Comparision of Nicardipine with Nitroprusside for Controlled Hypotensive Anesthesia in Spinal Fusion

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Introduction

After approval of intervertebral fusion cages in the U.S. in 2006 by FDA, spinal fusion has been steadily increased for spinal stenosis, as estimated 10.8 of 100,000 persons who are older than 20 years and 90 of 100,000 persons who are older than 60 years in US.(1)

Although more than 80% of the patients who underwent spinal fusion were relieved some degree of symptom by the surgery, Doyo et al.(2) reported that the blood transfusion rate during spinal fusion was 5.8 times greater compared to the elderly patients undergoing spinal surgery without spinal fusion and Lee et al.(3) revealed that postoperative delirium after spinal surgery was significantly related to the intraoperative blood loss and hemoglobin and hematocrit levels at first day after surgery in Korean population. Controlled hypotensive anesthesia (CHA) technique is used mainly to decrease bleeding during surgery and consequently diminish the chance of the homologous blood products transfusion for fear of comorbidity related to transfusion. Nicardipine (NIC) has an excellent vasodilating action while decreasing mean arterial pressure (MAP), maintaining coronary blood flow, myocardial contractility cardiac filling pressures and cardiac output, and limited rebound tachycardia.(4) Although NIC is superior to sodium nitroprusside (SNP) in less probability of profound hypotension,(5) coronary steal phenomenon, increased intracranial pressure and no cyanide toxicity in long-term use,(6) clinical experience and use of NIC for hypotensive anesthesia has been limited.

The aim of this study was to compare the amount of transfusion, hemodynamic profiles, like cardiac index (CI) and stroke volume index (SVI) and comorbidity related to transfusion in NIC group on long duration hypotensive anesthesia in lumbar spinal fusion with those of SNP.

Methods

This study was approved by the Institutional Review Board of our institute and informed consent was
obtained. Twenty-three patients, ASA physical status I or II, scheduled for spinal surgery were enrolled in this study. Patients who had uncontrolled hypertension, coronary artery disease, congestive heart failure, liver disease, renal disease, and abnormal coagulation profile were excluded. Same surgeon performed lumbar spinal fusion for spinal stenosis (range from L3 to S1).

Anesthesia was induced with propofol 1 mg/kg and fentanyl 2 $\mu$g/kg. Intubation was facilitated by vecuronium 0.15 mg/kg. Anesthesia was maintained with isoflurane 0.6 vol% and fentanyl 2 $\mu$g/kg/h, supplemented with 50% nitrous oxide in oxygen and intermittent doses of vecuronium. Lungs were mechanically ventilated with tidal volume 10 ml/kg and respiration rates were adjusted to maintain normocapnia.

Perioperative monitoring included electrocardiogram, pulse oximetry, capnography, nasopharyngeal temperature, invasive blood pressure, and urine output. In addition, cerebral hemoglobin oxygen saturation using Cerebral Oximeter™ (Somanetics Corp., Michigan, USA) and hemodynamic variables using Esophageal Doppler Monitor™ (Deltex Medical Inc., West Sussex, UK) were continuously measured. A prospective, randomized study was planned. Before surgery, patients were randomly allocated using Research Randomizer (4) to one of two groups. Attending anesthesiologists knew only the agent of intraoperative controlled hypotension and the target hemoglobin (above 9 g/dL).

We allowed them to use the parameters measured by Esophageal Doppler Monitor™ for fluid management including crystalloid, colloid and 400 ml-pack red blood cells (PRBCs). At surgical incision, SNP (0.25 mg/ml, Nitropress®, Abbott Laboratory, USA) or NIC (0.2 mg/mL, Perdipine®, Yamanouchi Pharmaceuticals, Korea) infusion was started through central venous route in internal jugular vein. In SNP group (n=10), infusion was initiated at 0.5 $\mu$g/kg/min and adjusted to maintain mean arterial pressure (MAP) to 75% of that of baseline (T0). In NIC group (n=13), infusion was initiated at 10 $\mu$g/kg/min and adjusted to maintain MAP to 75% of baseline (T0). Both agent was stopped after instrumentation.

