A CASE-CONTROL STUDY TO DETERMINE THE EFFECT OF INTRATHECAL NEOSTIGMINE WITH BUPIVACAINE ON THE DURATION OF ANALGESIA IN A TERTIARY CARE CENTER, KOTTAYAM

Unnikrishnannair Muralikrishnan

1Additional Professor and HOD, Department of Anaesthesia, Government Medical College, Kottayam, Kerala.

ABSTRACT

BACKGROUND

Pain is derived from the Latin word “poena”, which means penalty or punishment.1 The relief of pain is one of the paramount goals of medical science. The surgical operation causes extensive tissue damage, thereby causing stress response, which peaks during the postoperative period and has major effects on almost all body systems.

MATERIALS AND METHODS

Patients aged between 30 to 50 years scheduled for surgery below the umbilicus were systematically randomised into 2 groups. Both the groups received bupivacaine with transdermal nitroglycerine patch, only group 1 received neostigmine. Both the group were assessed for vitals, duration of analgesia, number of analgesia requirement and adverse effects.

RESULTS

The mean age was 36.1 ± 10.4 in group I and 35.9 ± 9.22 years in group II. There was no statistically significant difference in the vitals. Duration of analgesia was longest in group I and the difference between two groups was statistically significant. Requirement of rescue analgesic in 1st 24 hrs. was least in group I.

CONCLUSION

Addition of 5 mcg neostigmine alone to bupivacaine does not produce much difference in duration of analgesia and analgesic requirement.

KEYWORDS

Neostigmine, Transdermal Nitroglycerine Patch.

HOW TO CITE THIS ARTICLE: Muralikrishnan U. A case-control study to determine the effect of intrathecal neostigmine with bupivacaine on the duration of analgesia in a tertiary care center, Kottayam. J. Evid. Based Med. Healthc. 2017; 4(54), 3316-3318. DOI: 10.18410/jebmh/2017/658

BACKGROUND

Pain is derived from the Latin word “poena”, which means penalty or punishment.1 The relief of pain is one of the paramount goals of medical science. The surgical operation causes extensive tissue damage, thereby causing stress response, which peaks during the postoperative period and has major effects on almost all body systems.

Therefore, an acceptable anaesthetic technique should not only have rapid onset and reversal of effects, but also it must maintain stable haemodynamics during operation and reduce the postoperative pain, nausea, vomiting and requirement for additional analgesics.2 A pain-free and stress-free postoperative period reduces morbidity and mortality of any surgical operation. Spinal anaesthesia remains one of the basic techniques in modern anaesthesia despite waxing and waning of its popularity over 100 years since its introduction into clinical practice.3

Various drugs have been tried in the subarachnoid space along with local anaesthetics with the aim of improving the duration of postoperative analgesia. In the present study, we are determining the effect of neostigmine on postoperative pain.

MATERIALS AND METHODS

The present study was conducted among patients aged between 30 to 50 years scheduled for surgery below the umbilicus at Medical College Kottayam over a period of one year. Patients were randomised into 2 groups consisting of 30 patients in each group. Group I patients received intrathecal injection of 15 mg bupivacaine with 1 mL of normal saline with transdermal nitroglycerine patch (5 mg/24 hours). Group II patients received intrathecal injection of 15 mg bupivacaine with 5 mcg of neostigmine and transdermal nitroglycerine patch (5 mg/24 hours) applied on a non-anaesthetised area after 20 minutes. All patients were familiarised with 0-10 cm Visual Analogue Scale for Pain (VAS P) and Visual Analogue Scale for Nausea (VAS N). Rating scale of 0 equal to “no pain or nausea” and 10 equal to “worst possible pain or nausea.” All patients received Tab. Alprazolam 0.25 mg and Tab. Ranitidine 150 mg orally on the previous night of surgery. Patients were premedicated 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. Vitals were monitored throughout the surgery. Postoperatively, patients were assessed for pain by VAS rating scale at 15 minutes, 2 hours, 4 hours, 6 hours, 8 hours, 18 hours and 24 hours. Sedation score was evaluated at the above-mentioned time intervals and was recorded using Ramsay scale. Patients were also assessed for the side effects like nausea, vomiting, sedation, hypotension, bradycardia, sweating and palpitation at the above-mentioned time intervals.

