Original Research Article

Effect of transdermal nitroglycerin patch on intrathecal neostigmine with bupivacaine for post operative analgesia

Viralben P. Patel[1*], Prakash Patel[2], Shweta S. Mehta[3], Gunvanti B. Rathod[4]

[1]Assistant Professor, Department of Anesthesia, GMERS Medical College, Himmatnagar, Gujarat, India
[2]Senior Resident, Department of Medicine, GMERS Medical College, Gandhinagar, Gujarat, India
[3]Associate Professor, Department of Anesthesia, Smt. NHLM Medical College, Ahmedabad, Gujarat, India
[4]Assistant Professor, Department of Pathology, GMERS Medical College, Himmatnagar, Gujarat, India
[*]Corresponding author email: **4viral@gmail.com**

International Archives of Integrated Medicine, Vol. 3, Issue 2, February, 2016.

Available online at http://iaimjournal.com/
ISSN: 2394-0026 (P) **ISSN: 2394-0034 (O)**
Received on: 15-01-2016 **Accepted on:** 31-01-2016
Source of support: Nil **Conflict of interest:** None declared.
How to cite this article: Patel VP, Patel P, Mehta SS, Rathod GB. Effect of transdermal nitroglycerin patch on intrathecal neostigmine with bupivacaine for post operative analgesia. IAIM, 2016; 3(2): 31-40.

Abstract

Background: The international association for the study of pain has defined pain as unpleasant and emotional experience associated with actual or potential tissue damage or described in terms of such damage. Spinal anesthesia was first produced by Corning in 1885 and first used deliberately by Bier in 1898. Glucose containing solution for spinal anesthesia was introduced by Barker in 1907. Since then hyperbaric solutions are in use for spinal anesthesia. All these advantages of spinal anesthesia are offset by complain of postoperative pain when effect of local anesthesia wears off due to relatively shorter duration of action of local anesthetic drug.

Aim: The present study was designed to evaluate the effect of intrathecal bupivacaine 0.5% heavy 3.0 ml (15 mg) with neostigmine 5 mcg and bupivacaine 0.5% heavy 3.0 ml (15 mg) with neostigmine 5 mcg and nitroglycerin patch (5 mg/24 hour) in various surgeries divided 2 groups, 25 patients in each group. The objectives of study were to observe onset and duration of sensory and motor blockade, to observe duration of post operative analgesia, to observe perioperative hemodynamic stability, to observe perioperative complications.

Materials and methods: The study was conducted by taking 50 randomly selected patients for various surgeries. Patients belonged to ASA Grade I/II aged 18 to 60 years were included. Patients were divided into 2 groups. **Group - A:** 0.5% heavy bupivacaine 3 ml (15 mg) + preservative free neostigmine 5 mcg. **Group - B:** 0.5% heavy bupivacaine 3 ml (15 mg) + preservative free neostigmine 5 mcg + transdermal nitroglycerin patch (5 mg/24 hours), applied on a non anaesthetised area after 20 minutes. All the patients were evaluated preoperatively and those having history of allergy to any drug, having any contraindications to spinal anesthesia, any neurological disorder and psychiatric illness were excluded from the study. Detailed preoperative history of past and present illness was taken. Systemic and general examination was done and back of patients were examined to rule out any spinal deformity and infection at local site. Patients were investigated for laboratory investigations like complete blood count, blood Sugar, renal function test, serum electrolytes, serum bilirubin and chest X-Ray, ECG were reviewed.

Results: In our study of 50 patients we observed that intrathecal neostigmine 5 mcg with bupivacaine 15 mg with transdermal nitroglycerin patch (5 mg/day) markedly prolong duration of post operative analgesia than intrathecal neostigmine with bupivacaine alone. Intra-operative complication like bradycardia do occur but it was not significant, and other complication like hypotension occur with both groups but more in group B which requires monitoring .

Conclusion: Transdermal nitroglycerin patch increases post-operative analgesia of low dose intrathecal neostigmine with bupivacaine in spinal anesthesia with less side effects.

Key words

Transdermal nitroglycerin patch, Intrathecal neostigmine, Bupivacaine, Post-operative analgesia.

