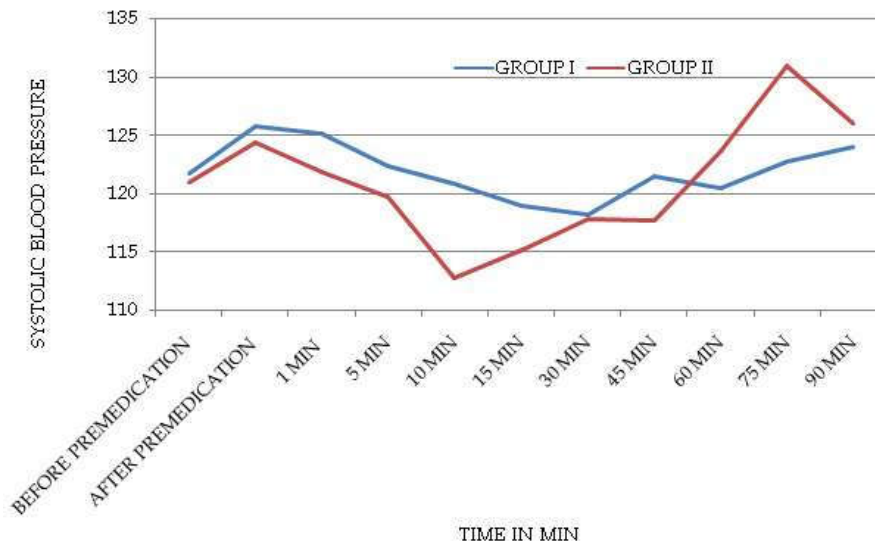
Duration (Min)	Group I (N=30)	Group II(N=30)
21-40	18	14
41-60	07	10
61-80	02	04
81-100	03	02
Mean \pm SD	46.17 ± 18.06	47.17 ± 15.14
t value	0.19	
p value	>0.05	

Table 9: Intra Operative 4 Point Pain Score

Pain Score	No. of Cases	
	Group I	Group II
0	18	19
1	10	08
2	01	02
3	01 ($O_2 + N_2O$)	01 (Ketamine)
p Value	>0.05	



Graph 1: Showing the Changes in Mean Pulse Rate



Graph 2: Showing the Changes in Mean Systolic Blood Pressure

Hemodynamically the patients stayed well controlled as compared to the pre operative values which are shown in Graph 1 (changes in pulse rate) and Graph 2 (change in systolic blood pressure). Post operatively patients were also observed for the sedation caused by use of these drugs using Cook’s sedation score (Table 2) almost all the patients had a score of more than 11 all through out suggestive of no sedation.

Discussion

The basic mechanism behind the local analgesic effect of Promethazine Hydrochloride is similar to other local analgesics drugs. It exhibits its action through membrane stabilization and directly blocking the sodium channels. It was in 1943 Watrous WG [1] explored the local anesthetic property of promethazine in animals and was of

conclusion that it was more potent than procaine a ester local anesthetic preparation. But owing to its antanalgesic property when given intravenously its property of local analgesic action was not much studied. In 1997, Kumar S. [2] published a pilot case study showing the use of Promethazine as an infiltrative local analgesic agent in direct inguinal hernia repair.

In our study, we used Inj. Promethazine hydrochloride in dose of 2 mg/kg diluted to a volume of 20 ml (Group I) to explore its use as local analgesic agent in superficial surgeries in comparison to Inj. Bupivacaine 0.25% diluted to a volume of 20 ml (Group II) (a routinely used local anesthetic).

It was found that the onset time of analgesia in Group I (mean of 1.95 ± 0.7 min) was significantly earlier than Group II (3.325 ± 1.25 min). As far as the efficacy of the drug was concerned in terms of feeling of pain, discomfort and patient compliance, both drugs were comparable. We observed the patients for any pain during the surgery using four point pain score which was around score '0' for 18 & 19, score '1' for 10 & 8, score 2 for 1 & 2 and score 3 for one patient in each group respectively. We supplemented with mask ventilation of $O_2 + N_2O$ and intravenous Inj. Ketamine in analgesic dose to alleviate the pain. This suggests that both drugs do provide a good pain free comfort to the patients. Kumar et al. (1997) [2] observed mild sedation during use of Promethazine as local infiltrant for inguinal surgeries. Sedation is commonly seen with intravenous use of Promethazine but it was not found in any of our case when used in regional and local blocks.

Hemodynamically the patients stayed stable as they didn't perceive the pain and had bare minimum stress sympathetic response keeping the pulse, Blood pressure as near as pre operative values. No any other complications like respiratory depression were observed except for burning sensation felt during the infiltration of drug in

group I but this was not hampering to the patients compliance.

Our study concluded that Promethazine is a safe and efficacious local analgesic in peripheral nerve blocks given individually and even along with other local anesthetics. So it can turn out to be a safe alternative in patients where use of local anesthetics may be limited owing to the known hypersensitivity. The mild sedation if at all occurs can be an added advantage along with its anti emetic and anti histaminic effect.

Conclusion

Analgesic effect of Promethazine is as comparable to local anesthetics when used solely in peripheral nerve blocks along with field block and local infiltration. It can turn out to be a safe alternative in patients where use of local anesthetics may be limited owing to the known hypersensitivity. The mild sedation if at all occurs due to systemic absorption from the infiltration site can be an added advantage along with its anti emetic and anti histaminic effect.

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