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Evaluating the Effect of Different Types of Anesthesia on Intraoperative Blood Glucose Levels in Diabetics and Non-Diabetics Patients: A Systematic Review and Meta-Analysis

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Abstract

Background and aim: the aim of present Systematic Review and Meta-Analysis was evaluate the effect of different types of anesthesia on intraoperative blood glucose levels of diabetes patients.

Method: From the electronic databases, PubMed, Cochrane Library, Embase, ISI have been used to perform a systematic literature over the last twenty years between February 2011 and January 2021. For Data extraction, two reviewers blind and independently extracted data from abstract and full text of studies that included.Prior to the screening, kappa statistics was carried out in order to verify the agreement level between the reviewers. The kappa values were higher than 0.80. Mean difference with 95% confidence interval (CI), fixed effect model and Invers-variance were calculated. Random effects were used to deal with potential heterogeneity and I^2 showed heterogeneity. I^2 values above 50% signified moderate-to-high heterogeneity. The Meta analysis have been evaluated with the statistical software Stata/MP v.16 (The fastest version of Stata).

Result:431 studies were selected to review the abstracts, finally ten studies were selected. Mean difference of post-operative blood glucose level between spinal and general anesthesia in non-diabetics patients was 22.12 (MD, 22.12 95% CI 21.79, 22.46; p=0.00), between epidural + general and general anesthesia in diabetics patients was -4.30 (MD, -4.30 95% CI -15.63, 7.03; p=0.46).

Conclusion:compared to different types of anesthesia in diabetic and non-diabetic populations, general anesthesia has better control in postoperative blood glucose levels.

Key words: general anesthesia, epidural anesthesia, spinal anesthesia, combined anesthesia

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Introduction

Diabetes mellitus (DM) is a disorder in which the body does not respond normally to insulin and causes abnormally high blood sugar (glucose) levels. This multisystem metabolic disease has recently become common in diabetics(1, 2). Studies have reported that about 2 to 4 percent of patients who undergo surgery have diabetes(3, 4). Perioperative for diabetics, complications such as a sharp rise in blood glucose, increase in acute complications and diabetic infections, delayed wound healing, and eventual postoperative mortality may occur (5-7).Therefore, discussing the better type of anesthesia and taking glycemic control were necessary. Studies have shown that surgical stress and anesthesia promotes hyperglycemia in a diabetic patient. However, few studies have reported that glucose levels between 150 and 200 mg / dL (8 to 11 mmol / L) should be maintained during surgery(8). Due to the importance of the subject and few studies in this field, the aim of present Systematic Review and Meta-Analysis was evaluate the effect of different types of anesthesia on intraoperative blood glucose levels of diabetes patients.

Methods

Search strategy

From the electronic databases, PubMed, Cochrane Library, Embase, ISI have been used to perform a systematic literature over the last twenty years between February 2011 and January 2021. Therefore, a software program (Endnote X8) has been utilized for managing the electronic titles. Searches were performed with mesh terms:

("Diabetes Mellitus"[Mesh] OR "Diabetes Mellitus, Type 2"[Mesh] OR “Diabetes Mellitus, Type 1"[Mesh]) OR "Diabetes Insipidus"[Mesh]) OR "Diabetes Complications"[Mesh]) OR ("Diabetes Insipidus, Neurogenic"[Mesh] OR "Diabetes Insipidus, Nephrogenic"[Mesh] OR "Diabetes, Gestational"[Mesh] OR "Diabetes Mellitus, Lipoatrophic"[Mesh])) AND "Anesthesia"[Mesh]) OR "Anesthesia, General"[Mesh]) OR ("Anesthesia, Caudal"[Mesh] OR "Anesthesia, Epidural"[Mesh])) OR "Anesthesia, Spinal"[Mesh]) AND ("Blood Glucose Self-Monitoring"[Mesh] OR "Glycemic Control"[Mesh])) AND ("General Surgery"[Mesh] OR "surgery" [Subheading] OR "Surgical Procedures, Operative"[Mesh])) OR "Perioperative Period"[Mesh]) OR "Postoperative Period"[Mesh]. Other databases were searched using the following keywords, spinal anesthesia OR general anesthesia OR epidural anesthesia OR subarachnoid anesthesia OR combined anesthesia AND Diabetic patients OR Diabetes Mellitus OR Diabetes AND blood glucose levels.

This systematic review has been conducted on the basis of the key consideration of the PRISMA Statement–Perfumed Reporting Items for the Systematic Review and Meta-analysis(9), and PICO strategy (Table1).

Table1. PICO strategy

PICO strategy	Description
P	Population: diabetics and non-diabetics patients undergoing operations with anesthesia
I	Intervention: different types of anesthesia

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C	Comparison: control group (any types of anesthesia)
O	Outcome: blood glucose levels

Selection criteria

Inclusion criteria

1. Randomized controlled trials studies, controlled clinical trials, Prospective and retrospective cohort studies, cross-sectional studies.
2. Diabetics and non-diabetics patients
3- Different types of anesthesia
4- Reported blood glucose levels
5. English language

Exclusion criteria

1. In vitro studies, reviews, case-control studies, case report and animal studies
2. Incomplete or inconsistent data for the purpose of the present study.