Introduction

The international association for the study of pain has defined pain as unpleasant and emotional experience associated with actual or potential tissue damage or described in terms of such damage [1]. Spinal anesthesia was first produced by Corning in 1885 and first used deliberately by Bier in 1898. Glucose containing solution for spinal anesthesia was introduced by Barker in 1907. Since then hyperbaric solutions are in use for spinal anesthesia. All these advantages of spinal anesthesia are offset by complain of postoperative pain when effect of local anesthesia wears off due to relatively shorter duration of action of local anesthetic drug [1].

In this study local anesthetic bupivacaine was selected as basic drug as this drug is rarely associated with neurological symptoms in therapeutic dose as compared to lignocaine. Various intrathecal adjuvant have been tried with local anesthetic agent to prolong It's duration of action. The adjuvant action is directed towards decreasing sensory input to CNS. Their site of action is different from that of Local Anesthetic Agent. Intrathecal neostigmine causes dose dependent post operative analgesia by inhibiting breakdown of acetylcholine in dorsal horn and spinal meninges. Acetylcholine causes analgesia through direct action on spinal cholinergic muscarinic receptors m1 and m3.

Nitric oxide (NO) has been suggested to act as a second messenger in the central nervous system and has been shown to play an important role in the mechanisms of antinociception. Acetylcholine produces analgesia indirectly through stimulation of release of the second messenger system nitric oxide in spinal cord. The transdermal nitroglycerin patch has been related to nitric oxide formation during degradation of organic nitrate and enhances the antinociception produced by low dose neostigmine intrathecally.

This study was undertaken to evaluate efficacy and potency of intrathecally administered bupivacaine with neostigmine (source of

Acetylcholine) and bupivacaine and neostigmine with nitroglycerin patch (source of exogenous NO) on onset and duration of sensory and motor blockade, hemodynamic stability, duration of post operative analgesia and side effects in various surgeries.

Aim and objectives

The present study was designed to evaluate the effect of intrathecal bupivacaine 0.5% heavy 3.0 ml (15 mg) with neostigmine 5 mcg and bupivacaine 0.5% heavy 3.0 ml (15 mg) with neostigmine 5 mcg and nitroglycerin patch (5 mg/24 hour) in various surgeries divided 2 groups, 25 patients in each group.

The objectives of study were

- To observe onset and duration of sensory and motor blockade.
- To observe duration of post operative analgesia.
- To observe perioperative hemodynamic stability.
- To observe perioperative complications.

Material and methods

The study was conducted by taking 50 randomly selected patients for various surgeries. Patients belonged to ASA Grade I/II aged 18 to 60 years were included. Patients were divided into 2 groups.

Group - A: 0.5% heavy bupivacaine 3 ml (15 mg) + preservative free neostigmine 5 mcg.
Group - B: 0.5% heavy bupivacaine 3 ml (15 mg) + preservative free neostigmine 5 mcg + transdermal nitroglycerin patch (5 mg/24 hours), applied on a non anaesthetised area after 20 minutes.

All the patients were evaluated preoperatively and those having history of allergy to any drug, having any contraindications to spinal anesthesia, any neurological disorder and psychiatric illness were excluded from the study.

Detailed preoperative history of past and present illness was taken. Systemic and general examination was done and back of patients were examined to rule out any spinal deformity and infection at local site.

Patients were investigated for laboratory investigations like complete blood count, blood Sugar, renal function test, serum electrolytes, serum bilirubin and chest X-Ray, ECG were reviewed.

Procedure and VAS score were explained and informed consent was taken and fasting for minimum 6 hours was advised.

Inside the operation theatre, intravenous line taken and each patient was preloaded with 10 ml/kg of ringer's lactate solution. Pulse oximeter, non invasive blood pressure and ECG monitors were applied and baseline readings were taken.

Standard spinal anesthesia tray was prepared with 23G lumbar puncture needle, 5 cc syringe, 10 cc syringe, 18G and 22G hypodermic needles, cotton swabs, swab holding forceps, an ampoule of bupivacaine 0.5% heavy and preservative free neostigmine, nitroglycerin patch, and normal saline.

An emergency crash cart kept ready with all cardiopulmonary resuscitation equipments. Anesthesia trolley and circuit were checked and kept ready.

