Impact of Anesthesia Type on Blood Glucose in Intraoperative Diabetic Patients: A Systematic Review and Meta-Analysis
Randomized Control Trial

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REVIEW ARTICLE

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Background: systematic literature review investigating the impact of different anesthetics on intraoperative blood glucose levels of diabetic patients. Method: Databases including ProQuest, PubMed, ScienceDirect, and Wiley were searched for RCTs (randomized controlled trials) that examined the effects of various anesthetics on intraoperative blood glucose levels in diabetic patients. In one study, two researchers independently used eligibility criteria to examine the literature, extracted the data, and used RevMan 5.3 software to perform the meta-analysis. Results: We used trials for meta-analysis with seven randomized controlled trial overall with a total sample of 519 intraoperative diabetic patients. Compared with general anesthesia, it was found that the general anesthesia-epidural combination had superior glycemic control in intraoperative blood glucose levels, based on the meta-analysis results (SMD -1.78, 95% confidence interval [CI] -4.57 to -3.41), however epidural anesthesia did not show comparable superiority. Conclusions: Combined general-epidural anesthesia offers better glycemic control for postoperative blood sugar levels compared to general anesthesia, based on existing data.

Keywords: blood glucose control, anesthesia, diabetes, meta-analysis

Introduction

The percentage of diabetic patients has increased substantially in recent years. Diabetes, also known as DM, is a multisystem metabolic disease, according to one study, 2% to 4% of those undergoing surgery have diabetes [1].

Diabetes Mellitus (DM) is a chronic, global health concern that significantly impacts the quality of life of affected individuals due to its potential for chronic complications. Uncontrolled DM can lead to several complications, such as peripheral microcirculation and the development of Diabetes Foot Syndrome (DFS), which can have a detrimental impact on the structural integrity, energy levels, and overall well-being of patients' feet [2,3]. According to reports from the International Diabetes Federation (IDF), the prevalence of DM is projected to increase by 46% by 2021, with an estimated 537 million people affected (IDF). The prevalence is expected to further increase to 783 million in the age group 20-79 years by 2045, particularly in developing countries undergoing economic transition from low to middle income [4]. Diabetes-related perioperative challenges including infection, delayed wound healing, and postoperative mortality can arise from unexpected elevated blood sugar levels in these individuals [5].

Therefore, it is important to consider the best anesthesia and perform glycemic control. This study will comprehensively
analyze the effects of different types of anesthesia on intraoperative blood glucose levels in diabetic patients and offer the necessary data to make the right choice about anesthesia.

Methods
Search Method
The three authors independently searched for studies in five databases from ProQuest, PubMed, ScienceDirect, and Wiley from September 2014 to July 2022. Several combinations of keywords used were anesthesia AND blood glucose control AND diabetes OR diabetes mellitus AND randomized controlled trial AND clinical trial. During this study search process, a librarian conducted the supervision, and the limitations were only English language studies with full text.

Eligibility criteria
The next one is the inclusion requirement: RCT; anesthesia for surgery in diabetic patients; general anesthesia, epidural anesthesia, subarachnoid (spinal) anesthesia, or conjunctival anesthesia; reporting intraoperative blood glucose levels as an outcome; Publication is in Chinese or English. The next one is the inclusion requirement: RCT; anesthesia for surgery in patients with diabetes; general anesthesia, epidural anesthesia, subarachnoid (spinal) anesthesia, or conjunctival anesthesia; reporting intraoperative blood glucose levels as an outcome; Publication prepared in English.

Selection of studies and assessment of risk of bias
The titles, abstracts, and overall text of the included papers were reviewed independently by two reviewers, and any discrepancies were resolved by discussion or contact with a third reviewer. The quality of the included literature was evaluated by three reviewers (AB, IS and SMS) using the Cochrane risk of bias assessment tool [6], which includes 7 aspects: random sequence generation, allocation concealment, participant and staff masking, outcome assessment masking, incomplete outcome data, selective reporting, and other biases data.

Extraction
Three reviewers (AB, IS and SMS) independently extracted data using a common data extraction template with the following details: year of publication, first author, institution, journal, and blood sugar levels of the intervention group and control group. We also verified the data with each other.

