Safety and Consumption of Sevoflurane Versus Desflurane Using Target Controlled Anesthesia in Children

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Abstract

Background: Recently a concept of target controlled inhalational anesthesia (TCA) is introduced in which the fresh gas flow and its composition are automatically delivered to the patients with the least possible flow. The aim of this study was to compare safety, consumption and cost of both sevoflurane and desflurane when delivered by TCA using closed circuit anesthesia.

Patient and Method: Sixty pediatric patients aged 2-12 years and ASA status I-II with normal liver and kidney function scheduled for procedures longer than two hours. The patients were classified into two groups according to the anesthetic delivered by auto control mode: S Group (n=30) in which sevoflurane was delivered D Group (n=30): In which desflurane was delivered. Anesthetic agent and O₂ consumption, cost and number of adjustments were assessed. Blood samples were obtained preoperatively and at 24, 48 and 72h postoperatively for measuring serum creatinine, BUN, AST and ALT. Twenty-four hour urine samples were collected for 3 consecutive days to measure glucose, microprotein and Creatinine for estimation of creatinine clearance.

Results: Sevoflurane group had a lower O₂, anesthetic consumption and cost than desflurane group. Also both groups had higher levels of serum urea and creatinine together with urinary microproteins and glucose in the first three postoperative days compared to preoperative values. However there was no statistically significant difference between the two groups. All values were within normal values in both groups by the 3rd day.

Conclusion: Sevoflurane is as safe as desflurane when delivered by auto control mode of Zeus machine with decreased anesthetic consumption and cost.

Key Words: Autocontrol mode – Target controlled anesthesia – Desflurane – Sevoflurane.

Introduction

LOW flow anesthesia has various advantages which include decreased consumption of medical gases and volatile anesthetics with its economic impact, reduction of anesthetic gas loss into the atmosphere with its environmental impact and finally conservation of temperature and humidity of the airway [1].

More recently a concept of target controlled inhalational anesthesia (TCA) is introduced in which the fresh gas flow and its composition are automatically delivered to the patients with the least possible flow. Theoretically target controlled anesthesia has many advantages in inhalational anesthesia practice which include decreased time to achieve a desired alveolar anesthetic gas concentration together with decreased overshoots and fluctuation of anesthetic agent. Another advantage is that the need for repeated anesthetic adjustments is markedly minimized decreasing the work of anesthetist [2].

Modern anesthesia machines that implemented the target controlled concept has an auto control mode that deliver target controlled anesthesia with a fully closed circuit through blower-driven ventilator, an electronically-controlled gas and vapor delivery system and a servo-controlled valve system [3].

The last generations of halogenated anesthetics (desflurane and sevoflurane) have certain pharmacokinetic and pharmacodynamic properties which have been greatly magnified in minimal flow states. These anesthetic agents have low potency and low solubility in tissues, which fastens equilibration between concentrations of the alveoli and the brain. This makes these agents ideal for minimal flow and closed circuit conditions; hence their Minimum Alveolar Concentration (MAC) in the inspiratory mixture is easily reached [4].

Despite being synthesized before the 1970’s, one of the major barriers to their use is the high cost together with greater amount of agent required. This is evident in desflurane which has the highest MAC known among all anesthetic agents increasing its consumption and overall cost [4].
The side effects of accumulated volatile substances as an outcome of metabolism of sevoflurane are another aspect to be considered and may add to barriers of its use in minimal flow conditions.

The aim of this study is to compare between sevoflurane and desflurane anesthesia regarding safety, consumption and cost when delivered by auto-control mode of Zeus machine that deliver target controlled anesthesia (TCA) using fully closed circuit conditions.

**Patients and Methods**

After approval of the hospital review board and obtaining parental written, informed consent, 60 pediatric patients aged 2-12 and ASA status I-II with normal liver and kidney functions scheduled for procedures longer than two hours duration at the Children’s Cancer Hospital of Egypt from March 2013 – Nov. 2013 were included in this study.

After arrival of the patients into the holding area, I.V cannula was inserted; midazolam 0.05 mg.kg\(^{-1}\) and atropine 0.02mg.kg\(^{-1}\) were administered intravenously for anxiolysis. Patients then were transferred into the operating theatre where the non invasive monitoring including electrocardiogram, non-invasive blood pressure, pulse oximetry, axillary temperature and bispectral index (BIS) were applied. All patients had warming blanket to maintain a body temperature between 34-36ºC throughout surgery. Anesthesia was induced with fentanyl (2µg.kg\(^{-1}\)), propofol (2.5 mg.kg\(^{-1}\)) and atracurium (0.5mg.kg\(^{-1}\)) to facilitate endo-tracheal intubation. Then, all patients were mechanically ventilated using target controlled anesthesia (TCA) through the autocontrol mode with a mixture of air-oxygen (50% oxygen + 50% air) in addition to the anesthetic agent according to the study group using the anesthesia workstation (Zeus®, Dräger, Luebeck, Germany). Tidal volume was set at 8mL/kg and adjusting respiratory frequency in order to maintain an end-tidal CO\(_2\) between 30-35mmHg.

