EFFECT OF TRANSDERMAL NITROGLYCERINE WITH BUPIVACAINE PLUS NEOSTIGMINE SPINAL ON THE DURATION OF ANALGESIA- A CASE CONTROL STUDY

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ABSTRACT

BACKGROUND
Neostigmine with bupivacaine is widely used for improving postoperative analgesia. However, to reduce the adverse effects and to prolong post-operative intrathecal analgesia other adjuvants have been used along with neostigmine.

MATERIALS AND METHODS
Patients aged between 30 to 50 years scheduled for surgery below the umbilicus, were systematically randomized into 2 groups. Both the groups received bupivacaine with neostigmine, only group 2 received transdermal nitroglycerine patch. Both the group were assessed for vitals & duration of analgesia.

RESULTS
The mean age was 34.5 ± 9.51 years in group I and 36.1 ±10.4 years in group II. There was no statistically significant difference in the vitals. Duration of analgesia was longest in group II and the difference between two groups was statistically significant.

CONCLUSION
Addition of transdermal nitroglycerine patch to bupivacaine + neostigmine spinal anaesthesia produced significant increase in duration of analgesia.

KEYWORDS
Nitroglycerine, Transdermal Analgesa.

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BACKGROUND
Surgical pain or “post-operative pain” is a universal phenomenon experienced by millions of patients, who undergoes surgical operation due to the severe tissue damage following the surgery.1 A pain free postoperative period aids in early mobilization and thereby reduces mortality and morbidity of any surgical operation.2

The importance of peripheral and central modulation in nociception has fostered the concept of “preemptive analgesia” in patients undergoing surgery. This type of management pharmacologically induces an effective analgesic state prior to the surgical trauma. This may involve infiltration of the wound with local anesthetic, central neural blockade, or the administration of effective doses of opioids, NSAIDS or ketamine. Experimental evidence suggests that preemptive analgesia can effectively attenuate peripheral and central sensitization to pain. Although some studies have failed to demonstrate preemptive analgesia in humans, other studies have reported significant reduction in postoperative analgesic requirements in patients receiving preemptive analgesia. Multimodal therapy is defined as two or more analgesic agents or techniques used in combination. The American Society of Anesthesiologists (ASA) “Practice Guidelines for Acute Pain Management in the Perioperative setting” contains the following statement: During the administration of anaesthetics for surgery, the needs of many patients may be best met by taking advantage of the combined effects of several agents. Similarly, there is growing conviction that a multimodality approach to providing perioperative analgesia has advantages over the use of a single modality. The literature supports the efficacy of two or more analgesic techniques (including non-pharmacologic methods) used in combination for the control of perioperative pain, especially when different sites and/or mechanisms of action are involved and/or when synergy of effect is achieved. The literature also indicates that multimodality approaches are associated with side effects, no greater than those resulting from single analgesic techniques for perioperative pain management.

Various drugs have been tried in the subarachnoid space along with local anesthetics with the aim of improving the duration of post-operative analgesia. The cholinesterase inhibitor, neostigmine is one such adjuvant which is widely used. However, it was associated with many unwanted side effects, hence to reduce the adverse effects and to prolong post-operative analgesia, other adjuvants have been used along with neostigmine.
The aim of this study was to systematically review current evidence of analgesic enhancement of intrathecal neostigmine by the addition of transdermal nitroglycerine patch on bupivacaine spinal anaesthesia.

**MATERIALS AND METHODS**

After approval from Ethical Committee, the study was conducted at Medical College Kottayam over a period of one year. This prospective study was conducted on 60 adult patients of ASA physical status I and II, aged 30 to 50 years scheduled for surgery below the umbilicus.

**Exclusion Criteria**

- Patient refusal.
- Patients having cardio-pulmonary illness.
- Patients having metabolic disorders.
- Patients with nervous system disorders.
- History of hypersensitivity reaction to any of the study medications.
- Patients having gastrointestinal disorders.
- Patients with sinus bradycardia.
- Bleeding disorder.
- Infection at the site of lumbar puncture.
- Patients on opioids or chronic analgesic abuse.