Statistical analysis
We calculated the mean difference and 95% confidence interval (CI) for continuous outcomes. We calculated the odd ratio (OR) and 95% CI for dichotomous data. Using the Q test, we found heterogeneity p=0.05, which indicates heterogeneity [7]. The I2 statistic, which is used to measure inconsistency among studies, was specifically developed to analyze heterogeneity. An I2 value of 75% or more indicates significant inconsistency. If data were available, comparable enough, and of high enough quality, we summarized them statistically [6]. The latest edition of the Cochrane Handbook for Systematic Reviews of Interventions guides our statistical analysis. Sensitivity analysis will be performed to look at the causes of heterogeneity when it is apparent or substantial. Statistical analysis was performed with RevMan 5.4.1 [8].

Quality appraisal of the studies
Quality analysis of research studies was conducted using the guidelines of the Preferred Reporting Items for Systematic
Review and Meta-Analysis [9]. Furthermore, the methodological analysis of the systematic quantitative.

Risk of Bias

The assessment for the quality of the RCT study methodology was conducted using the Cochrane Guideline for Risk of Bias (RoB 2).
review was conducted using the RCT from the Joanna Briggs Institute, with a score of 0 to 13. Bias analysis was performed using the Risk of Bias Quality Assessment from Rev-Man 5.4.1 [8].

**Ethical clearance**

This study is a journal review and only article samples were analyzed, thus we confirm that this study is not ethical.

**Results of the search**

We reported 733 studies after analysis and validation with five international databases, and we also found duplicate publications (n=150). Furthermore, 23 full-text studies were taken, reviewed, and analyzed to assess study eligibility criteria. Exclude by title (n=213), Non diabetes (n=155), outcome is not blood glucose (n=46), abstract (n=121), no authors (n=25), outcome analysis is irrelevant and not comprehensive (n=4), article discuss the effective cost of the economy (n=3), not-english article (n=3), article in the form of protocol and review (n=2) and article population is not homogenous (n=4). Therefore, 7 RCT studies fulfilled the selection criteria and were included in this study.

Thus, 7 RCT studies met the requirements of the selection criteria and proceeded to the next stage of the study. We reported 519 populations from seven studies included in the meta-analysis [10–16]. The process of identifying studies in the database then, screening, eligibility and include can be seen in the PRISMA flow chart (Figure 1).

**Assessment of risk of bias**

Risk of bias analysis of the 7 included studies revealed that none of the studies involving blinded patients or investigators in any of the trials reported randomization.
Allocation concealment and outcome assessment blinding were not reported in any of the trials (Figure 3).
Table 1. Baseline characteristics of included studies.

<table>
<thead>
<tr>
<th>No</th>
<th>Title/Name</th>
<th>Country</th>
<th>Design</th>
<th>Result</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>Effect of Subcutaneous Tirzepatide vs Placebo Added to Titrated Insulin Glargine on Glycemic Control in Patients with Type 2 Diabetes</td>
<td>Japan</td>
<td>Randomized Control Trial</td>
<td>Among patients with type 2 diabetes and inadequate glycemic control despite treatment with insulin glargine, the addition of subcutaneous tirzepatide, compared with placebo, to titrated insulin glargine resulted in statistically significant improvements in glycemic control</td>
</tr>
<tr>
<td>2</td>
<td>Effect of sevoflurane versus desflurane on blood glucose level in patients undergoing intracranial neurosurgery: A randomised controlled study</td>
<td>India</td>
<td>Randomized Control Trial</td>
<td>Desflurane caused an initial rise followed by a decline, whereas a gradual increase in intraoperative blood glucose level was seen with sevoflurane use in non-diabetic adults undergoing elective neurosurgery. The intraoperative change in blood sugar was statistically significant but was within the normal clinical range.</td>
</tr>
<tr>
<td>3</td>
<td>The Effects of Propofol and Isoflurane on Blood Glucose during Abdominal Hysterectomy in Diabetic Patients</td>
<td>Iran</td>
<td>Randomized Control Trial</td>
<td>Blood glucose increased during maintenance of anesthesia with isoflurane compared to propofol during the surgery.</td>
</tr>
<tr>
<td>4</td>
<td>The effect of anti-emetic doses of dexamethasone on postoperative blood glucose levels in non-diabetic and diabetic patients: a prospective randomised controlled study</td>
<td>United State America</td>
<td>Randomized Control Trial</td>
<td>Dexamethasone administration was a significant predictor of maximum postoperative blood glucose increase (p &lt; 0.01) after adjusting for potential confounders. There was no interaction between baseline blood glucose level, or presence or absence of diabetes, and dexamethasone administration.</td>
</tr>
<tr>
<td>5</td>
<td>Effects of Glucose Load on Catabolism during Propofol-Based Anesthesia with Remifentanil in Patients with Diabetes Mellitus: A Prospective Randomized Trial</td>
<td>Japan</td>
<td>Randomized Control Trial</td>
<td>Suggested that continuous infusion of propofol at a clinical dose is sufficient to reduce the requirement for glucose infusion during surgery in patients with diabetes.</td>
</tr>
<tr>
<td>6</td>
<td>A prospective randomized study on the impact of low-dose dexamethasone on perioperative blood glucose concentrations in diabetics and nondiabetics</td>
<td>India</td>
<td>Randomized Control Trial</td>
<td>The maximum rise in blood glucose was within the range of 40-45 mg/dl in the patients who received dexamethasone. The clinician should use his clinical judgment before administering dexamethasone for PONV prophylaxis/treatment.</td>
</tr>
<tr>
<td>7</td>
<td>Changes in blood glucose level during and after light sedations using propofol fentanyl and midazolam fentanyl in diabetic patients who underwent cataract surgery</td>
<td>Iran</td>
<td>Randomized Control Trial</td>
<td>Light sedation methods of propofol + fentanyl and midazolam + fentanyl did not have any differences in alteration of blood glucose levels.</td>
</tr>
</tbody>
</table>
Analysis of intraoperative blood glucose levels during combined general-epidural anesthesia and general anesthesia [10,12,14,16], and the results are depicted in Fig. 2. The "combined general-epidural" group showed a decrease in blood glucose levels (SMD -1.78, 95% confidence interval [CI] –4.57 to -3.41), when a confounding analysis was performed using the fixed-effect model. Based on the findings mentioned above, combining general and epidural anesthesia improves blood glucose management during surgery (figure 1).