Heart rate (HR), MAP, cerebral hemoglobin oxygen saturation (ScO2), cardiac index (CI), and stroke volume index (SVI) were measured and plasma concentration of epinephrine (Epi), norepinephrine (NE), dopamine (Dopa), and renin activity (RA) were estimated by amperometry at the following times: at baseline before induced hypotension (T0), 80 minutes after vasodilator start (T1), just before the end of vasodilator infusion (T2), and then, 20 and 80 minutes after (T3 and T4) discontinuation of each agent. Using Esophageal Doppler Monitor, Peak velocity (Pv) and corrected flow time (FTc) were measured and compared at T0, T1, T2, and T3. Because the esophagus is assumed to lie parallel to the descending aorta and the body of the Doppler probe is in line with the esophagus, the esophageal Doppler monitor can show the descending aorta Pv measured during systole and flow the time of systolic aortic blood flow. FTc is the time of systolic aortic blood flow corrected for heart rate and inversely correlated with the systemic vascular resistance.(9) Although stroke volume is derived in Esophageal Doppler Monitor by Pv and FTc, we recorded Pv and FTc because there are some assumption to calculate stroke volume.

Estimated blood loss (EBL) was derived from the amount of collected blood in suction bottle and the weight difference between dried gauze and blood soaked gauze.

Statistics analyses were performed with the SAS 8.2 version. Mann-Whitney test, fisher’s exact test, independent t-test and repeated measured ANOVA was employed. A P<0.05 indicated statistical significance.
Table 1. Demographic Characteristics of Patients Presenting for Spinal Surgery

<table>
<thead>
<tr>
<th></th>
<th>SNP group</th>
<th>NIC group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>60.2±11.5</td>
<td>56.9±9.8</td>
<td>0.410</td>
</tr>
<tr>
<td>Sex (Female : Male)</td>
<td>6 : 4</td>
<td>8 : 5</td>
<td>1.0000</td>
</tr>
<tr>
<td>ASA group (I : II)</td>
<td>8 : 2</td>
<td>10 : 3</td>
<td>1.0000</td>
</tr>
<tr>
<td>Fusion Level</td>
<td>2.1±0.4</td>
<td>1.9±0.4</td>
<td>0.446</td>
</tr>
<tr>
<td>Length of Stay (days)</td>
<td>15.1±6.2</td>
<td>13.1±7.9</td>
<td>0.313</td>
</tr>
</tbody>
</table>

Values are mean±standard deviation. There were no differences between the SNP and NIC groups. SNP: Sodium Nitroprusside, NIC: Nicardipine.

Table 2. Intraoperative Variables of Patients Presenting for Spinal Surgery

<table>
<thead>
<tr>
<th></th>
<th>SNP</th>
<th>NIC</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before Surgery</td>
<td>12.3±1.7</td>
<td>12.2±1.3</td>
<td>1.0000</td>
</tr>
<tr>
<td>At PACU</td>
<td>9.1±1.3</td>
<td>10.5±1.1</td>
<td>0.0429</td>
</tr>
<tr>
<td>Anesthetic Time (minutes)</td>
<td>368.8±197.1</td>
<td>266.3±60.7</td>
<td>0.2436</td>
</tr>
<tr>
<td>Operation Time (minutes)</td>
<td>312±136</td>
<td>239±37</td>
<td>0.4423</td>
</tr>
<tr>
<td>Crystalloid (ml)</td>
<td>3762.5±1083.6</td>
<td>3362±962.4</td>
<td>0.393</td>
</tr>
<tr>
<td>Colloid (mL)</td>
<td>625±231.5</td>
<td>675±271.2</td>
<td>0.413</td>
</tr>
<tr>
<td>PRBCs (units)</td>
<td>3.2±1.3</td>
<td>1.8±1.2*</td>
<td>0.0418</td>
</tr>
<tr>
<td>Blood Loss (mL)</td>
<td>3005.4±1756.7</td>
<td>1412.5±364.3*</td>
<td>0.0253</td>
</tr>
<tr>
<td>U/O (ml/hr)</td>
<td>127.3±60.3</td>
<td>138.3±93.1</td>
<td>0.963</td>
</tr>
</tbody>
</table>

Values are mean±standard deviation. SNP: Sodium Nitroprusside, NIC: Nicardipine, PACU: Postanesthetic Care Unit, PRBCs: Packed Red Blood Cells. * P<0.05 compared with SNP group.

Results

No difference was observed between two groups with respect to age, sex, ASA group, operation time, preoperative hemoglobin level, and units of transfused 400 ml-PRBC (Table 1). But, hemoglobin level at 30 minutes after arrival at postanesthesia care unit was significantly higher (P<0.05) and estimated blood loss was significantly less in NIC group (P<0.05) compared with those of SNP group (Table 2). There was no significant difference in administered fluid amount and hourly urine output. The length of hospital stay was shorter in NIC group than in SNP group, even though it was statistically insignificant.