In both the groups, the drug solution was prepared by the anesthesiologist who performed the lumbar puncture. Inj. neostigmine 0.5 mg was diluted in 10 cc with normal saline and 1 cc is taken from it and again diluted in 10 cc and from it 1 cc (5 mcg) was taken with 3 cc (15 mg) of 0.5% hyperbaric bupivacaine. Total volume of 4 ml was used. Under all aseptic and antiseptic precaution spinal anesthesia was performed in sitting/ lateral position at L_2L_3 or L_3L_4 inter vertebral space with 23G quincke spinal needle. After completion of procedure patients were immediately turned to supine position and time to subarachnoid injection was noted. Highest T6-T8 level was achieved. An eye cover was placed

and O_2 was given by Hudson mask at the rate of 4 L/min by the anesthesia machine. In group B, after hemodynamic stabilisation the transdermal nitroglycerin patch was applied on the thorax (ventral, T2-T4), in a non-anesthetised area, 20 minutes after spinal puncture. The total nitroglycerin content of transdermal nitroglycerin patch was 25 mg; the total drug releasing area was 10 cm^2. It delivered nitroglycerin at the rate of 20-25 $\mu g/cm^2$ per hour or 5 mg /24 hours.

Evaluation

Sensory block was checked by using pin prick method with the tip of 24 G hypodermic needle

- Time of onset of sensory blockade in minutes.
- Time of two segment regression of sensory block in minutes.

Motor block was assessed by modified Bromage scale.

- Complete motor blockade: (it was defined as the time from intrathecal drug injection to time to attain modified Bromage grade 3)
- Duration of motor block: ((it was defined as time interval from intrathecal drug injection to when modified Bromage scale grade become 0 again)

Intra-operative vital parameters

Pulse rate, Blood pressure and SPO2 were monitored at every 5 min till first 30 minutes then every 10 min till 1 hour and then every 30 min till the end of surgery.

Intra-operative complications

Intra-operative complications like hypotension, respiratory depression, nausea, vomiting, shivering were treated as follow.

Hypotension greater than 15% below the baseline value was treated by the incremental dose of Injection mephenteramine 6 mg IV. Any fall in the heart rate below 60 beats per minute was treated with incremental doses of Inj. atropine 0.3 mg IV. Intra-operative nausea was treated with Inj. Ondansetron 4 mg intravenous. Shivering was treated with 100% oxygen, warm fluids and adequate covering. No other sedation or analgesic drug given to the patients.

Post-operative period

Time from subarachnoid injection to administration of first rescue analgesic was taken as total duration of analgesia.

Method of judging post-operative analgesia was by VAS (Visual Analogue Scale). At this time, patients were given rescue analgesic Inj. Diclofenac Sodium 1.5 mg/kg IM. Vital parameters were recorded initially at 30 min interval for 1 hr then hourly for 7 hour then 2 hourly for 4 hours (total 14 hours).

Pain assessment

It was done every 30 min for initial 1 hour then hourly for 7 hour and then 2 hourly for 4 hour by using Visual Analogue Scale (VAS).

It is a 10 cm scale graded from 0-10 in such a way that 0 denotes no pain and 10 denote most excruciating pain. Patients were asked to mark the point on the scale that corresponded to their level of pain intensity at the time of observation.

Transdermal Nitroglycerin patch was removed after giving the rescue analgesia.

Post-operative vital parameters

Vital parameters were recorded initially at 30 min interval for 1 hr then hourly for 7 hour then 2 hourly for 4 hours (total 14 hours).

Post-operative complications

Post-operative complications like bradycardia, hypotension, respiratory depression, nausea, vomiting, shivering, post dural puncture headache, backache were observed and treated accordingly.

The results of the study were tabulated and statistically compared among the two groups. The Student t test was used for quantitative data. Data were presented as mean and mean$\pm$SD. The

p-value was considered significant as shown below.

- P > 0.05 not significant
- P < 0.05 significant
- P < 0.001 highly significant

Results

There were 25 patients in each group and their demographic characteristics were as per **Table – 1.** There was no statistically significant (*P*>0.05) difference among two groups in terms of demographic data like age, weight and ASA grade as per **Table - 1**.