Patients were systematically randomized into 2 groups, consisting 30 patients in each group. Group I patients received intrathecal injection of 15 mg bupivacaine with 5 mcg of neostigmine and transdermal placebo patch (control group). Group II patients received intrathecal injection of 15 mg bupivacaine with 5mcg of neostigmine and transdermal nitroglycerine patch (5 mg/24 hours), applied on a non-anaesthetized area after 20 minutes (case group). Pre-anaesthetic checkup was done, all patients were familiarized with 0-10 cm visual analogue scale, for pain (VAS P) and nausea (VAS N). All patients received tab alprazolam 0.25 mg and tab ranitidine 150 mg orally on the previous night of surgery. Patients were pre-medicated with midazolam 0.05 mg/kg intravenously and hydration with ringer's lactate solution 10 ml/kg preoperatively in the holding room. Lumbar puncture was performed at L3-L4 level, with 26 gauge spinal needle and the drug solution was injected intrathecally over 30 seconds as per the group allocation. Heart rate and SpO2 were monitored continuously. Any fall in the heart rate below 60 beats per minute was treated with incremental doses of intravascular (IV) atropine 0.3 mg injection. Intraoperative nausea was treated by IV ondansetron 4 mg injection. Vitals were monitored throughout the surgery.

Data thus obtained were analyzed using Microsoft Excel 2003, Chi square test (Fisher Exact Probability Test) and student t test for comparison between groups. A 'p' value of <0.05 was considered significant.

**RESULTS**

In the present study, we included two groups with 30 study subjects in each group. The mean age was 34.5 ± 9.51 years in group I and 36.1 ± 10.4 years in group II.
Duration of analgesia was longest in group II and this difference was statistically significant.

**DISCUSSION**

Surgical operation involves tissue damage followed by post-operative pain, which delays the recovery and thereby increases the morbidity and mortality. An acceptable anaesthetic technique must have characteristics such as rapid onset and reversal of effects. It must maintain stable hemodynamic during operation without need to increase blood transfusion. Lastly, an excellent anaesthetic must decrease recovery room stay, while reducing postoperative pain, nausea, vomiting, and requirement for additional analgesics.

The aim of this study was to systematically review current evidence of analgesic enhancement of intrathecal neostigmine by the addition of transdermal nitroglycerine patch on bupivacaine spinal anaesthesia.

It has been proved that intrathecal neostigmine alone can be used to provide analgesia, but at higher doses which produces distressing adverse effects like severe nausea, vomiting and evacuation of bowel and bladder. This has precluded the use of neostigmine as a sole analgesic agent. When used in very low doses along with local anaesthetics like lignocaine or bupivacaine, it did not prolong postoperative analgesia.

In our study the duration of analgesia was analysed as period between complete onset of sensory blockade to the time at which patient started complaining of pain or first rescue analgesic was given using VAS score. On statistical analysis, patient belonging to group I complained of pain earlier than group II. There was statistically significant delay in the onset of pain in group II. Our study showed a mean duration of 7.142 (SD ± 1.81) hours inpatients belonging to group II. We came to conclusion that addition of a transdermal nitroglycerine patch (5 mg/24 hr) provides a good duration of postoperative analgesia and this correlates with the findings of Lauretti et al. and Gurvinder Kaur et al. 

Lauretti et al. in 2000 conducted a study to determine whether association of transdermal nitroglycerine would enhance analgesia from a low dose of intrathecal neostigmine in patients undergoing gynaecologic surgery during spinal anaesthesia. Their study shown that there were no significant changes on cardiovascular parameters, while using nitroglycerine transdermal patch along with intrathecal neostigmine.

**CONCLUSION**

Duration of analgesia was longest in bupivacaine + neostigmine + transdermal nitroglycerine group. Addition of transdermal nitroglycerine patch to bupivacaine + neostigmine spinal anaesthesia produced significant increase in duration of analgesia.

**REFERENCES**


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<tr>
<th>Group I</th>
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<td>Mean ± SD</td>
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<tr>
<td>2.36 ± 0.41</td>
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**Table 4. Comparison of Duration of Analgesia (Hours)**
