ABSTRACT

Aim: a tight control of blood glucose is critical. We compare blood glucose level between isoflurane and desflurane in neurosurgical patients for further application.

Methods: one hundred and eight patients scheduled for neurosurgery under general anesthesia were recruited and divided into two groups; fentanyl-isoflurane-nitrous oxide based and fentanyl-desflurane-nitrous oxide based randomly. Vital signs, end tidal gas concentration, amount of narcotics usage and blood glucose level were recorded at induction (T0) and intraoperative hourly thereafter (T1-T8). Independent t-test and ANOVA were used. The statistical significance was considered if p-value < 0.05.

Results: there were 107 patients enrolled excluded one from isoflurane group because of the schedule changes. The amounts of fentanyl usage (0.89±0.41mcg/kg/hr, 0.88±0.48 mcg/kg/hr), the end tidal inhales’ tension (0.71%±0.32, 3.13%±1.63) were equivalent in isoflurane and desflurane group. The blood glucose levels at various period of time had no statistical difference but there was a significant (p<0.05) increasing from T1 to T8 comparing to T0 in both groups (3.88±0.93 mg%/hr and 5.55±1.14mg%/hr).

Conclusion: desflurane has demonstrated the indistinguishable blood glucose level and hemodynamic response from isoflurane anesthesia intraoperatively in neurosurgical patients, confirming a comparable pattern of blood glucose concentration intensifying over time spends.

Key words: inhaled anesthetic agents, hyperglycemia, neurological damage.
depression effect may occur similar to other inhalation agents.

In vitro pharmacokinetic study, desflurane has no direct effect on the metabolism of glucose but in vivo intraoperative blood glucose level may rise with many different aspects. From the literature review, there were no studies showed the difference of blood glucose level among isoflurane and desflurane anesthesia in the randomized control trial dissimilar to isoflurane and sevoflurane. Thus, we propose this research to compare blood glucose level intraoperatively between those two anesthetic inhalation agents in neurosurgical patients for further applicable clinical practice.

**METHODS**

This study was conducted with the approval of the Institutional Research Ethics Board of Prasat Neurological Institute, Department of Medical Services, Ministry of Public Health. One hundred and eight patients estimated sample size from 20% difference between two population proportions and expected 10% drop out, physical status classified by the American Society of Anesthesiologists (ASA) I – II aged 15 – 75 years scheduled for neurosurgery under general anesthesia in Prasat Neurological Institute were recruited from the first list of the operative schedule which were not started beyond 9 A.M. during November 1st, 2006 – July 31st, 2007. The patients who had any endocrine disorders which produced abnormal glucose metabolism; e.g. Diabetes Mellitus, hyperthyroidism, hypothyroidism; or renal, hepatic disease; pregnant or lactating women; or the patients who received any medications known to interfere with or affect blood glucose or insulin release; i.e. steroids, beta adrenergic blocking agents, insulin, sulphonylurea, alcohol at least 1 week preoperatively were excluded.

After the thorough explanation of the purpose and procedure of the study, the written informed consent was obtained. The randomization was done by selecting sealed envelope and allocated equally into 2 groups, i.e. isoflurane and desflurane group. Blood glucose level was measured on the day of surgery after fasting 6-8 hours overnight (TW) by using blood glucose reagent strips (Medisense®, Abbott laboratories, UK) and glucometers (Optium®, Abbott laboratories, USA) which have been investigated and verified the precision, accuracy, efficiency, and safety for clinical use. Isotonic balanced salt solution without glucose containing was given intravenously 4 ml/kg on the first 10 kg body weight, 2 ml/kg on the second 10 kg and the last 1 ml/kg for the remaining 4 hours before the operation. The patients were transferred to the operating room where non-invasive blood pressure, pulse oximetry, electrocardiography, body temperature were monitored and recorded every 5 minutes while end tidal carbon dioxide tension, inspired and expired inhaled anesthetic agent concentration were recorded every 15 minutes.

