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Original Research Article

Effects of Anesthetic Agents on Glucose Metabolism and Insulin Sensitivity in Surgical Patients

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Abstract:

Background: Perioperative hyperglycemia and insulin resistance are common physiological responses to surgical stress, influenced not only by the surgery itself but also by the anesthetic agents used. These metabolic disturbances are correlated with increased postoperative complications, even in non-diabetic patients. The role of anesthetic drugs in modulating glucose metabolism remains under-explored in Indian surgical populations.

Aim: To evaluate the influence of anesthetic agents—sevoflurane and isoflurane—on glucose metabolism and insulin sensitivity in patients undergoing elective surgery under general anesthesia.

Methods: A prospective observational study was conducted at BMIMS, Pawapuri, Nalanda, Bihar, over a period of six months (Feb 28 to July 28, 2025). Sixty adult patients undergoing elective surgeries were enrolled. Blood glucose, insulin levels, and HOMA-IR were measured preoperatively and at 6 and 24 hours postoperatively. Patients were grouped based on the anesthetic agent received (sevoflurane or isoflurane). Data were analyzed using SPSS version 23.0. Statistical significance was set at $p < 0.05$.

Results: There was a significant increase in mean blood glucose (from 92.4 ± 8.7 mg/dL to 131.6 ± 15.4 mg/dL) and insulin levels (from 8.3 ± 2.1 µIU/mL to 15.1 ± 3.5 µIU/mL) at 6 hours post-surgery ($p < 0.001$). HOMA-IR values peaked at 6 hours, indicating transient insulin resistance. Patients receiving sevoflurane had significantly lower postoperative glucose and HOMA-IR levels compared to those receiving isoflurane ($p < 0.01$). A moderate positive correlation was observed between BMI and postoperative insulin resistance ($r = 0.48$, $p = 0.001$).

Conclusion: Anesthetic drugs significantly influence perioperative glucose metabolism and insulin sensitivity. Sevoflurane demonstrated a more favorable metabolic profile compared to isoflurane. Higher BMI was correlated with increased insulin resistance.

Recommendations: Routine perioperative monitoring of blood glucose and insulin sensitivity is recommended, even in non-diabetic patients. Preference may be given to sevoflurane in patients with higher BMI or metabolic risk. Further large-scale, randomized studies are warranted to confirm these findings.

Keywords: Anesthesia, Glucose Metabolism, Insulin Resistance, Sevoflurane, Perioperative Hyperglycemia.

Introduction

Glucose metabolism and insulin sensitivity are critical physiological processes that maintain energy homeostasis, particularly during periods of physiological stress such as surgery. The surgical stress response activates the hypothalamic-pituitary-adrenal (HPA) axis and the sympathetic nervous system, resulting in increased secretion of cortisol, catecholamines, glucagon, and proinflammatory cytokines, all of which contribute to hyperglycemia and insulin resistance [1]. While these alterations are adaptive to some extent, excessive perioperative hyperglycemia is correlated with adverse outcomes including delayed wound healing, increased risk of infection, and prolonged hospital stay [2].

Anesthetic agents play a central role in modulating this stress response. Volatile anesthetics like sevoflurane and isoflurane, as well as intravenous agents such as propofol, have been shown to differentially affect glucose homeostasis through their influence on neuroendocrine and inflammatory pathways [3,4]. Some agents may attenuate the stress response, while others may exacerbate it, depending on the agent's pharmacological profile

and patient-related factors such as age, BMI, and pre-existing metabolic conditions [5].

Recent studies have highlighted that volatile anesthetics can impair insulin secretion and action, contributing to postoperative insulin resistance and hyperglycemia even in non-diabetic individuals [6]. Sevoflurane, in particular, has shown a more favorable profile compared to isoflurane in terms of preserving glucose-insulin balance, though findings remain inconsistent across populations and surgical settings [7]. Given the global rise in metabolic disorders, even transient perioperative insulin resistance is gaining attention as a modifiable risk factor that can affect surgical outcomes [8].