Table - 1: Demographic profile of groups with Mean and S.D. values.

Parameter	Group A	Group B
No. of patients	25	25
ASA grade (I/II)	15/10	15/10
Age (Years)	37.24±12.3	37.64±11.82
Weight (kg)	55.12±3.59	55.60±4.04

There was statistically insignificant difference in two groups with regards to preoperative hemodynamic parameters (p>0.05) as per **Table - 2**.

Table – 2: Pre-operative hemodynamic parameters (Mean ±SD).

Parameter	Group A	Group B
Pulse (beats/ min)	90.48±12.18	90.96±12.83
Blood pressure (Systolic/ Diastolic) (mm of Hg)	127.6±8.86/ 83.36±6.62	128.72±10.98/ 82.64±7.95
SPO_2 %	98.76±0.66	99.04±0.73
Respiratory rate (per min.)	15.84±1.17	14.92±0.86

Duration of two segment regression of sensory block was 137.36± 3.45 min in Group-A as compared to 139.72± 3.57 min in Group -B. There was no significant difference in two groups with regards to duration of two segment regression of sensory block as per **Table - 3**.

Table – 3: Characteristics of sensory block.

	Group A	Group B
Time to achieve sensory block (Mean ± SD) minutes	3.12±0.60	3.52±0.96
Duration of two segment regression of sensory block (Mean ± SD) minutes	137.36±3.45	139.72±3.57

There was no significant difference in total duration of motor blockade as 201.52 ± 7.41 min in Group-A as compare to 200.16 ± 10.19 min in Group-B. There was no significant difference in two groups with regards to time to achieve grade 3 block and duration of grade 3 to grade 0 level(p>0.05) as per **Table – 4**.

Table – 4: Characteristics of motor blockade.

	Group A	Group B
Time to achieve Grade 3 block (Mean ± SD) minutes	5.48±0.87	5.52±0.87
Time taken for Grade 3 to Grade 0 level (Mean ± SD)minutes	201.52±7.41	200.16±10.19

There was statistically insignificant difference between two groups with regards to duration of surgery (P > 0.05) as per **Table - 5**. There was more hypotension at 20, 25 and 30 min in Group-B as compare to Group-A. There was no significant difference in mean pulse rate at 5, 10, 15, 20, 25 and 30 min intra- operatively (P > 0.05) in both Groups. There was statistically

insignificant difference between two groups with regards to hemodynamic parameters (P > 0.05) as per **Table - 6**.

Table – 5: Duration of surgery.

Time (in min)	Numbers of patients	
	Group A	Group B
50-70	7	7
71-90	12	13
91-110	6	5
Mean ± SD	79.0± 11.80	78.64 ± 11.98

There was statistically insignificant difference between two groups with regards to postoperative hemodynamic parameters (P>0.05) as per **Table - 7**. Duration of post operative analgesia was significantly prolonged in Group-B (580.8 ± 34.87) min. as compare to Group-A (408 ± 30.27) min. Highly significant difference between total duration of analgesia in both groups (p<0.01) was evident as per **Table - 8**.

More hypotension was noted in group B than group A and incidence of bradycardia was same in both groups as per **Table - 9**.

Table – 6: Intra-operative hemodynamic monitoring (mean).

Time	Group-A			Group-B		
	Pulse (Per min)	Blood pressure (mmHg)		Pulse (Per min)	Blood pressure (mmHg)	
		Systolic	Diastolic		Systolic	Diastolic
5 min	83.88	124.88	77.92	85.0	125.92	78.96
10 min	81.92	121.36	77.60	82.04	121.28	77.52
15 min	80.40	114.32	72.16	80.36	113.84	72.24
20 min	77.28	108.72	67.68	76.52	108.64	67.72
25 min	73.88	106.48	64.88	75.12	105.92	65.44
30 min	71.08	107.12	66.64	74.36	101.68	62.56
40 min	73.08	109.2	68.88	73.08	106.08	67.92
50 min	72.08	110.16	71.2	72.08	110.16	71.2
60 min	72.72	112.48	73.04	72.72	112.24	72.24
90 min	73.84	116.56	72	73.84	116.32	71.52
120 min	77.76	118.64	75.28	77.76	118.64	75.28

Table – 7: Post-operative hemodynamic monitoring.