The patients were randomly assigned –using an envelop technique– into one of two groups according to the anesthetic agent used: S Group (n=30): In which sevoflurane was delivered by auto control mode of Zeus machine and D Group (n=30): In which desflurane was delivered by auto control mode of Zeus machine.

Anesthesia was maintained by readjusting the administered anesthetic agent.

During maintenance, the BIS values were maintained between 40-60 and this was achieved by adjusting the end tidal concentration of the administered agents accordingly. Adequate neuromuscular blockade was achieved by administering atracurium boluses 0.1mg.kg\(^{-1}\) every 20min.

During skin closure, anesthetic was discontinued and the patient received 100% O\(_2\). At 25% recovery of the first response to train-of-four stimulation, neuromuscular blockade was reversed by neostigmine (4µg.kg\(^{-1}\)) and atropine (15µg.kg\(^{-1}\)).

Consumption of O\(_2\) and the used anesthetic agent were monitored and recorded from the integrated Zeus delivery system and calculated as per hour consumption. Cost was calculated as per hour cost by the Egyptian pound. Also the number of adjustments required to maintain the BIS value between 40 and 60 were recorded.

Blood samples were obtained immediately preoperatively and at 24, 48 and 72h after the end of surgery for measuring serum creatinine, BUN, aspartate aminotransferase (AST) and alanine aminotransferase (ALT).

Normal values were defined by the commercial laboratory and the results were expressed in conventional units.

Twenty-four hours urine samples were collected for 3 consecutive days to measure glucose, protein in urine as sensitive indicators for renal tubular insult. Creatinine was also measured in urine for estimation of creatinine clearance.

**Statistical analysis:**

Data were analyzed using the Statistical Package for Social Sciences for windows (SPSS 13.0.1; SPSS Inc; Chicago, II, USA).

Quantitative variables were expressed as means (SD) or median (range) according to normality of distribution. Categorical variables were expressed as number (%). Differences between groups were assessed using the Students - t- test for normally distributed data, or Mann Whitney U test for non-normally distributed data. Changes from Preanesthesia to postanesthesia at 24, 48, and 72 hours were analyzed using either Paired - t- test or Wilcoxon signed rank test for normally and non-normally distributed data, respectively. Categorical variables were compared using the chi-square test or Fisher’s exact test as appropriate. \( p < 0.05 \) was considered to indicate statistical significance.
Results

Regarding patients’ demographics, mean age, weight, sex, duration of surgery and MAC-hour results were comparable in both groups. There were no statistically significant differences between the groups. (Table 1).

Table (1): Patient’s demographic data in the studied groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>S group n=30</th>
<th>D group n=30</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>7.7±1.36</td>
<td>6.6±1.83</td>
<td>0.09</td>
</tr>
<tr>
<td>Male/female</td>
<td>16/14</td>
<td>14/16</td>
<td>0.20</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>23±5.4</td>
<td>21±6.2</td>
<td>0.18</td>
</tr>
<tr>
<td>Duration of anesthesia (hr)</td>
<td>5.3±1.6</td>
<td>5.1±2.97</td>
<td>0.81</td>
</tr>
</tbody>
</table>

Data are presented as mean±SD and ratio.

Consumption of Oxygen and anesthetic agent, number of adjustments and cost were significantly lower in S group than in D group. (Table 2).

Table (2): Oxygen and anesthetic consumption, number of adjustments and cost among the studied groups.

<table>
<thead>
<tr>
<th>Variables</th>
<th>S group n=30</th>
<th>D group n=30</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>O₂ consumption (L/h)</td>
<td>15.65±8.4</td>
<td>11.74±30.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Agent consumption (ml/h)</td>
<td>3.1±1.3</td>
<td>16.4±7.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cost (Egyptian pound/h)</td>
<td>13.4±4.6</td>
<td>33.6±6.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Number of adjustments</td>
<td>3.65±0.75</td>
<td>5.45±1.9</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Results are represented as mean±SD.

Serum creatinine levels were significantly higher at all the assessment time points during postanesthesia when compared with the preanesthetic values in both groups. However, there were no significant difference between both groups. (Tables 3,4).

Table (3): Serum creatinine levels (mg/dl).

<table>
<thead>
<tr>
<th></th>
<th>S group n=30</th>
<th>D group n=30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-anesthesia</td>
<td>0.29±0.13</td>
<td>0.26±0.12</td>
</tr>
<tr>
<td>24h</td>
<td>0.52±0.14*</td>
<td>0.48±0.09*</td>
</tr>
<tr>
<td>48h</td>
<td>0.47±0.13*</td>
<td>0.46±0.11</td>
</tr>
<tr>
<td>72h</td>
<td>0.44±0.14*</td>
<td>0.44±0.09*</td>
</tr>
</tbody>
</table>

Data are represented as mean±SD.

Normal range = 0.4-1.4mg/dl.

Serum AST and ALT levels were not significantly different from the pre-anesthetic values in either group all over the study period. Also there were no statistically significant differences between both groups. (Fig. 1).

