Hemodynamic Effects of Sevoflurane versus Dexmedetomidine

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ABSTRACT

Background: Cardiac catheterization procedures produce challenges for the anesthetist because of the increased need to provide support in sedating and/or anesthetizing patients.

Objective: To compare pulmonary and systemic hemodynamics of two anesthetic regimens: sevoflurane as volatile induction maintenance anesthesia and dexmedetomidine as total intravenous anesthesia in pediatric patients suffering from congenital heart disease with left-to-right intracardiac shunt.

Design: A Prospective Randomized Study.

Setting: Mansoura University Children Hospital (MUCH), Egypt.

Method: Sixty pediatric patients of both sexes were referred for elective cardiac catheterization. Patients were randomly allocated into two equal groups, consisted of 30 patients. In the first group, the patients received volatile induction maintenance anesthesia (VIMA) with sevoflurane (GS group) while in the second, the patients received total intravenous anesthesia (TIVA) with dexmedetomidine (1 μg/kg) intravenous bolus dose over 10 minutes, anesthesia was maintained by intravenous infusion of dexmedetomidine at a rate of 1-2 μg/kg/hour (GD group).

Result: The present study showed that the heart rate (HR), Pulmonary blood flow index (QpI), Systemic blood flow index (QsI) and Qp/Qs ratio were comparable in both groups. Pulmonary vascular resistance index (PVRI) and Systemic vascular resistance index (SVRI) were significantly lower in GS group after induction of general anesthesia (GA) if compared with the basal value maintaining PVR/SVR at baseline value. However, PVRI and SVRI were insignificantly higher in GD group after induction of GA if compared with the basal value; thus, maintaining PVR/SVR. The Systemic Mean arterial blood pressure (MAP) decreased in both groups.

Conclusion: Total intravenous anesthesia with dexmedetomidine provided hemodynamic stability. It is comparable to volatile induction and maintenance of anesthesia with sevoflurane when administered to pediatric patients suffering from congenital heart disease with left-to-right intracardiac shunt during cardiac catheterization.

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INTRODUCTION

Cardiac catheterization procedures produce challenges for the anesthetist because of the increased need to provide support in sedating and anesthetizing these patients. The goals of anesthetic management during cardiac catheterization are adequate analgesia, sedation, and immobility. The agents used should have a minimal influence on cardiac function and respiratory drive.

Although a wide variety of pharmacologic agents and techniques have been successfully used for these procedures, studies that have examined the hemodynamic consequences of anesthetic agents mostly focused on changes in heart rate and blood pressure. Sevoflurane is considered to be an improvement in inhalational anesthesia according to all modern textbooks of anesthesia. The most striking advantage of sevoflurane is the ease of induction of anesthesia with short recovery time. The superiority of sevoflurane over halothane in preserving cardiac output and contractility renders it an attractive choice for anesthesia in pediatric patients with congenital heart disease.

Dexmedetomidine is a highly selective α2-adrenoceptor agonist with sedative, anxiolytic and analgesic properties. It is a very helpful drug in pediatric anesthesia due to its cardiovascular and respiratory stability.

The aim of this study is to compare pulmonary and systemic hemodynamics of two anesthetic regimens: sevoflurane as volatile induction maintenance anesthesia and dexmedetomidine as total intravenous anesthesia in pediatric patients suffering from congenital heart disease with left-to-right intracardiac shunt.

METHOD

An informed consent was obtained from parents. Sixty pediatric patients of both sexes, aged 1-10 years had left to right intracardiac shunt submitted for elective diagnostic cardiac catheterization.

The exclusion criteria were the following:
1. Patients with major cardiac problem requiring inotropic support
2. Patients with major endocrinal, respiratory, renal or hepatic disorders
3. Patients having aortic stenosis, pulmonary stenosis, aortic regurgitation or pulmonary regurgitation
4. Hypersensitivity to dexmedetomidine
5. Presence of airway abnormalities that may increase the risk of obstruction or make it difficult to produce adequate mask ventilation

Medical and anesthetic history was obtained; patients were subjected to clinical examination one day before the procedure. The following investigations were obtained: complete blood count, complete liver profile, serum creatinine, coagulation profile, chest X-ray, ECG and transthoracic echocardiogram. Fasting guidelines were followed.
Ingested material and Minimal fasting Period recommended before induction of anesthesia: Clear liquids 2 hours, Breast milk 4 hours, Infant formula and Non-human milk 6 hours, Light meal 6 hours.

The eutectic mixture of local anesthetics (EMLA) cream was applied on both hands and groins of the children one hour before entering the catheterization laboratory and an appropriately sized intravenous catheter was inserted in a peripheral vein. Lactated Ringer's solution was administered at a rate of 4 ml/kg/hour.