The average infusion rate of SNP and NIC was 0.5 and 1.9 g/kg/min, respectively. Median time of obtaining target blood pressure level in NIC and SNP group was 8.5 min (interquartile range=6.5~18.0) and 18.5 min (interquartile range=8.2~21.9), respectively (P=0.336). Median time of returning to baseline blood pressure level in NIC and SNP group was 27.00 min (interquartile range=26.0~35.0) and 15.0 min (interquartile range=11.8~27), respectively (P<0.05).

MAP, HR, SVI, and CI between baseline and hypotension were similar between the two groups. In NIC group, MAP at T3 remained significantly lower than T0 and HR continues to increase till T4, while increasing CI and maintaining SVI in both groups (Table 3). In NIC group, Pv was significantly increased at T1 and T3 (P<0.05), and FTc was significantly increased at T1 (P<0.05) and there was no significant difference in ScO2 between two groups (Table 4). Interestingly, in NIC group, plasma concentration of Epi and NE was significantly increased till T4 (P<
Table 3. Hemodynamic Variables Before, During, and After Nitroprusside and Nicardipine Administration

<table>
<thead>
<tr>
<th>Time Point</th>
<th>MAP (mmHg)</th>
<th>P-value</th>
<th>HR (per min)</th>
<th>P-value</th>
<th>CI (L/min/m²)</th>
<th>P-value</th>
<th>SVI (ml/m²)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNP T0</td>
<td>76±12</td>
<td>-</td>
<td>74±10</td>
<td>-</td>
<td>2.9±0.7</td>
<td>-</td>
<td>37±9</td>
<td>-</td>
</tr>
<tr>
<td>T1</td>
<td>59±11*</td>
<td>0.0024</td>
<td>74±13</td>
<td>1.0000</td>
<td>4.3±1.9</td>
<td>0.2816</td>
<td>51±9*</td>
<td>0.0006</td>
</tr>
<tr>
<td>T2</td>
<td>58±11*</td>
<td>0.0006</td>
<td>80±9</td>
<td>0.4092</td>
<td>3.7±1.1</td>
<td>0.6294</td>
<td>38±11</td>
<td>1.0000</td>
</tr>
<tr>
<td>T3</td>
<td>72±12</td>
<td>1.0000</td>
<td>81±13</td>
<td>0.3366</td>
<td>3.1±1.2</td>
<td>1.0000</td>
<td>34±5</td>
<td>0.8358</td>
</tr>
<tr>
<td>T4</td>
<td>81±10</td>
<td>1.0000</td>
<td>83±13*</td>
<td>0.0336</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>NIC T0</td>
<td>77±19</td>
<td>-</td>
<td>67±10</td>
<td>-</td>
<td>2.5±0.8</td>
<td>-</td>
<td>35±15</td>
<td>-</td>
</tr>
<tr>
<td>T1</td>
<td>54±9*</td>
<td>0.0006</td>
<td>68±5</td>
<td>1.0000</td>
<td>3.6±1.5*</td>
<td>0.0420</td>
<td>43±18</td>
<td>0.7446</td>
</tr>
<tr>
<td>T2</td>
<td>55±10*</td>
<td>0.0006</td>
<td>72±7</td>
<td>1.0000</td>
<td>2.7±1.1</td>
<td>1.0000</td>
<td>37±17</td>
<td>1.0000</td>
</tr>
<tr>
<td>T3</td>
<td>64±12*</td>
<td>0.0414</td>
<td>76±10</td>
<td>0.1956</td>
<td>4.0±2.0</td>
<td>0.0816</td>
<td>41±15</td>
<td>1.0000</td>
</tr>
<tr>
<td>T4</td>
<td>79±9</td>
<td>1.0000</td>
<td>95±8*</td>
<td>0.0006</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Values are mean±standard deviation. SNP: Sodium Nitroprusside, NIC: Nicardipine, PACU: Postanesthetic Care Unit, PRBCs: Packed Red Blood Cells. * P<0.05 compared with SNP group.