Time	Group-A			Group-B		
	Pulse (Per min)	Blood pressure (mmHg)		Pulse (Per min)	Blood pressure (mmHg)	
		Systolic	Diastolic		Systolic	Diastolic
150 min	73.84	116.56	72	77.4	120.08	75.92
180 min	77.76	118.64	75.28	78.72	119.84	76.4
240 min	77.4	120.08	75.92	80.68	120.96	75.6
300 min	81.84	122.08	78.08	81.68	121.76	77.84
360 min	82.88	122.8	77.68	82.84	122.48	77.44
420 min	84.16	123.12	77.92	84.2	122.88	77.84
480 min	84.92	123.44	77.92	84.96	123.6	78.08
540 min	83.12	125.52	78.4	82.96	125.28	78.48
600 min	82.68	126.88	80.8	82.52	126.64	80.48
720 min	83.92	124.88	82.0	83.6	124.72	81.6
840 min	84.56	124.64	83.12	84.32	124.48	82.64

Table – 8: Total duration of analgesia.

Time in Minutes	No. of Patients	
	Group A	Group B
300-350	2	0
351-400	6	0
401-450	17	0
451-500	0	0
501-550	0	5
551-600	0	13
601-650	0	7
Mean time ± S.D.	408 ± 30.27	580.8 ± 34.87

Table – 9: Perioperative complications.

Complications	No. of patients			
	Group-A		Group-B	
	Intra-operative	Post-operative	Intra-operative	Post-operative
Nausea/ Vomiting	0	0	0	0
Hypotension	5 (20%)	0	9 (36%)	0
Bradycardia	5 (20%)	0	5 (20%)	0
Respiratory depression	0	0	0	0
Shivering	0	0	0	0

Discussion

Effective control of post operative pain remains one of the most important and pressing issues in the field of surgery and anesthesia with significant impact on our health care system.

The most important factors influencing the occurrence, intensity, quality and duration of postoperative pain includes.

- Site, nature and duration of operation, type of incision and amount of intra-operative trauma.
- Anxious nature of the patient.
- Presence of serious complications related to operation.
- Anesthetic management before, during and after operation.
- The quality of postoperative care.

The aim of this study was to evaluate that nitroglycerin patch (source of exogenous NO) would enhance the analgesic efficacy of intrathecal neostigmine (source of acetylcholine) with bupivacaine.

The study was conducted by taking 50 randomly selected patients for various surgeries. Patients were divided into 2 groups.

Group-A: 0.5% heavy bupivacaine 3 ml (15 mg) + neostigmine 5 mcg.
Group-B: 0.5% heavy bupivacaine 3 ml (15 mg) + neostigmine 5 mcg + transdermal nitroglycerin patch (5 mg/24 hours).

Concern of intrathecal Neostigmine

Hood B, et al. [2] in 1995 proved that intrathecal neostigmine is safe.

Yaksh TL, et al. [3] in 1995 studied that intrathecal neostigmine causes no spinal tissue toxicity in rats and dogs.

Naguib M, et al. [4] in 1997 studied increased level of acetyl choline binds to muscarinic and nicotinic receptors in the spinal cord dorsal horn and neostigmine increase level of acetylcholine in cerebrospinal fluid and acetylcholine bioavailability at cholinergic nerves within the spinal cord. Acetylcholine causes analgesia through direct action on spinal cholinergic muscarinic receptors M1, M3 and indirectly through the second messenger Nitric Oxide in spinal cord.

Concern of transdermal Nitroglycerin Patch

Ahmed, et al. [5] (2010) study showed that the combination of 5 mg/day transdermal nitroglycerin patch and intrathecal low dose neostigmine (5 mcg) resulted in an average of 10 hours of postoperative analgesia after total abdominal hysterectomy.

Meller ST, et al. [6], 1993 studied that NO synthase has neurons located in laminae I and II of the dorsal horn of spinal cord and probably function as interneuron modulating the sensory processing in spinal cord. The activation of descending pain pathways involves the participation of nitric oxide, which include activation of second messengers such as cyclic guanosine monophosphate (cGMP).