Patients were premedicated with intravenous midazolam (0.03 mg/kg) and intravenous atropine (0.01 mg/kg) 30 minutes before the procedure. Routine monitors were applied upon arrival to the operating theater including electrocardiogram, non-invasive arterial blood pressure and pulse oximetry.

Sedation was achieved before femoral cannulation by boluses of intravenous midazolam (0.03mg.kg⁻¹) and ketamine (0.5mg.kg⁻¹) to keep the patients appropriately sedated for the cardiac catheterization procedure.

All patients breathed air spontaneously; if oxygen saturation is less than 5% from the baseline, mixture of oxygen and air (50%:50%) was given via an appropriate facemask and a modified Jackson-Rees breathing system. Supplemental oxygen was maximized during cardiac catheterization.

Transthoracic echocardiography was performed and catheterization of femoral artery and vein under the fluoroscopic guidance was done by the same cardiologist. The left and right cardiac catheters were attached to pressure transducers for continuous pressure monitoring.

Patients were randomly assigned to two equal groups. In the first group, the patients received volatile induction maintenance anesthesia (VIMA) with sevoflurane (GS group) while in the second group, the patients received total intravenous anesthesia (TIVA) with dexmedetomidine (GD group).

All patients received 100% oxygen for 3-5 minutes and intravenous fentanyl 1 μg/kg before induction of general anesthesia.

In GS group, induction of anesthesia was done with sevoflurane in oxygen. The initial delivered dose of sevoflurane was 1% and the concentration was increased by 1% increments every three breaths until the onset of rhythmic breathing and loss of the eyelid reflex occurred. In GD group, induction of anesthesia was done with dexmedetomidine 1 μg/kg intravenous bolus dose over 10 minutes.

Intravenous vecuronium was given with an initial dose of 0.1 mg/kg; endotracheal intubation was done 2-3 minutes after the administration of vecuronium.

The patient was maintained on closed circuit with total fresh gas flow 1-2 liters/min with FiO₂ 0.21-0.30. The mean airway pressure was maintained less than 20 cmH₂O with inspiratory: expiratory ratio of 1:2-1:3. End tidal partial pressure of carbon dioxide (PetCO₂) was maintained at 30-35 mmHg.
In GS group, the delivered concentration of sevoflurane was adjusted to keep changes in heart rate (HR) and blood pressure (BP) within ± 20% of basal values. In GD group, anesthesia was maintained by intravenous infusion of dexmedetomidine at a rate of 1-2 μg/kg/hour. Once the procedure started, the infusion rate was adjusted to keep changes in HR and BP within ±20% of basal values.

The following parameters were measured or calculated at the three intervals: basal 15 minutes after induction of GA and 15 minutes after ventilation with 100% oxygen.

1. Mean arterial blood pressure (MAP) and heart rate (HR)
2. Pulmonary vascular resistance index (PVRI)
3. Systemic vascular resistance index (SVRI)
4. Pulmonary to Systemic vascular resistance ratio (PVR:SVR)
5. Pulmonary blood flow index (QpI)
6. Systemic blood flow index (cardiac index) (QsI)
7. Pulmonary to systemic blood flow ratio (Qp/Qs)

If the cardiac assessment was complete, sevoflurane administration was stopped and the anesthetic drug infusion was discontinued. The residual effects of muscle relaxant was reversed (after good attempts of spontaneous respiration) using 20 μg/kg atropine and 40 μg/kg neostigmine. The patients were fully awake at the time of tracheal extubation.

Statistical Analysis

The statistical analysis of data was done by using excel program and SPSS 11. The significance between groups was done by using Student t-test for quantitative data (mean ± SD) and Chi-square test for qualitative data (frequent and proportion). P is considered significant if < 0.05.

RESULT

Age, sex, body surface area (BSA), type of shunt and duration of the procedure were comparable in both groups, see table 1. There were no statistically significant differences between the two groups in HR. However, the MAP was significantly lower after induction of general anesthesia and 15 minutes after ventilation with 100% oxygen compared to the basal readings (P < 0.05) in the both groups, see table 2.