Data Extraction and method of analysis

The data have been extracted from the research included with regard to the study, years, and study design, Sample Size, surgery, anesthesia, intervention and control group. Cochrane Collaboration's tool (10) used to assessed quality of the studies that included in present meta-analysis. The scale scores for low risk was 1 and for High and unclear risk was 0, Scale scores range from 0 to 6 and higher score means higher quality. Newcastle-Ottawa Scale (NOS) (34) used to assessed quality of the cohort studies and case-control studies, this scale measures three dimensions (selection, comparability of cohorts and outcome) with a total of 9 items. In the analysis, any studies with NOS scores of 1-3, 4-6 and 7-9 were defined as low, medium and high quality, respectively.

For Data extraction, two reviewers blind and independently extracted data from abstract and full text of studies that included.Prior to the screening, kappa statistics was carried out in order to verify the agreement level between the reviewers. The kappa values were higher than 0.80.

Mean difference with 95% confidence interval (CI), fixed effect model and Invers-variance were calculated. Random effects were used to deal with potential heterogeneity and I^2 showed heterogeneity. I^2 values above 50% signified moderate-to-high heterogeneity. The Meta analysis have been evaluated with the statistical software Stata/MP v.16 (The fastest version of Stata).

Results

According to aim of present study, in the initial search with keywords, 456 articles were found. In the first step of selecting studies 431 studies were selected to review the abstracts. Then, studies that did not meet the inclusion criteria were excluded from the study (n=385). In the second step, the full text of 46 studies was reviewed, in this step 36 article were excluded and finally ten studies were selected (Figure1).

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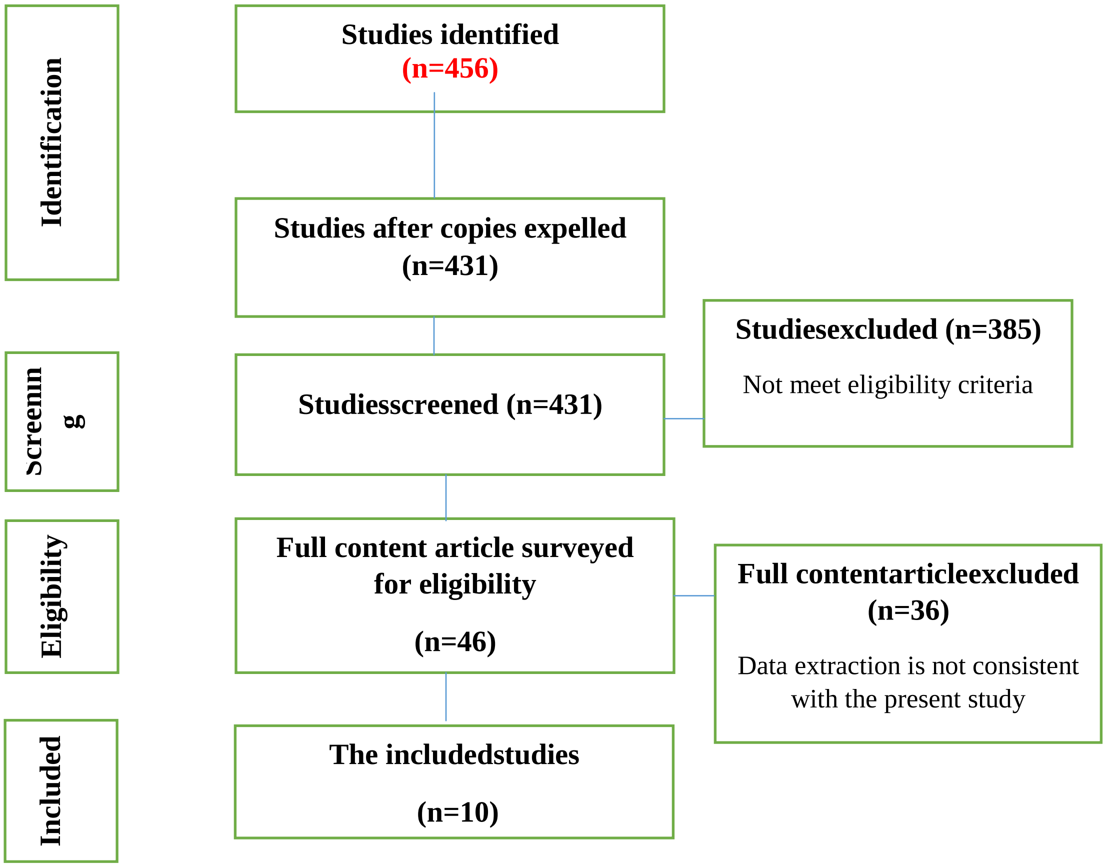
Figure 1. Study Attrition



Characteristics

Ten studies have been included in present article. The basic characteristics of the ten studies are summarized in Table 2. The number of patients a total was 980.