Table 4. Changes of the Cardiac Function and Metabolic Variable Before, During, and After Nitroprusside and Nicardipine Administration

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Time Point</th>
<th>FTc (ms)</th>
<th>P-value</th>
<th>P(velocity (cm/sec)</th>
<th>P-value</th>
<th>ScO₂ (%)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNP T0</td>
<td>376.0±60.0</td>
<td>-</td>
<td></td>
<td>59.2±21.0</td>
<td>-</td>
<td>66.9±13.9</td>
<td>-</td>
</tr>
<tr>
<td>T1</td>
<td>402.3±57.0</td>
<td>1.0000</td>
<td>75.8±30.8*</td>
<td>0.0222</td>
<td>64.3±13.5</td>
<td>0.5934</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>345.6±42.2</td>
<td>0.9618</td>
<td>66.8±24.8</td>
<td>0.0984</td>
<td>60.1±12.4</td>
<td>0.0594</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>364.6±49.5</td>
<td>0.2670</td>
<td>57.5±23.6</td>
<td>0.0630</td>
<td>59.7±13.4</td>
<td>0.2406</td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td>345.6±42.2</td>
<td>0.2826</td>
<td>66.8±24.8</td>
<td>1.0000</td>
<td>61.3±12.2</td>
<td>0.2160</td>
<td></td>
</tr>
<tr>
<td>NIC T0</td>
<td>326.1±67.1</td>
<td>-</td>
<td></td>
<td>60.0±23.3</td>
<td>-</td>
<td>61.9±6.9</td>
<td>-</td>
</tr>
<tr>
<td>T1</td>
<td>384.9±42.4*</td>
<td>0.0246</td>
<td>71.9±24.6*</td>
<td>1.0000</td>
<td>67.4±8.7</td>
<td>0.2598</td>
<td></td>
</tr>
<tr>
<td>T2</td>
<td>340.1±72.1</td>
<td>1.0000</td>
<td>65.5±25.9</td>
<td>0.0024</td>
<td>60.9±8.7</td>
<td>1.0000</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>363.5±68.5</td>
<td>1.0000</td>
<td>68.1±24.7*</td>
<td>0.0630</td>
<td>58.2±7.6</td>
<td>1.0000</td>
<td></td>
</tr>
<tr>
<td>T4</td>
<td>322.3±82.3</td>
<td>1.0000</td>
<td>65.5±25.9</td>
<td>1.0000</td>
<td>59.6±5.9</td>
<td>1.0000</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean±Standard deviation. SNP: Sodium Nitroprusside, NIC: Nicardipine, FTc: Corrected Flow Time, P(velocity: Peak Velocity, ScO₂: Cerebral Hemoglobin Oxygen Saturation, CI: Cardiac Index, SVI: Stroke Volume Index, T0: at baseline before induced hypotension, T1: 80 minutes after vasodilator start, T2: just before the end of vasodilator, T3: 20 minutes later discontinuation of each agent, T4: 80 minutes later discontinuation of each agent. Within the groups: *P<0.05 compared to T0.

Discussion

There have been some clinical studies comparing NIC with other various agents and most of them used SNP to compare for the CHA.(8-11) However, they failed to prove the superiority of NIC to SNP in a decrease of blood loss and transfusion rate. There was no difference in preoperative hemoglobin level and the amount of packed RBCs, but, hemoglobin level at postanesthesia care unit was significantly higher in NIC group, even though we used same transfusion strategy. In our study, bias including uncontrolled hypertension, coronary artery disease, congestive heart failure, liver disease, renal disease, and abnormal coagulopathy were ruled out as in the previous studies, it will be clinically worthy to prove the usefulness of the CHA - bleeding
Table 5. Plasma Catecholamine Concentration and Renin Activity Before, During and After Nitroprusside and Nicardipine Administration