Premedication was provided with fentanyl 1-2 mcg/kg intravenously then an indwelling catheter was inserted into a radial or dorsalis pedis artery under local anesthesia for obtaining arterial blood samples for glucose examination at T0 before anesthesia. All patients were preoxygenated with oxygen 6 L/min via face mask and induced with propofol 2-2.5 mg/kg intravenously followed by atracurium bromide 0.6 mg/kg for tracheal intubation. Anesthesia was maintained with either isoflurane or desflurane 0.5-1 MAC in 50% nitrous oxide and oxygen according to the end tidal gas monitor including fentanyl 0.5-1 mcg/kg intravenously incrementally every 45-60 minutes for analgesia and atracurium bromide 0.3-0.5 mg/kg/hr continuous infusion to attain complete muscle relaxation. The total gas flow was set at 4 L/min for 5 minutes and decrease to 1.2 L/min later. Normocapnia was provided by controlled mechanical ventilation with end tidal carbon dioxide tension values ranging from 28-32 mmHg. A balanced electrolyte solution was infused as maintenance fluid during the operation; no glucose or other carbohydrates were given. Blood component was considered when indicated. The periodic glucose level was measured hourly after induction at T1, T2, T3, until complete anesthesia by collecting 1 mL sampling blood in 3 mL syringe after discarded prior blood and flushing fluid 10 mL from arterial line. The number coded syringe was labeled and assessed in double blinded fashion. If blood glucose level was less than 70 mg%, the study would be discontinued. The promptly treatment would be done by giving 50% glucose intravenously together with glucose containing solution continuous infusion. Contrarily, if blood glucose level was over 200 mg%, regular insulin would be infused to maintain blood glucose level within 150-180 mg% range and monitored in every single hour until the end of the surgery. Nevertheless all cases would be collected and included in statistical analysis to avoid selection bias.

Within 30-45 minutes before the end of the operation, atracurium bromide infusion was discontinued. The inhalation agent was switched off and ventilated with 100% oxygen 3-5 L/min at the end of surgery. Residual muscle relaxation was antagonized with atropine 0.02 mg/kg and prostigmine 0.04 mg/kg intravenously. Extubation is cogitated if the ventilatory support was unnecessary.
Descriptive statistic was evaluated in part of demographic data and demonstrated in mean, standard deviation, frequency and percentage. Independent t-test was applied to determine the mean differences of the variables between groups; e.g. blood sugar level at 1 hour after induction between isoflurane and desflurane group, etc. Within group comparison of variable; e.g. blood sugar level between 1, 2, 3 and 4 hour after induction in desflurane group, was made by one-way ANOVA with Bonferroni correction. The statistical significance was considered if p-value is less than 0.05 at the power of 80%.

RESULTS

There were 107 patients enrolled in this study. One from isoflurane group was excluded because of the operative schedule changes. Four patients were discontinued because the blood sugar level was not in expected range; two from isoflurane and one from desflurane group had blood glucose level less than 70 mg% at T0 period and another one from desflurane group had high blood glucose level (235 mg%) at T8 period. There were no differences between the two groups regarding sex, age, ASA physical status, body weight, diagnosis, intraoperative body temperature, anesthetic and surgical duration (Table 1). The synthetic colloid fluid, 6% hydroxyethyl starch, was used 13.46% and 15.09% in isoflurane and desflurane group. Nevertheless, both groups were similar with respect to type and amount of fluid utilization, urine output and the extent of blood loss.

According to the end tidal carbon dioxide tension, the mean values were 31.03 ± 1.92 mmHg in isoflurane group and 30.98±2.70 mmHg in desflurane group which were not statistically different. Since the anesthetic level was controlled with inhalation agents and narcotics, the results had shown the comparable amount of fentanyl usage; i.e. 0.89 ± 0.41mcg/kg/hr, 0.88 ± 0.48 mcg/kg/hr together with the equivalent end tidal inhalation agents’ tension; i.e. 0.71% ± 0.32, 3.13% ± 1.63 in isoflurane and desflurane group in order.

The blood glucose levels at various period of time between isoflurane and desflurane groups had no statistical difference but there was a significant increasing of blood glucose level from T1 to T8 comparing to T0 within both groups (p<0.05); average change per hour in isoflurane group was 3.88 ± 0.93 mg% and in desflurane group was 5.55 ± 1.14mg% as demonstrated in Figure 1.

There was an upsurge in systolic blood pressure, diastolic blood pressure and heart rate at T0 period compared to TW in both groups but had no statistical significant between each inhalation agent. (Figure 2, 3)

Table 1. Summary of patients’ characteristics demonstrated in number (percent) and mean ± standard deviation