Twenty-four hour urinary protein and glucose levels were significantly higher from the pre-anesthetic values in both groups at 24, 48, 72hr. However there were no statistically significant differences between both groups. (Tables 5,6).

Table (5): Twenty-four hour urinary protein level in both studied groups. (mg/day).

<table>
<thead>
<tr>
<th></th>
<th>S group n=30</th>
<th>D group n=30</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-anesthesia</td>
<td>32 (15-86)</td>
<td>73 (22-108)</td>
</tr>
<tr>
<td>24h</td>
<td>65 (40.5-187.5)*</td>
<td>189.5 (44.75-262.5)*</td>
</tr>
<tr>
<td>48h</td>
<td>64 (28.5-205)*</td>
<td>260 (27.25-406.5)*</td>
</tr>
<tr>
<td>72h</td>
<td>52 (26.3-172.8)**</td>
<td>173 (35-227.5)*</td>
</tr>
</tbody>
</table>

Data are presented as median (inter-quartile range).

Serum AST and ALT in groups of patients under investigation.

![Fig. (1): Serum AST and ALT in groups of patients under investigation.](image-url)
Discussion

This study revealed that sevoflurane group had a lower O\textsubscript{2}, anesthetic consumption and cost than desflurane group. Also both groups had higher levels of serum urea and creatinine together with urinary microproteins and glucose in the first 3 post operative days compared to preoperative values indicating minor tubular insult. However, there were no statistically significant differences between the two groups. It is worthy to mention that by the 3\textsuperscript{rd} day all values were within normal values in both groups.

Sofie et al., compared desflurane consumption during auto-control mode of Zeus anesthesia machine and conventional anesthesia machine with low fresh gas flow and concluded that desflurane consumption was higher in auto control mode [6]. Another study for cost analysis using two anesthetic machines: “Primus” and “zeus” showed that the consumption of sevoflurane and isoflurane was also higher in auto control mode [7], and this was contrary to a study by Lortat et al., that assessed clinical and pharmaco-economic benefits of TCA and showed decreased desflurane consumption in auto control mode [8].

In the present study the higher consumption of desflurane may be due to the higher MAC that needs more time by the machine to reach the target expired setting of desflurane with more oxygen and desflurane consumption. Also because of the automatic control of fresh gas and volatile agent flow, any change in the targeted concentration of volatile agent in the circle system was achieved using maximum fresh gas flow rates of oxygen for rapid equilibration. This means that with each adjustment to the desired inspired expired and anesthetic agent, the circle system became more toward higher flows as open breathing circuits with higher oxygen and agent consumption [7]. In our study, higher number of adjustments was reported with desflurane that also may add to higher desflurane consumption.

Lately in the last century there was controversy about safety of low flow sevoflurane due to accumulation of toxic metabolite in the anesthetic circuit however many literatures supported its safety. A retrospective study evaluated pooled renal laboratory data from 22 different clinical trials that compared sevoflurane with isoflurane, enflurane, or propofol. The trials examined postoperative changes in serum creatinine and blood urea nitrogen levels from a total of 3,436 adult surgical patients. The incidences of increased serum creatinine and blood urea nitrogen concentrations were similar among patients administered sevoflurane and those administered control drugs. Additionally, no trends specific to sevoflurane were observed as regard to postoperative serum creatinine concentration with the fresh gas flow rate and concurrent treatment with nephrotoxic antibiotics, or type of carbon dioxide absorbent [8].

In another study, 17 patients with stable renal insufficiency were anesthetized with sevoflurane or isoflurane at a total flow of 1L/minute. Renal function was assessed with serum creatinine and blood urea nitrogen. The results showed no significant changes of blood urea nitrogen levels, serum creatinine concentrations, or creatinine clearance after anesthesia within each group [9]. A study by Song and his colleagues evaluated the influence of sevoflurane or propofol on renal function in 200 patients undergoing liver resection and concluded that the sevoflurane did not seem to impair postoperative renal function even in cirrhotic patients who are prone to renal dysfunction after anesthesia [10].

Also recently, sahin and coworkers [11] evaluated the effect of moderate duration low-flow sevoflurane on renal and hepatic functions in 80 patients, with an operation time of 120-240min. They reported similar results to the current study. They found that postoperative serum BUN, creatinine and urine glucose were significantly higher from the preoperative values. However, all values were within the normal range.

In 80 children aged 5-15 years, no significant effect on renal and hepatic functions was found after low flow sevoflurane anesthesia [12]. Many factors common to anesthesia and surgical procedures have been concerned in the cause of renal dysfunction/injury. Antibiotics, surgical stress, preexisting renal disease, intraoperative blood pressure, site of surgery, and anesthetics are some of the suggested factors.

It is revealed in the current study that an additional factor which may adds to sevoflurane safety with auto control mode of the Zeus anesthesia machine is the automatic flushing that occurs with each anesthetic agent adjustment increasing the flow towards open circuit that may wash any toxic metabolite in the circuit.

In conclusion:

Sevoflurane is as safe as desflurane when delivered by auto control mode of Zeus anesthesia machine and is associated with decreased anesthetic consumption and cost.
References


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