The objective of our study was to observe effect of transdermal nitroglycerin patch on the efficacy of low dose of intrathecal neostigmine with bupivacaine.

Demographic and surgical variables

Both the groups were comparable regarding demographic data like Age, Weight and ASA grade (p>0.05).

Different types of surgical cases were selected and allocated randomly in the two groups.

There was also no statistically significant difference between the two groups regarding duration of surgery as it was 79±11.80 min in Group A and 78.64+11.98 min in Group B.(P>0.05).

Preoperative vital parameters were also comparable in both groups.

Characteristics of sensory blockade

Ahmed, et al. [5] in 2010 studied that onset of sensory block was faster in neostigmine using groups.

In our study there was no statistically significant difference present regarding time of onset of sensory blockade as it was 3.12+0.60 min in Group A and 3.52+0.96 min in Group B (P>0.05).

Anand, et al. [7] in 2008 studied that two segment regression of sensory blockade was prolonged in neostigmine group (122.86+5.05 min) as compared to bupivacaine group (86.7+5.77 min).

Ahmed, et al. [5] (2010) studied there was no statistically significant difference was present regarding duration of regression time of sensory block by two segments.

In our study there was no statistically significant difference was present regarding time of two segment regression of sensory block as it was 136± 35.08 min in Group A and 139.72± 3.57 min in Group B (P>0.05).

Characteristic of motor blockade

Onset of motor block

Ahmed, et al. [5] in 2010 studied that there was no significant difference between onsets of motor block in neostigmine using group as compared to other groups.

Anand, et al [7] in 2008 studied that there was not any significant difference between two groups regarding time to achieve Grade 3 motor block.

In our study we did not find any significant difference between two groups regarding time to achieve complete motor blockade as it was 5.48+0.87 min in Group A and 5.52+0.87 min in Group B (P>0.05)

Duration of motor blockade

Ahmed, et al. [5] in 2010 studied that there was no significant difference between the duration of motor block in group using neostigmine as compared to group using neostigmine with nitroglycerin patch.

Anand, et al. [7] in 2008 studied that there was not any significant difference between two groups regarding time taken for Grade 3 to Grade 0 level of motor block.

In our study we did not find any significant difference between two groups regarding duration of motor block as it was 200 ± 6.75min in Group A and 201± 6.84 min in Group B (P>0.05).

Intra-operative hemodynamics monitoring

Hood B, et al. [2] (1995) in their study found that 150 mcg intrathecal neostigmine produces prolonged motor weakness and 750 mcg intrathecal neostigmine produces significant tachycardia and increase in blood pressure.

Gabrriela, et al. [8] in (2000) observed no bradycardia and hypotension in their study.

In our study we observed bradycardia in both groups in intra-operative period. It was 83.88±9.37, 82.04±8.51, 80.36±8.27, 77.28±8.04, 74.36±8.06, 71.16±13.71 at 5, 10, 15, 20, 25 and 30 minutes in Group A as compare to 85±9.29, 82.04±8.51, 80.365±8.27, 77.32±8.03, 75.28±7.15, 74.36±8.06 in Group B. Thereafter pulse rate was comparable in both the groups.

In our study significant fall in blood pressure was noted after 25 min in Group B **(**106.32±4.44, 65.68±4.02 min) as compare to Group A (107.52±4.87, 64.8±5.22 min) patients. Thereafter blood pressure was comparable in both the groups.

Post-operative hemodynamic monitoring

In our study there was no significant difference between two groups regarding postoperative hemodynamic monitoring both groups up to 12 hours.

Total duration of Analgesia

Lauretti GR, et al. [9] in 1996 studied that spinal neostigmine produces analgesia for vaginoplasty surgery similar in duration to spinal morphine and that the combination of morphine and neostigmine may allow a reduction in the dose of each component for postoperative analgesia.

Krukowski, et al. [10] in 1997 studied that intrathecal neostigmine can produce 10 hr post Cesarean section analgesia.

Lauretti GR, et al. [11] in 1999 evaluated the influence of transdermal nitroglycerin on the analgesic action of spinal sufentanil in patients undergoing Orthopedic surgery.