Rescue analgesia was administered at VAS 4 or >4 (moderate pain). Duration of effective analgesia was measured from the time of intrathecal drug administration to the patient’s first request for analgesic.

Data thus obtained were analysed using Microsoft Excel 2003, Chi-square test (Fisher Exact Probability Test) and Student’s t-test for comparison between groups. A ‘p’ value of <0.05 was considered significant.

RESULTS

In the present study, 60 study subjects were randomly allocated into two groups with 30 each. The mean age, height and weight were 36.1 ± 10.4 years, 167.2 ± 7.49 cms and 68.0 ± 7.41 kgs in group I and 35.9 ± 9.22 years, 166.8 ± 8.03 kg, respectively in group II. However, the difference was not statistically significant.

There was no statistically significant difference in heart rate among the two groups.

<table>
<thead>
<tr>
<th>Heart Rate</th>
<th>Group I</th>
<th>Group II</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>76.43 ± 8.68</td>
<td>74.76 ± 7.45</td>
<td>0.42</td>
</tr>
<tr>
<td>Intraoperative</td>
<td>72.46 ± 7.51</td>
<td>71.36 ± 6.59</td>
<td>0.54</td>
</tr>
<tr>
<td>Postoperative</td>
<td>75.3 ± 7.68</td>
<td>74.76 ± 6.83</td>
<td>0.77</td>
</tr>
</tbody>
</table>

Table 1. Comparison of Heart Rate among the Two Groups

There was no statistically significant difference in mean arterial pressure in two groups. Duration of analgesia was longest in group I, which was 7.14 ± 1.81 and the duration of analgesia was 2.58 ± 0.49 in group II and this difference was statistically significant (p-value 0.0001).

<table>
<thead>
<tr>
<th>Mean Arterial Pressure</th>
<th>Group I</th>
<th>Group II</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative</td>
<td>86.76 ± 6.53</td>
<td>87.5 ± 5.9</td>
<td>0.64</td>
</tr>
<tr>
<td>Intraoperative</td>
<td>81.53 ± 4.81</td>
<td>83.73 ± 4.55</td>
<td>0.07</td>
</tr>
<tr>
<td>Postoperative</td>
<td>84.06 ± 4.41</td>
<td>85.93 ± 4.58</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Table 2. Comparison of Mean Arterial Pressure among Both the Groups

There was no statistically significant difference in sedation score in group I and group II.

<table>
<thead>
<tr>
<th>Sedation Scores</th>
<th>Group I</th>
<th>Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>9</td>
<td>9</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>11</td>
<td>12</td>
</tr>
</tbody>
</table>

Table 4. Comparison of Sedation Scores among the Two Groups

Both the groups had similar adverse events.

DISCUSSION

Although, main action of local anaesthetics in subarachnoid space is on the nerve roots and root ganglia, both at the same time, a subtle effect on the spinal cord tracts. This becomes apparent in segmental spinal anaesthesia, i.e. segment where the anaesthetic agent is deposited that area is fully blocked and segments below this, the finer sensations such as touch, temperature and two-point discrimination, which are conducted by more superficially located fibers in cord maybe blocked. However, sensations such as pain, pressure and proprioception, which are conducted by ascending fibers located deeper in spinal cord are not blocked and these impulses are carried past the segmental area completely blocked. Indirect effects of spinal anaesthesia are through paralysis of nerves.

Blockade of autonomic nervous system varies with the extent of anaesthesia. This is evident by haemodynamic changes. Sympathetics are usually blocked two segments higher than sensory blockade.