<table>
<thead>
<tr>
<th>Time point</th>
<th>Epi (pg/mL)</th>
<th>P-value</th>
<th>NE (pg/mL)</th>
<th>P-value</th>
<th>Dopa (L/min/m²)</th>
<th>P-value</th>
<th>RA (ng/ml/h)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNP</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>33.6±25.1</td>
<td>-</td>
<td>243.7±121.1</td>
<td>-</td>
<td>22.9±12.3</td>
<td>-</td>
<td>3.2±2.9</td>
<td>-</td>
</tr>
<tr>
<td>T1</td>
<td>79.5±99.2</td>
<td>1.0000</td>
<td>283.1±69.4</td>
<td>1.0000</td>
<td>36.6±24.7</td>
<td>0.2316</td>
<td>4.5±5.6</td>
<td>1.0000</td>
</tr>
<tr>
<td>T2</td>
<td>122.9±120.1</td>
<td>0.2046</td>
<td>462.6±423.1</td>
<td>1.0000</td>
<td>30.2±30.2</td>
<td>1.0000</td>
<td>4.2±4.2</td>
<td>0.8286</td>
</tr>
<tr>
<td>T3</td>
<td>64.7±72.4</td>
<td>1.0000</td>
<td>394.9±251.2</td>
<td>0.8700</td>
<td>37.1±17.5</td>
<td>0.5868</td>
<td>4.4±4.6</td>
<td>1.0000</td>
</tr>
<tr>
<td>T4</td>
<td>251.0±143.1</td>
<td>0.0012</td>
<td>415.3±192.1</td>
<td>0.1704</td>
<td>38.3±16.1</td>
<td>0.1248</td>
<td>4.3±5.6</td>
<td>1.0000</td>
</tr>
<tr>
<td>NIC</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>T0</td>
<td>16.1±6.5</td>
<td>-</td>
<td>198.4±52.7</td>
<td>-</td>
<td>22.0±19.9</td>
<td>-</td>
<td>3.4±3.2</td>
<td>-</td>
</tr>
<tr>
<td>T1</td>
<td>80.6±72.6</td>
<td>0.0744</td>
<td>276.9±108.6</td>
<td>0.1266</td>
<td>25.9±10.3</td>
<td>1.0000</td>
<td>7.0±4.0*</td>
<td>0.0432</td>
</tr>
<tr>
<td>T2</td>
<td>62.1±59.3</td>
<td>0.1284</td>
<td>334.1±125.6</td>
<td>0.0012</td>
<td>29.6±18.5</td>
<td>1.0000</td>
<td>9.0±5.7</td>
<td>0.1464</td>
</tr>
<tr>
<td>T3</td>
<td>56.4±15.7*</td>
<td>0.0006</td>
<td>329.8±94.1</td>
<td>0.0006</td>
<td>34.9±12.1</td>
<td>0.4440</td>
<td>8.1±6.9</td>
<td>0.5634</td>
</tr>
<tr>
<td>T4</td>
<td>234.3±86.9*</td>
<td>0.0006</td>
<td>377.9±78.0</td>
<td>0.0006</td>
<td>32.0±17.7</td>
<td>1.0000</td>
<td>7.8±4.3</td>
<td>0.1350</td>
</tr>
</tbody>
</table>

Values are mean±Standard deviation. SNP: Sodium Nitroprusside, NIC: Nicardipine, Epi: Epinephrine, NE: Norepineprine, Dopa: Dopamine, RA: Renin, T0: at baseline before induced hypotension, T1: 80 minutes after vasodilator start, T2: just before the end of vasodilator, T3: 20 minutes later discontinuation of each agent, T4: 80 minutes later discontinuation of each agent. Within the groups: *P<0.05 compared to T0.

reduction with little side effects.

NIC antagonizes the cellular entry of calcium through calcium channels to produce vasodilatation on coronary, cerebral and systemic vasculature through relaxation of smooth muscle fiber and inhibition of sympathetic nerve.(4) The sympathetic nerve reactions limit a decrease of cardiac contractility and produce an increase of cardiac output. It prevents rebound hypertension and reduces blood loss as a consequence of a prolonged hypotension, despite of an increase in plasma renin activity and catecholamine concentration.(5) It shows fast onset time of 1 or 2 minutes and the mean duration of action of 24 minutes.(4)

SNP is regarded as a reference agent of CHA because of the very fast onset and offset time since the 1950s.(5) This agent initially relaxes the resistance vessels by way of causing venous dilatation and reducing venous return, and secondarily dilates the arterial vasculature to produce a direct peripheral vasodilatation. (5) The peripheral vasodilatation leads to baroreceptor-induced reflex tachycardia and an increase in myocardial contractility. Its disadvantages involve tachyphylaxis, rebound hypertension, increased intrapulmonary shunt, inhibition of platelet aggregation and cyanide toxicity. The activation of sympathetic and renin-angiotensin system, which increase cardiac output, plasma catecholamine concentration and renin activity, is accountable for rebound hypertension through long lasting effects even after its discontinuation.

