Comparing the effects of oral clonidine premedication with intraoperative dexmedetomidine infusion on anesthesia requirement and recovery from anesthesia in patients undergoing major spine surgery.

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**Background**

Alpha 2 (α2) agonists - sedative, anxiolytic, analgesic, opioid and anesthetic sparing effects and attenuates the hemodynamic stress response to intubation and surgery, improves the quality of recovery.

It potentiated the analgesic effects of the opioid without increasing their hyperalgesic properties and side effects by acting on the different receptors and by different mechanisms.

Clonidine and Dexmedetomidine are the commonly used α2 agonists.

Dexmedetomidine has more selectivity towards the α2 receptor (α2/α2-ratio 1620:1) compared to clonidine (α2/α2-ratio 200:1). We wanted to compare the effects of these two drugs.

Primary outcome - Anesthetic requirement and recovery time.

Secondary outcome - Intraoperative hemodynamic response, analgesic requirement, blood loss, adverse events.

**Methods, Randomization, Blinding, Study Protocol**

Inclusion Criteria: ASA 1,2 patients between 18-60 years undergoing 2 or >2 level spinal decompression and fusion between Feb 2012 – October 2012.

Exclusion Criteria: ASA 3, 4 or patients, with the H/O liver or renal diseases or H/O allergy to study drugs, patients who are on chronic β blocker treatment with low baseline heart rate (less than 60/min) and pregnant patients.

Double blind, randomized control trial (patients and anesthesiologists involved in the patient care were blinded about the study drug).

Computer generated set of randomized numbers by using block randomization.

Two groups: Group A: Clonidine premedication (200 µg) 60 min prior to surgery

Group B: Dexmedetomidine infusion 1 µg/kg bolus 1b 0.5µg/kg/hr

Standard anesthesia protocol for induction and maintenance using Air, Oxygen and Isoflurane. Anesthetic concentrations was titrated to keep the BISs between 40-50.

Morphine and intravenous paracetamol was given for analgesia.

Hypotension was treated with propofol and fentanyl bolus. Hypotension was treated with ephedrine or phenylephrine boluses. Bradycardia associated with hypotension was treated with atropine.

HR, BP, ET iso concentration at 1, 5, 10 min during the bolus and at 15,15 min after pronging then every 15 min during the study drug infusion was noted.

Demographic, hemodynamic parameters, total dose of fentanyl and propofol used, duration of surgery (from the time of skin incision to end of skin closure), blood loss during surgery, recovery time (time of stopping the Isoflurane to the time of extubation), Number of episodes of hypotension, hypertension and bradycardia needed treatment were noted.

At the end of procedure, all patients were extubated after reversing the muscle relaxant effect with neostigmine and glycopyrrolate.

**Clinical Study Statement**

**Enrolment**

- Assessed for eligibility (n= 80)
- Excluded (n= 6)
- Randomized (n= 74)

**Allocation**

- Group A
  - Allocated to clonidine premedication (n= 37)
  - Received clonidine (n= 37)
  - Not received clonidine (n= 0)

- Group B
  - Allocated to dexmedetomidine (n= 37)
  - Received clonidine (n= 37)
  - Not received clonidine (n= 0)

**Follow up**

- Lost to follow up (n=0)
- Follow up

**Analysis**

- Analysed (n= 37)
  - Excluded from analysis (n=0)
  - Analysed (n= 37)
  - Excluded from analysis (n= 2)
  - Data missing, 1- Analgesia not titrated to BIS.

The mean with standard deviation and frequency with percentages were calculated. The statistical analysis was performed using independent sample t-test. P value < 0.05 was considered statistically significant.

**Statistical analysis**

The ET Iso concentration to maintain the BIS of 40-50 was similar between the two groups at intubation, 1, 5 and 15 minutes after prong position.

At 30 minutes to till the end of skin closure, the ET Iso concentration was lower in dexmed group compared to clonidine group. This was statistically significant at two hours and one after the pronging with α value of 0.001 and 0.003 respectively. (Figure 1)

At intubation, there was 17% reduction in ET Iso concentration in clonidine group (ET Iso 0.96) compared to clonidine group. This was statistically significant at one and two hours after the intubation.

There was no significant difference in recovery time (p=0.239) between the two agents. (Table 1).

There was no statistically significant difference in HR between the two groups during the study drug infusion.

Patients who received dexmed had significant drop in MBP during the first 30 min of pronging. After 30 min there was no difference in MBP between the two groups.

The episodes of hypotension and hypertension were similar between the two groups.

Two patients had bradycardia in clonidine group of which, one needed treatment with atropine.

Four patients had bradycardia in dexmed group where none required treatment with atropine.

**Conclusions**

Both clonidine and dexmedetomidine have anesthetic sparing effect; however, it was more with dexmedetomidine compared to clonidine.

Recapture from isoflurane anesthesia was similar between both groups.

Both are equally effective in controlling the hemodynamic response and reducing the blood loss during spine surgery.

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**Table 1: Demography and Intraoperative parameters**

<table>
<thead>
<tr>
<th>Character</th>
<th>Group A (Clonidine)</th>
<th>Group B (Dexmedetomidine)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total no of patients</td>
<td>37</td>
<td>33</td>
<td></td>
</tr>
<tr>
<td>Age (years ± SD)</td>
<td>48±6.12</td>
<td>44±13.6</td>
<td></td>
</tr>
<tr>
<td>Sex (Male:Femail)</td>
<td>18:19</td>
<td>18:15</td>
<td></td>
</tr>
<tr>
<td>Weight (Kg ± SD)</td>
<td>60.2±16.7</td>
<td>59.3±8.13</td>
<td></td>
</tr>
<tr>
<td>Duration of surgery (hours ± SD)</td>
<td>3.68±1.0973</td>
<td>3.37±0.9064</td>
<td></td>
</tr>
<tr>
<td>Recovery time (in minutes)</td>
<td>8.15±5.15</td>
<td>8.51±3.79</td>
<td>0.239</td>
</tr>
<tr>
<td>Total dose of fentanyl used (µg/kg ± SD)</td>
<td>3.14±0.93</td>
<td>2.83±1.05</td>
<td>0.206</td>
</tr>
<tr>
<td>Total dose of Propofol used (mg/kg ± SD)</td>
<td>2.35±0.94</td>
<td>2.46±1.03</td>
<td>0.644</td>
</tr>
<tr>
<td>Average blood loss (mL ± SD)</td>
<td>350±218</td>
<td>340±103</td>
<td>0.880</td>
</tr>
<tr>
<td>Average amount of crystalloid given (mL ± SD)</td>
<td>1135±253</td>
<td>1106±242</td>
<td>0.623</td>
</tr>
<tr>
<td>Average amount of colloid given (mL ± SD)</td>
<td>672±241</td>
<td>560±165</td>
<td>0.505</td>
</tr>
<tr>
<td>Average amount of packed red cell transfusion</td>
<td>350±000</td>
<td>480±230</td>
<td>0.423</td>
</tr>
</tbody>
</table>

**Figure 1: ET Isoflurane concentration at various time period during the study drug infusion.**