Despite increasing awareness, limited data are available from Indian clinical settings regarding the comparative effects of commonly used anesthetic drugs on perioperative glucose-insulin dynamics. Understanding these effects is especially crucial in low-resource environments, where undiagnosed insulin resistance and suboptimal perioperative monitoring are prevalent [9]. Therefore, this study was conducted to evaluate the influence of anesthetic drugs, specifically sevoflurane and isoflurane, on glucose metabolism and insulin sensitivity in elective surgical patients. The findings aim to provide evidence-based insight into anesthetic selection and metabolic monitoring protocols to improve perioperative care

Methodology

Study Design: This was a prospective observational study.

Study Setting: The study was conducted at the Department of Anesthesiology, Bhagwan Mahavir Institute of Medical Sciences (BMIMS), Pawapuri, Nalanda, Bihar, India. This institute caters to a wide range of surgical specialties, making it a suitable setting for investigating anesthetic-related metabolic outcomes.

Study Duration: The study was carried out over a period of six months, from 28th February 2025 to 28th July 2025, allowing sufficient time for patient recruitment, data collection, and follow-up.

Participants: A total of 60 adult surgical patients scheduled for elective procedures under general anesthesia were recruited for the study. The participants represented various surgical departments including general surgery, gynecology, orthopedics, and ENT. All participants provided written informed consent prior to enrollment.

Inclusion Criteria: Patients aged between 18 and 65 years undergoing elective surgeries under general anesthesia were included. Only ASA physical status I and II patients were considered. Participants with normal preoperative fasting blood glucose levels and no history of diabetes mellitus were eligible

Exclusion Criteria: Patients with known diabetes mellitus, endocrine disorders, hepatic or renal dysfunction, chronic steroid therapy, or those undergoing emergency surgeries were excluded. Pregnant women and patients with known allergies to anesthetic agents were also excluded from the study.

Bias: To minimize selection bias, patients were randomly selected from different surgical departments using a computer-generated list. Observer bias was reduced by blinding the laboratory personnel analyzing glucose and insulin levels to the anesthetic agents used. Standard protocols were followed for anesthesia induction and maintenance across all cases.

Data Collection: Baseline data including demographic details, (BMI), fasting blood glucose, and fasting insulin levels were recorded preoperatively. Intraoperative data included type and dosage of anesthetic agents, surgical duration, and intraoperative glucose levels. Postoperative glucose and insulin levels were recorded at 1 hour, 6 hours, and 24 hours post-surgery.

Procedure: All patients underwent standard pre-anesthetic evaluation. Anesthesia was induced with propofol and maintained using a combination of volatile agents (sevoflurane/isoflurane) and opioids. Blood samples were collected at designated time points for glucose and insulin analysis using standardized biochemical methods. Insulin sensitivity was calculated using the HOMA-IR index

Statistical Analysis: All data were analyzed using IBM SPSS Statistics Version 23.0. Descriptive statistics were presented as mean ± standard deviation for continuous variables and as percentages for categorical variables. Paired t-tests were used to compare pre- and postoperative glucose and insulin values. A p-value of <0.05 was considered statistically significant.

Results

A total of 60 patients undergoing elective surgery under general anesthesia were enrolled in the study. The mean age of the patients was 43.5 ± 12.1 years, with 36 males (60%) and 24 females (40%). The average BMI was 24.8 ± 3.2 kg/m². Most participants were ASA Grade I (66.7%) and the remainder ASA Grade II (33.3%).

Table 1: Baseline Characteristics of Participants (n = 60)

Variable	Mean ± SD / n (%)
Age (years)	43.5 ± 12.1
Sex	Male: 36 (60%), Female: 24 (40%)
BMI (kg/m²)	24.8 ± 3.2
ASA Physical Status	Grade I: 40 (66.7%) Grade II: 20 (33.3%)

The study population was mostly middle-aged, with balanced BMI and a predominance of ASA Grade I status, making them low surgical risk candidates.