Table 1: Personal Data, Duration of the Procedure, and Shunt Type

<table>
<thead>
<tr>
<th></th>
<th>GS (n=30)</th>
<th>GD (n=30)</th>
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<tbody>
<tr>
<td>Age (year)</td>
<td>4.5 ± 2.9</td>
<td>4.8 ± 3.9</td>
</tr>
<tr>
<td>BSA (m²)</td>
<td>0.65 ± 0.34</td>
<td>0.67 ± 0.28</td>
</tr>
<tr>
<td>Sex (M/F)</td>
<td>(14/16)</td>
<td>(15/15)</td>
</tr>
<tr>
<td>Duration of the procedure (minute)</td>
<td>129 ± 11.9</td>
<td>127 ± 12.6</td>
</tr>
<tr>
<td>Shunt type</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>Atrial septal defect</td>
<td>8</td>
<td>6</td>
</tr>
<tr>
<td>Atrio-ventricular septal defect</td>
<td>5</td>
<td>6</td>
</tr>
</tbody>
</table>

GS (Sevoflurane group), GD (Dexmedetomidine group). Values are mean ± SD or number. No significant differences between groups (P >0.05%).

Table 2: Heart Rate (HR) and Mean Arterial Blood Pressure (MAP) Changes
GS (Sevoflurane group), GD (Dexmedetomidine group). Values are mean ± SD. *Statistically significant difference when compared with basal values (P < 0.05%). HR Changes (Beat Per Minute) and MAP Changes (Mmhg).

There were no statistically significant differences between the two groups regarding any of the studied parameters. In both groups, QpI and Qp/Qs were significantly higher after administration of 100% oxygen compared with the basal readings (P < 0.05), see table 3.

Table 3: Comparison of Blood Flow

<table>
<thead>
<tr>
<th></th>
<th>GS (n=30)</th>
<th>GD (n=30)</th>
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<tbody>
<tr>
<td>Basal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR (l/min/m²)</td>
<td>123.4 ± 14</td>
<td>125.5 ± 10.8</td>
</tr>
<tr>
<td>MAP</td>
<td>74.3 ± 11.8</td>
<td>65.9 ± 8.5</td>
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<tr>
<td>After induction of GA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR (l/min/m²)</td>
<td>121.5 ± 15.2</td>
<td>121.6 ± 10.2</td>
</tr>
<tr>
<td>MAP</td>
<td>63.8 ± 12.2 *</td>
<td>55.4 ± 9.2 *</td>
</tr>
<tr>
<td>After 100% oxygen</td>
<td></td>
<td></td>
</tr>
<tr>
<td>HR (l/min/m²)</td>
<td>120.6 ± 16.7</td>
<td>119.3 ± 9.6</td>
</tr>
<tr>
<td>MAP</td>
<td>64.3 ± 11.9 *</td>
<td>56.5 ± 11.3 *</td>
</tr>
</tbody>
</table>

Table 4 shows vascular resistance data where PVRI and SVRI were significantly lower in GS group after induction of GA compared with the basal values. However, PVRI and SVRI were slightly higher (no statistical significance) in GD group after induction of GA compared with the basal value, thus maintaining PVR/SVR. Administration of 100% oxygen for 15 minutes was associated with significant decrease in PVRI and PVR/SVR ratio in both groups.

Table 4: Comparison of Resistance

<table>
<thead>
<tr>
<th></th>
<th>GS (n=30)</th>
<th>GD (n=30)</th>
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<tbody>
<tr>
<td>Basal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PVRI (Wood. m²)</td>
<td>4.3 ± 2.2</td>
<td>5.1 ± 2.8</td>
</tr>
<tr>
<td>SVRI (Wood. m²)</td>
<td>14.6 ± 5.7</td>
<td>12.9 ± 3.9</td>
</tr>
<tr>
<td>PVRI/SVRI</td>
<td>0.34 ± 0.2</td>
<td>0.43 ± 0.2</td>
</tr>
<tr>
<td>After induction of GA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>PVRI (Wood. m²)</td>
<td>3.3 ± 2.4*</td>
<td>5.3 ± 2.7</td>
</tr>
<tr>
<td>SVRI (Wood. m²)</td>
<td>11.3 ± 4.1*</td>
<td>13.1 ± 4.4</td>
</tr>
<tr>
<td>PVR/SVR</td>
<td>0.34 ± 0.3</td>
<td>0.38 ± 0.3</td>
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<tr>
<td>After 100% oxygen</td>
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DISCUSSION

There is no ideal anesthetic technique that can be universally used in pediatric patients undergoing cardiac catheterization. Cardiac anomaly will dictate the modification of technique needed for each patient. The main goal of anesthetic management is the safety of patient (cardiac and respiratory profile) during catheterization.

Ketamine-Midazolam combination is used to provide sedation because it possesses short duration of action with relatively minimal respiratory depressive effect. Adding midazolam greatly reduces or even eliminates the unwanted cardiovascular effects of ketamine.