We observed no rebound hypertension but only tachycardia in both groups in 80 minutes after discontinuation. Kim et al.(12) revealed that continuous NIC infusion during tracheal intubation attenuated an increase in blood pressure while it significantly stimulated an increase of HR. Although NIC is regarded as an excellent vasodilator with less reflex tachycardia than SNP, there have been several studies that its administration may result increase in HR.(13-14) In our study, HR showed to increase till 80 minutes later discontinuation and only HR recorded at 80 minutes later discontinuation in both group was statistically significant. The tachycardia may result from the sympathetic activation responding to the decreased arterial BP and the elevated catecholamine according to
the continuous infusion of NIC and surgical stimula-
tion. While SNP group showed elevated Epi concentra-
tion only in 80 minutes after discontinuation, NIC
group presented persistently elevated Epi and NE from
20 minutes to 80 minutes after discontinuation of NIC.
The extended study interval to reinstate catecholamine
concentration affecting MAP, HR and SVR addressed
the question whether the favorable effect of NIC to
reduce bleeding and transfusion rate is owing to a
prolonged effect to increase of SVR through stimulated
catecholamine after discontinuation. In spite of this
issue, compared with SNP, NIC is more favorable and
suitable for controlled hypotension because NIC is
photosensitive, water-soluble and metabolically neutral,
rapidly distributed, extensively metabolized in the liver,
and rapidly eliminated.(15)

Degoute(6) hypothesized that the factor to decide the
quantity of bleeding is dependent on the vascular
resistance. He explained that bleeding is an amount of
flowed blood to the operative field in a given time and
this flow can be expressed in pressure over vascular
resistance. If the pressure decreases to the target
pressure, and the resistance remains constant or
increases (vasoconstriction), the flow would decrease.
On the other hand, if both the pressure and the
resistance (vasodilatation) are stable, the flow would
remain constant or change little. Among our measuring
values, the pressure can be substituted by MAP and
resistance can be switched by FTC because the FTC is
inversely correlated with the systemic vascular
resistance.(13) According to this hypothesis, we could
expect the quantity of bleeding using FTC times MAP.
SNP group showed larger numeric value of MAP times
FTC than NIC during infusion of each agent. Despite
the limitation that there are many methods to predict
the quantity of bleeding and to prove the statistical
analysis, the calculated values of our study showed that
there was a quite difference in flow (bleeding) between
each agent and we could find a tendency of lesser
blood loss in NIC group than SNP group. The lesser
blood loss may lead to lesser fluid administration,
lesser transfusion, and greater hemoglobin at PACU
(Table 2).

We performed transfusion to maintain a certain level
of hemoglobin (9 g/L) because we thought that it is
unethical to avoid transfusion in the belief in favor of
the controlled hypotension anesthesia. However, there
was a significant difference of hemoglobin at PACU
between both groups. It seemed to be unreliable to
compare postoperative hemoglobin and hematocrit with
those of preoperative values as the parameter to expect
blood loss due to preoperative fluid administration.
However, there was no significant difference in the
administered fluid amount and the factors reflecting
regional blood flow such as ScO₂ and hour urine
output between two groups in our study. Also, there
was no evidence of rebound hypertension in both
groups. Twenty minutes after discontinuation of
infusion of the agents, MAP of NIC group significantly
decreased while that of SNP group was normalized to
the level before its administration. We thought that this
extended hypotensive duration in NIC group contrib-
uted to lesser blood loss than SNP group. Factors
involving in bleeding are not only regional blood flow
which was determined by MAP and SVR, but also
another elements such as 1) the applied technique: the
action of the agents used on the cardiovascular system,
2) the mechanisms that these agents antagonise, and 3)
the counter-regulatory mechanisms.(5) Furthermore,
those factors may make our results more reliable. Our
results showed accordance with those of Byeon et al.
(4) and they recommended that NIC is more ideal
agent for CHA than any other antihypertensive drugs.

CHA may result in the better and drier operative
field. And it probably allows more accurate dissection
and lesser surgical complications such as unintentional
Table 6. Quality of Surgical Field

<table>
<thead>
<tr>
<th>Score</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>5</td>
<td>Massive uncontrollable bleeding</td>
</tr>
<tr>
<td>4</td>
<td>Bleeding, heavy but controllable, that significantly interferes with dissection</td>
</tr>
<tr>
<td>3</td>
<td>Moderate bleeding that moderately compromises surgical dissection</td>
</tr>
<tr>
<td>2</td>
<td>Moderate bleeding, a nuisance but without interfering with accurate dissection</td>
</tr>
<tr>
<td>1</td>
<td>Bleeding, so mild it was not even a surgical nuisance</td>
</tr>
</tbody>
</table>

surgical trauma to vessels, infection, hematoma or related reoperation and, consequently, to reduce the total operation time. Table 2 shows the advantages of NIC compared with SNP. In NIC group, the length of stay and the operation time were shorter as well as the unit of transfused packed RBCs and the amount of blood loss were smaller than SNP group. We experienced only one patient in SNP group got an emergency hematoma removal on 3rd day after operation.