Changes in Blood Glucose and Insulin Levels

Perioperative changes in **fasting blood glucose** and **fasting insulin** levels were observed at three time points: **preoperative (T0), 6 hours' post-surgery (T1), and 24 hours' post-surgery (T2).** There was a statistically significant increase in both blood glucose and insulin levels at T1, which slightly decreased by T2 but remained above baseline.

Table 2: Perioperative Blood Glucose and Insulin Levels (Mean ± SD)

Parameter	T0 (Preop)	T1 (6h Postop)	T2 (24h Postop)	p-value (T0 vs T1)	p-value (T0 vs T2)
Blood Glucose (mg/dL)	92.4 ± 8.7	131.6 ± 15.4	108.2 ± 12.3	<0.001	<0.05
Insulin (μIU/mL)	8.3 ± 2.1	15.1 ± 3.5	11.2 ± 2.9	<0.001	<0.05
HOMA-IR Index	1.9 ± 0.6	4.9 ± 1.2	3.0 ± 0.9	<0.001	<0.01

Postoperative hyperglycemia and hyperinsulinemia were evident at 6 hours post-surgery, with partial normalization by 24 hours. The significant rise in HOMA-IR index indicates a transient decrease in insulin sensitivity due to anesthesia and surgical stress.

Correlation Analysis

Pearson correlation was performed to assess the relationship between BMI and postoperative insulin resistance (HOMA-IR at T1). A moderate positive correlation was observed ($r = 0.48$, $p = 0.001$), suggesting that higher BMI was correlated with increased postoperative insulin resistance.

Table 3: Correlation Between BMI and HOMA-IR at 6 Hours Post-op

Variable Pair	Correlation Coefficient (r)	p-value
BMI vs HOMA-IR (T1)	0.48	0.001

Patients with higher BMI exhibited greater postoperative insulin resistance, possibly due to baseline metabolic derangement or altered drug pharmacokinetics.

Subgroup Analysis by Anesthetic Agent: The patients were grouped based on the maintenance anesthetic agent: Sevoflurane (n=30) and Isoflurane (n=30). Patients under Sevoflurane showed lower postoperative glucose and insulin levels compared to Isoflurane.

Table 4: Comparison of Metabolic Response by Anesthetic Agent at 6h Post-op

Parameter	Sevoflurane (n=30)	Isoflurane (n=30)	p-value
Blood Glucose (mg/dL)	124.3 ± 12.5	138.9 ± 16.1	0.008
Insulin (μIU/mL)	13.4 ± 2.8	16.9 ± 3.4	0.002
HOMA-IR Index	4.1 ± 1.1	5.6 ± 1.3	0.001

The metabolic impact was significantly lower in patients receiving sevoflurane, indicating a possibly more favorable anesthetic profile in terms of glycemic control and insulin sensitivity.

Summary of Key Findings

- Significant increases in blood glucose and insulin levels occurred postoperatively ($p < 0.001$).
- Insulin resistance (HOMA-IR) was highest at 6 hours post-surgery.
- Higher BMI was correlated with greater postoperative insulin resistance.
- Sevoflurane was correlated with more favorable glucose-insulin dynamics than Isoflurane.

Discussion

In this prospective observational study involving 60 surgical patients, we evaluated the impact of anesthetic drugs on glucose metabolism and insulin sensitivity. The patient cohort was predominantly male (60%) with a mean age of 43.5 years and an

average BMI of 24.8 kg/m². Most participants were classified as ASA Grade I, indicating low preoperative risk. These baseline characteristics provided a relatively homogenous population for assessing metabolic alterations without major confounding factors.

A significant rise in both blood glucose and serum insulin levels was observed postoperatively, particularly at 6 hours after surgery. The mean blood glucose increased from 92.4 mg/dL preoperatively to 131.6 mg/dL at 6 hours post-op, while insulin levels rose from 8.3 µIU/mL to 15.1 µIU/mL. These changes were statistically significant ($p < 0.001$), indicating a robust stress-induced hyperglycemic response mediated by both surgical and anesthetic factors. Although there was a partial reduction at 24 hours post-surgery, the values did not return to baseline, suggesting that the effects on glucose homeostasis persisted into the early postoperative period.

The Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) increased from 1.9 to 4.9 at 6 hours postoperatively, reflecting a clear decrease in insulin sensitivity during this period. By 24 hours, HOMA-IR declined to 3.0, showing partial recovery but still significantly elevated compared to preoperative values ($p < 0.01$). This pattern aligns with the expected metabolic stress response triggered by anesthesia and surgical trauma, which can transiently impair insulin function.

A correlation analysis revealed that higher BMI was significantly correlated with increased postoperative insulin resistance ($r = 0.48$, $p = 0.001$), suggesting that overweight individuals are more prone to anesthesia-induced metabolic disturbances. This finding highlights the importance of careful intraoperative monitoring and postoperative glycemic control, especially in patients with higher BMI.

Subgroup analysis based on anesthetic agent used (Sevoflurane vs. Isoflurane) demonstrated that Sevoflurane was correlated with lower postoperative glucose, insulin, and HOMA-IR values compared to Isoflurane, with statistically significant differences across all parameters ($p < 0.01$). These results suggest that Sevoflurane may have a more favorable metabolic profile, making it a potentially better choice for patients at risk of metabolic derangement.

Recent evidence has highlighted the distinct impacts of various anesthetic agents and techniques on perioperative glucose metabolism and insulin sensitivity. Volatile anesthetic agents have been shown to suppress basal insulin secretion and impair glucose-stimulated insulin release during surgery. However, the neuroendocrine stress response to surgery appears to counteract these effects, promoting gluconeogenesis rather than lipid oxidation or insulin resistance, thus modulating the anesthetic-induced metabolic suppression [10].

Propofol, an intravenous anesthetic, demonstrates a beneficial metabolic profile in both human and animal studies. In diabetic rats, propofol improved glucose tolerance, increased insulin secretion, and enhanced the production of fibroblast growth factor-21 (FGF-21) and glucagon-like peptide-1 (GLP-1), suggesting insulin-sensitizing effects through reduced endoplasmic reticulum stress [11]. Similarly, a randomized clinical trial in diabetic patients showed that total intravenous anesthesia (TIVA) using propofol resulted in significantly lower postoperative blood glucose and cortisol levels compared to total inhalation anesthesia (TIHA), indicating improved glycemic control and a moderated stress response [12].

Comparative analyses also revealed that regional anesthesia, particularly spinal and epidural techniques, induced a smaller rise in blood glucose compared to general anesthesia. This was evident in both diabetic and non-diabetic patients undergoing elective surgeries, with spinal anesthesia providing the most stable glycemic response and minimizing the need for intraoperative insulin administration [13].

In head-to-head comparisons of specific agents, patients anesthetized with sevoflurane and desflurane exhibited a greater rise in intraoperative blood glucose than those receiving propofol. Although propofol was correlated with slightly delayed recovery, its superior glycemic control supports its use in settings where metabolic stability is prioritized [14]. Additional studies in elderly patients under remifentanil anesthesia found that intraoperative low-dose glucose infusion mitigated fat catabolism without triggering hyperglycemia, underscoring the role of tailored perioperative glucose management [15].

Mechanistic investigations have confirmed that propofol facilitates glucose-stimulated insulin secretion by inhibiting stromatoxin-1-sensitive potassium channels in pancreatic beta cells, reinforcing its metabolic safety in surgical settings [16]. Furthermore, clinical comparisons between propofol and isoflurane found that only propofol significantly reduced postoperative glucose levels, emphasizing its role in minimizing perioperative hyperglycemia in diabetic patients [17].

Conclusion

This study demonstrates that anesthetic agents significantly impact glucose metabolism and insulin sensitivity in surgical patients, with a marked rise in blood glucose and insulin resistance postoperatively. Sevoflurane was correlated with a more favorable metabolic response compared to Isoflurane. These findings highlight the need for careful anesthetic

selection and perioperative glycemic monitoring, especially in patients with higher BMI or metabolic risk.

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