Sevoflurane preserves the cardiac output and the myocardial contractility more than any other inhalational agents. It is associated with less tachycardia than isoflurane; it has less myocardial depressant effect than halothane and it does not sensitize the myocardium to the arrhythmogenic effects of catecholamines.

Dexmedetomidine is a highly selective α2-adrenoceptor agonist with sedative and anxiolytic effects. It provides and augments analgesia and diminishes agitation postoperatively. The safety record of dexmedetomidine suggests that it can be used effectively and safely in children.

Cardiac output mainly determined in infants by the HR due to the poorly compliant left ventricle. The HR in the two groups had no statistical significance. Our result is similar to Rivenes et al who compared the cardiovascular effects of sevoflurane, isoflurane, halothane, and fentanyl-midazolam in 1 or 1.5 MAC concentrations or their equivalent in 54 children with congenital heart disease. They found that in sevoflurane group, HR was preserved at 1 and 1.5 MAC. In dexmedetomidine group, HR is preserved at all times. This is similar to the result of Munro et al who used a loading dose of 1 μg kg(-1) dexmedetomidine administered over 10 minutes followed by an infusion rate of 0.5-2 μg/kg/h. In that study of 20 patients, heart rate and blood pressure remained within 20% of baseline.

MAP was significantly lower after induction of general anesthesia and 15 minutes after ventilation with 100% oxygen in comparison with the basal value (P < 0.05) in the two studied groups. The decrease in MAP in GS group explained by decreased peripheral vascular resistance and to a lesser extent by minor decrease in cardiac contractility. In GD group, the hypotensive effects of dexmedetomidine are mediated via stimulation of central α2A and imidazoline type 1 receptors. The activation of these central receptors results in a decreased catecholamine release and an overall reduction in the sympathetic outflow from the locus ceruleus of the brainstem.

In GS group, it was found that the cardiac index (QsI) was insignificantly lower while the pulmonary blood flow index (QpI) was insignificantly higher after induction of general anesthesia in comparison with the basal values; however, these changes did not affect Qp/Qs significantly. These results are similar to other studies which found that QsI was preserved with sevoflurane. This study also showed that SVRI and PVRI were significantly lower in GS
after induction of GA compared with the basal value; it is similar to the result of Wodey et al who reported decreased SVRI from baseline when using 1 MAC and 1.5 MAC with sevoflurane \(^{14}\). Other studies found that SVRI was preserved at both 1.0 and 1.5 MAC concentrations of sevoflurane but decreased at 2.0 MAC concentration \(^{15}\).

In GD group, Qp, Qs and Qp/Qs were not changed significantly after induction of general anesthesia compared with basal values. PVRI and SVRI were slightly higher after induction of general anesthesia compared with the basal values rendering PVR/SVR maintained at baseline value. The increase in SVR and PVR in GD group were probably due to peripheral vasoconstriction \(^{16,17}\).

After administration of 100% oxygen, we found a significant decrease in PVRI and PVR/SVR and a significant increase QpI and Qp/Qs in both groups. This may be due to the relaxant effect of oxygen on the tone in the pulmonary arterial system in patients with reactive pulmonary vasculature. This decreased tone will lower PVR and lead to an increased Qp in patients with intracardiac shunting \(^{18}\).

This study has few limitations; firstly we did not study other factors affecting pulmonary vascular resistance and pulmonary blood flow such as positive pressure ventilation, hypoxia, hypercarbia, etc. Also, the anesthetist and cardiologists were not blinded to the study groups.

Finally, it was difficult to achieve similar depth of anesthesia in both groups by maintaining the HR and the MAP within ± 20% of the basal values. It was difficult to ensure similar depth of anesthesia for the two regimens where one regimen is inhalational and the other is intravenous. Relying upon maintaining HR and systemic MAP within ± 20% of the basal values was our tool to titrate the anesthetic depth.

**CONCLUSION**

Total intravenous anesthesia with dexmedetomidine provided hemodynamic stability comparable to volatile induction and maintenance of anesthesia with sevoflurane if administered to pediatric patients suffering from congenital heart disease with left-to-right intracardiac shunt during cardiac catheterization. However, sevoflurane and dexmedetomidine decreased the mean arterial blood pressure.

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**Author Contribution:** All authors share equal effort contribution towards (1) substantial contribution to conception and design, acquisition, analysis and interpretation of data; (2) drafting the article and revising it critically for important intellectual content; and (3) final approval of manuscript version to be published. Yes.

**Potential Conflicts of Interest:** None.

**Competing Interest:** None. **Sponsorship:** None.

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**Ethical Approval:** Approved by Mansoura University, Children Hospital, Egypt.

**REFERENCES**