<table>
<thead>
<tr>
<th>Variables</th>
<th>Isoflurane</th>
<th>Desflurane</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Male</td>
<td>27 (50.0%)</td>
<td>19 (35.2%)</td>
</tr>
<tr>
<td>- Female</td>
<td>27 (50.0%)</td>
<td>35 (64.8%)</td>
</tr>
<tr>
<td>Age (Years)</td>
<td>48.37±13.28</td>
<td>45.91±12.75</td>
</tr>
<tr>
<td>ASA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- I</td>
<td>21 (38.9%)</td>
<td>20 (37%)</td>
</tr>
<tr>
<td>- II</td>
<td>33 (61.1%)</td>
<td>34 (63%)</td>
</tr>
<tr>
<td>Body weight (Kg)</td>
<td>62.76±10.73</td>
<td>60.64±10.54</td>
</tr>
<tr>
<td>Diagnosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Cerebral tumour</td>
<td>22 (41.5%)</td>
<td>19 (35.2%)</td>
</tr>
<tr>
<td>- Cerebral aneurysm</td>
<td>4 (7.5%)</td>
<td>3 (5.6%)</td>
</tr>
<tr>
<td>- Cerebral infarction</td>
<td>0 (0%)</td>
<td>1 (1.9%)</td>
</tr>
<tr>
<td>- Spinal cord tumour</td>
<td>2 (3.8%)</td>
<td>2 (3.7%)</td>
</tr>
<tr>
<td>- Spinal spondylosis</td>
<td>4 (7.5%)</td>
<td>13 (24.1%)</td>
</tr>
<tr>
<td>- Herniated nucleus</td>
<td>13 (24.5%)</td>
<td>9 (16.7%)</td>
</tr>
<tr>
<td>- pulposus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Others</td>
<td>8 (15.1%)</td>
<td>7 (13%)</td>
</tr>
<tr>
<td>Intraoperative body temperature (°C)</td>
<td>35.43±0.67</td>
<td>35.71±0.66</td>
</tr>
<tr>
<td>Anesthetic duration (Hours)</td>
<td>5.21±2.34</td>
<td>4.50±2.18</td>
</tr>
<tr>
<td>Surgical duration (Hours)</td>
<td>4.39±2.29</td>
<td>4.09±2.13</td>
</tr>
</tbody>
</table>

TW = Time at 6-8 hours fasting overnight, T0 = Time before induction, T1 = Time at 1 hour after induction, T2 = Time at 2 hours after induction, T3 = Time at 3 hours after induction, T8 = Time at 8 hours after induction. *p-value<0.05 at the different period of time compared to T0.

Figure 1. The blood glucose level at the different period of time categorized by anesthetic inhalation agent.

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circumstance of the alteration in blood glucose concentration effect. Undoubtedly, the literature review has shown that volatile anesthetic agents inhibit insulin secretion and increase hepatic glucose production. These consequences contrast with the effect of narcotics which reduce the rate of hyperglycemia. Although we did not measure hormones, catecholamine plasma concentration, it was assumed that the systemic metabolism preoperatively did not differ; hence, the blood glucose concentration is motivated by neurohormonal stress response under anesthesia and surgery principally. The variability of anesthetic stages, specifically the lightness of anesthesia, is a part of burdens and influence on stress as mentioned but auspiciously this phenomenon was regulated by fentanyl which may depress catecholamine response and controlled similarly as demonstrated in the corresponding of hemodynamic, the average endtidal inhalation agent concentration and the total dose of narcotics usage. Therefore, the outcome of blood glucose measurement among isoflurane and desflurane group may perhaps show the after effect from the lowest identical stage of stress response altered with type of inhalation agents only. Although valuable information on the regulation and alteration of intraoperative stress response has been obtained, none of the currently used inhalation anesthetic agents has been able to prevent metabolic endocrine stress response without showing any differences between the substances.

As a result of the increased counter-regulatory neurohormonal response, the concentrations of blood glucose is stimulated to a greater degree under perioperative condition. We have found that blood glucose level is increasing with inclination related to the stress exposed time during the surgery under general anesthesia both with isoflurane and desflurane in the same fashion without significant difference similar to the prior studies. The mechanism of the hyperglycemia originates from reduced insulin secretion, depressed maximum insulin response to a glucose challenge and increased stimulation of glucose production during anesthesia.

Based on the results from isolated inhaled anesthetics on blood glucose level with the attempt to eliminate interfering surgical stimulation, it has been postulated that isoflurane anesthesia impairs glucose tolerance up to 1.5 MAC. Moreover, glucagon concentration may decrease after the long duration of anesthesia which result in high blood glucose level observation.

No differences were found in hemodynamic response among both groups. The present finding of increase blood...
pressure and heart rate during the time before induction (T0) is in agreement with Baris et al. demonstrating perioperative nervousness and anxiety. The sedative effect of midazolam in neurosurgical patient especially who had increased intracranial pressure is critical. This end result is in accordance with the abandonment of tranquilizing premedication in this study.

CONCLUSION

The new inhalation agent, desflurane has demonstrated the indistinguishable blood glucose level from isoflurane anesthesia intraoperatively in neurosurgical patients as well as the hemodynamic response, confirming a comparable pattern of blood glucose concentration intensifying over time spends.

REFERENCES