Three research investigations were included in the meta-analysis of intraoperative blood sugar levels comparing general anesthesia and epidural anesthesia [10,12,14,16], the findings of which are shown in Fig. 2. Pooling analysis using a random effects model showed no statistically significant variation between the blood glucose levels of the two groups (SMD -1.78, 95% confidence interval [CI] –4.57 to -3.41). According to the above data, compared with general anesthesia, epidural anesthesia has no discernible effect on intraoperative blood glucose levels (Figure 2).

Quality Assessment of Included Studies

A bias assessment was presented at the risk analysis stage, as seen in Figure 3. The fourteen studies on Random Sequence Generation showed a low risk of bias across all studies. Meanwhile, two studies with allocation hiding had a high risk of bias, but twelve showed a low-risk value [10–16]. Furthermore, four studies in dominant blinding outcome assessment had a high risk of bias, while ten showed a low risk [11,13,15].

Publication bias

We created a funnel plot using MD values as the X-axis and SE(MD) as the Y-axis in each of the seven studies that reviewed the impact of combining general epidural with general anesthesia on intraoperative blood glucose levels. The funnel plot (Fig. 4) indicated that the meta-analysis may have publication bias as it was not symmetrical and focused.

Discussions

Diabetic patients are prone to surgical trauma, higher risk, hyperglycemia, and potential stress. Blood glucose levels may increase by 1.12 mmol/L on average after minor and moderate surgery, 2.05 mmol/L on average after major surgery, and 0.55 mmol/L on average after anesthesia [11]. The danger of infection will increase during surgery, which will easily cause various problems and increase the risk of surgery. Therefore, choosing the right anesthesia is very important to ensure the stability of blood glucose level [17].
Our meta-analysis was conducted by combining controlled trials on the effects of various anesthesia modalities on intra-operative blood glucose levels of diabetic patients. Based on the findings of the meta-analysis, combined general-epidural anesthesia has a superior effect in controlling intra-operative blood glucose levels compared to single anesthesia. However, it is important to think about the advantages and disadvantages of various anesthesia options, and healthcare providers should choose a more appropriate anesthesia based on the needs and preferences of the individuals they treat. The following are some of the major limitations of this study: limited sample size in eligible studies; high risk of bias; and substantial clinical heterogeneity among the included studies. Therefore, there is a desire to conduct innovative and high-quality research.

Conclusions

Combined general epidural anesthesia offers better glycemic control for postoperative blood sugar levels compared to general anesthesia, based on existing data.

Acknowledgments

We thank the patients included in the selected studies as well as all the clinical researchers who worked on them.

Reference