On cardiovascular system, spinal anaesthesia is associated with slowing of the heart rate. The degree of bradycardia as well as the frequency with which it occurs can be roughly correlated with the extent of sympathetic denervation. A reduction in blood pressure is an variable accompaniment of spinal anaesthesia in unoperated humans. In general, diastolic blood pressure is not decreased remarkably. The systolic blood pressure falls and there is no proportional fall in diastolic blood pressure. Spinal anaesthesia theoretically could influence cerebral blood flow altering either blood pressure or cerebrovascular resistance or both.

On respiratory system, alterations in pulmonary variables in healthy patients during spinal anaesthesia are usually of little clinical consequence. Also, spinal anaesthesia can partially suppress the stress response during major surgeries or totally block the response during lower extremity surgeries. Reduction of catecholamine release may decrease preoperative arrhythmias.
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, there was statistically significant delay in the onset of pain in group I. Our study showed a mean duration of 7.142 (SD ± 1.81) hrs. in patients belonging to group I. We came to conclusion that addition of a transdermal nitroglycerine patch (5 mg/24 hrs.) provides a good duration of postoperative analgesia and this correlates with the findings of Lauretti et al,4 Gurvinder Kaur et al,5 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 gynaecological surgery during spinal anaesthesia. They concluded that neither intrathecal 5 mcg neostigmine alone nor transdermal nitroglycerine alone (5 mg/day) delayed the time to administration of first rescue analgesics, the combination of both provided an average of 14 hrs. of effective postoperative analgesia after vaginoplasty suggesting that transdermal nitroglycerin and the central cholinergic agent neostigmine may enhance each other’s antinociceptive effects at the dose studied.6

Gurvinder Kaur et al in 2007 conducted a study to assess the effect of transdermal nitroglycerin patch (5 mg/24 hours) on the analgesia of intrathecal neostigmine (5 mg) and incidence of untoward effects. They found a statistically significant longer duration of analgesia in patients who received both intrathecal neostigmine and transdermal nitroglycerine than in patients who received neostigmine alone.5

Saini S et al (2006) conducted a study to evaluate the efficacy and safety of intrathecal neostigmine in two different doses for the relief of postoperative pain in patients undergoing elective lower abdominal surgery under spinal anaesthesia. The two study groups used intrathecal neostigmine in doses of 50 mcg and 150 mcg with bupivacaine. They concluded that intrathecal neostigmine in dose of 50 mcg is ineffective for analgesia and is also associated with increased incidence of vomiting. The higher incidence of adverse effects might restrict the usefulness of intrathecal neostigmine as the sole analgesic.6

The quality of analgesia was assessed using the pain score and patients were asked to give a global assessment of the overall effectiveness of the analgesic treatment. Based on this score, the quality of pain, which the patient complained after the regression of postoperative analgesia was easily controlled with NSAIDs like diclofenac injection.

The present study showed nausea and vomiting, which was significantly higher in both the groups. Nausea and vomiting incidences were controlled by intravenous ondansetron injection of 4 mg. This finding was consistent with the findings observed in various other studies.6,7,8

Hood DD et al in 1995 conducted a study on the safety assessment of intrathecal neostigmine, methyl sulfate in humans and concluded that the incidence of neostigmine side effects appears to be affected by dose, method of administration and baricity of solutions.7

Cho SS et al conducted a study to evaluate the efficacy and safety of effect of intrathecal neostigmine on post-caesarean section analgesia. Study was conducted using 0.2 mL of normal saline or neostigmine 12.5 mcg or neostigmine 25 mcg intrathecally with 0.5% hyperbaric bupivacaine. There were significantly higher incidences of nausea and vomiting in neostigmine groups than in saline group.8

CONCLUSION
Duration of analgesia was longest in bupivacaine + neostigmine + transdermal nitroglycerine group. Addition of 5 mcg neostigmine alone to bupivacaine does not produce much difference in duration of analgesia and analgesic requirement.

REFERENCES