There are some potential limitations in our study. First, we did not evaluate the quality of operative field using objective criteria, even though we manifested the better surgical outcomes in NIC group. The most common method to evaluate the quality of operative field is the numerical scale by Fromme et al.(15) (Table 6). Second, we did not assess the effect of each agent on the platelet aggregation. There have been limited studies comparing how much SNP and NIC affect the platelet aggregation and perioperative bleeding. Most studies revealed that they decreased platelet aggregation.(2,16-17) It is unclear whether decreasing platelet aggregation contributes to increased blood loss in the SNP group than NIC group. Third, our patient numbers seemed to be small. Power analysis demonstrated that twenty eight patients in each group were sufficient to have a >80% chance of detecting a difference of 1.0 g/dL of hemoglobin at the 5% level of significance. Although it is hard to believe whether there is practical significance, our preliminary study can support nicardipine group showed obviously less perioperative transfusion amount and more post-operative hemoglobin level compared with SNP and further study based on this study can be revealed them with satisfactorily statistical power. Finally, our study did not investigate the potential advantages of CHA over normotensive anesthesia because we excluded normotensive anesthesia group.

In conclusion, continuous NIC infusion can be a easy and safe strategy for CHA in case of spinal fusion compared to SNP infusion. Continuing elevation of Epi and NE after discontinuation of NIC may affect the peripheral vasculature as well as MAP, even though it did not happen to present any obstacles in clinical situation. NIC showed its beneficial effect for spinal fusion because it reduces comorbidity related to transfusion and hemorrhage resulting from lesser blood loss as a reference agent for CHA than SNP.

Abstract

요척추 융합술에서 유도저혈압마취를 위한 니카디핀과 니트로푸루시드의 비교

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연구배경: 니카디핀(nicardipine)은 평균동맥압을 감소시키고, 심장충만압과 심박출량을 유지시키며 반동빠른맥을 제한시킨다. 니트로푸루시드(nitroprusside)는 정맥혈압과 심장혈관저항협을 동반할 전신혈관저항의 감소, 두개내압의 상승, 시안화물 독성의 특정을 보인다. 저자들은 혈류역학 효과, 교감신경 활성도, 실험과정 그리고 유도저혈압의 제어가능 정도의 관점에서 니카디핀과 니트로푸루시드를 비교하였다.

방법: 요척추 융합술이 예정된 23명의 환자를 대
상으로 전향적 임의선택연구가 시행되었다. 니카디핀 또는 니트로푸루시드가 수술 중 저혈압 유도를 위하여 지속적으로 주입되었다. 수술 전 (T0), 지속 주입 80분 후 (T1), 지속 주입의 중단 직전 (T2), 지속 주입의 중단 후 20분 (T3), 80분 (T4)에 수혈량, 실혈량, 심박동수, 평균동맥압, 심장박출지수, 박출량지수 그리고 에피네프린과 노르에피네프린의 혈장 농도를 측정하였다.

결과: 니카디핀군은 니트로푸루시드군에 비하여 실혈량이 적었고(\(P<0.05\)) 회복실에서 높은 혈색소치를 보였다. 니카디핀군은 수술 전에 비해서 T3까지 평균동맥압이 낮게 유지되었으며, 심박동수는 수술 전에 비해서 T4까지 증가되어 있었다. T1에서 심장박출지수는 니카디핀군에서, 박출량지수는 니트로푸루시드군에서 의미있게 증가되었다. 특히, 니카디핀군에서 에피네프린과 노르에피네프린의 혈장농도가 T4까지 의미있게 증가되어 있었다(\(P<0.01\)).

결론: 니카디핀은 요척추 융합술에서 합리적인 제어가능성을 보이며 니트로푸루시드군과 비교하여 출혈 및 수혈과 관련된 동반이환을 감소시키는 것으로 사료된다.

중심단어: 니카디핀, 니트로푸루시드, 레닌, 요척추융합술, 유도저혈압마취, 카테콜라민

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