Anand, et al. [7] in 2008 studied that duration of analgesia was longer in intrathecal neostigmine (50 mcg) group (322.2+25.76 min) as compare to bupivacaine (15 mg) group (185.8+10.90 min).

Gurvinder, et al. [12] (2007), Gabriel R, et al. [8] (2000) and Ahmed, et al. [5] in 2010 studied that transdermal nitroglycerin would enhance analgesia of a low dose of intrathecal neostigmine with bupivacaine in patients undergoing Gynecologic surgery.

In our study there was significant difference between total duration of analgesia as it was longer duration in Group B (580±34.87 min) as compare to Group A (408±30.27 min) (P<0.05).

Peri operative Complications

Ahmed, et al. [5] (2010), Gurvinder, et al. [12] (2007), Gabriel R, et al. [8] (2000) in their studies found that 5 mcg of intrathecal

neostigmine produces prolonged analgesia without any major adverse effects.

Krukowski, et al. [10] (1997) in their study observed that intrathecal neostigmine in doses of >50 mcg resulted in nausea and vomiting.

In our study incidences of hypotension were more in Group B (36%) as compare to Group A (20%). In our study 5 patients in each group had bradycardia. Any other complications like nausea, vomiting, respiratory depression and shivering were not present in both the groups.

Conclusion

In our study of 50 patients we observed that intrathecal neostigmine 5 mcg with bupivacaine 15 mg with transdermal nitroglycerin patch (5 mg/day) markedly prolong duration of post operative analgesia than intrathecal neostigmine with bupivacaine alone. Intra-operative complication like bradycardia do occur but it was not significant, and other complication like hypotension occur with both groups but more in group B which requires monitoring .

So from my study it can be concluded that transdermal nitroglycerin patch increases post operative analgesia of low dose intrathecal neostigmine with bupivacaine in spinal anesthesia with less side effects.

References

1. R.D. Miller. Miller's Anesthesia. 7th edition, Elsevier, 2009, Chapter-58, p. 1799-1808.
2. Hood B, et al. Subarachnoid neostigmine potentiation of alpha 2-adrenergic aganist analgesia. Reg Anesth., 1995; 20: 121-7.
3. Yaksh TL. Studies on the safety of chronically administered intrathecal neostigmine methylsulfate in rats and dogs. Anesthesiology, 1995; 82: 412-27.
4. Naguib M, et al. Characterization of muscarinic receptor subtypes that mediate antinociception in the rat spinal cord. Anesth Analg., 1997; 85: 847-53. .
5. Ahmed, et al. Transdermal nitroglycerine enhances postoperative analgesia of intrathecal neostigmine following abdominal hysterectomies. Indian journal anaesthesia, 2010; 54(1): 24-28.
6. Meller St., et al. Nitric oxide (NO) and nociceptive processing in the spinal cord. Pain, 1993; 52: 127–36.
7. Anand, et al. Transdermal nitroglycerine enhances postoperative analgesia of intrathecal neostigmine following abdominal hysterectomies, 2008; Thesis submitted to Rajiv Gandhi University.
8. Gabriel R, Oliveira AP, Julião MC, Reis MP, Pereira NL. Transdermal nitroglycerine enhances spinal neostigmine postoperative analgesia following gynecological surgery. Anesthesiology, 2000; 93: 943-6.
9. Lauretti GR, et al. Transdermal nitroglycerine enhances spinal sufentanil postoperative analgesia following orthopedic surgery. Anesthesiology, 1999; 90: 734-9.
10. Krukowski JA, et al. Intrathecal neostigmine for post-cesarean section analgesia: Dose response. Anesth Analg., 1997; 84: 1269-75.
11. Lauretti GR, et al. Dose response study of intrathecal morphine versus intrathecal neostigmine, their combination, or placebo for postoperative analgesia in patients undergoing anterior and posterior vaginoplasty. Anesth Analg., 1996; 82: 1182–7.
12. Gurvinder, et al. Effect of transdermal nitroglycerine patch on analgesia of low dose intrathecal neostigmine: An evaluation. J Anesth Clin Pharmacol., 2007; 23: 159-62.