Bias assessment

According to Cochrane Collaboration's tool, two studies had a total score of 4/6, no RCT reported allocation concealment and blinding of outcome assessment. Low risk of bias observed in two RCT studies (Table3).According to NOS tool, four studies had a total score of 7/9, two studies had a total score of 5/6, and one study had a total score of 9/9; 6/9; five studies had low risk of bias, three studies had medium quality (Table4).

Table2. Studies selected for systematic review and meta-analysis.

Study. Years	Study design	Study population	Number of patients		Types of surgical procedures	Type of anesthesia		outcome
			Intervention group	Control group		Intervention group	Control group	
Hani et al.,2021 (11)	prospective	non-diabetes patients	171	131	cesarean section	general anesthesia	spinal anesthesia	There was no significant difference in the number

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								of gestational diabetes patients between both groups
Kochhar et al.,2020 (12)	RCT	non-diabetes patients	15	14	elective head and neck cancer surgery	general anesthesia	spinal anesthesia + general anesthesia	No statistically significant difference was found in baseline and post-incision blood glucose levels
Har et al.,2019 (13)	cross-sectiona	non-diabetes patients	97	50	Any surgery	general anesthesia	spinal anesthesia	General anesthesia was significantly associated with postoperative hyperglycemia
Kumar et al.,2019 (4)	Retrospective	diabetes patients	50	50	Any surgery	general anesthesia	spinal anesthesia	The study concludes that there was an increased intraoperative blood glucose fluctuation, alterations in the BP and HR level among the diabetic patients upon administration of both general and regional anaesthesia.
El-Radaideh et al.,2019 (14)	Prospective	non-diabetes patients	23	35	cesarean section	general anesthesia	spinal anesthesia	There is a much lower increase in blood glucose concentration under spinal anesthesia than under general anesthesia.
Singh et al.,2019 (15)	cross-sectiona	non-diabetes patients	60	60	non-diabetes patients	general anesthesia	spinal anesthesia	Both the group were almost identical in demographic parameters

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Tabatabaie et al.,2017 (16)	RCT	diabetes patients	22	22	Coronary Artery Bypass Graft Surgery	general anesthesia + spinal anesthesia	general anesthesia	Spinal anesthesia along with general can control blood sugar in diabetics and reduce the need for insulin, as well as blood pressure and heart rate in improving the quality of anesthesia, improve the outcome of surgery, pain and quality of life of diabetic patients undergoing coronary artery bypass surgery.
Sağlık et al.,2015 (17)	prospective	non-diabetes patients	20	20	Hip and Knee Arthroplasty	general anaesthesia	epidural anaesthesia	No difference was found between the groups with regard to preoperative HR, blood pressure, cortisol, ACTH, insulin and glucose levels
VAGYANNAVAR et al.,2014 (18)	prospective	non-diabetes patients	30	30	elective major upper abdominal surgeries	general anaesthesia	epidural anaesthesia	There were no significance difference between baseline hemodynamic and biochemical parameters in both the groups
Werner et al.,2011 (19)	prospective	non-diabetes patients	20	20	major thoracic surgical	general and thoracic epidural anaesthesia	general anaesthesia	No significant differences between the groups were found with respect to mean ±SD blood

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								glucose levels or insulin requirements during anaesthesia.
Werner et al.,2011 (19)	prospective	diabetes patients	20	20	major thoracic surgical	general and thoracic epidural anaesthesia	general anaesthesia	No significant differences between the groups were found with respect to mean ±SD blood glucose levels or insulin requirements during anaesthesia

Table3. Risk of bias assessment (Cochrane Collaboration's)

study	Random sequence generation	allocation concealment	blinding of participants and personnel	blinding of outcome assessment	incomplete outcome data	selective reporting	Total score
Kochhar et al.,2020 (12)	+	+	-	?	+	+	4
Tabatabaie et al.,2017 (16)	+	+	?	?	+	+	4

Low (+), unclear (?), high (-)

Table4. Risk of bias assessment (NOS tools)

Study. Years	Selection (5 score)				Comparability (2 score)	Outcome (2 score)		Total score
	representative sample	Sample size	No respondents	Ascertainment of the exposure	Based on design and analysis	Assessment of outcome	Statistical test	
Hani et al.,2021 (11)	1	1	0	1	2	1	1	7
Har et al.,2019 (13)	1	1	0	2	2	1	0	7
Kumar et al.,2019 (4)	1	1	0	0	1	1	1	5

El-Radaideh et al.,2019 (14)	1	1	1	2	2	1	1	9
Singh et al.,2019 (15)	1	1	0	1	1	1	0	5
Sağlık et al.,2015 (17)	1	1	0	1	2	1	1	7
VAGYANNAVAR et al.,2014 (18)	1	1	0	0	2	1	1	6
Werner et al.,2011 (19)	1	1	1	1	2	1	0	7

Results of the meta-analysis

Spinal and general anesthesia

Mean difference of post-operative blood glucose level between spinal and general anesthesia in non-diabetics patients was 22.12 (MD, 22.12 95% CI 21.79, 22.46; p=0.00) among four studies and heterogeneity found (I^2= 98.98%; P =0.5100), there was statistically significant difference of post-operative blood glucose level between spinal and general anesthesia in non-diabetics patients (Figure2).

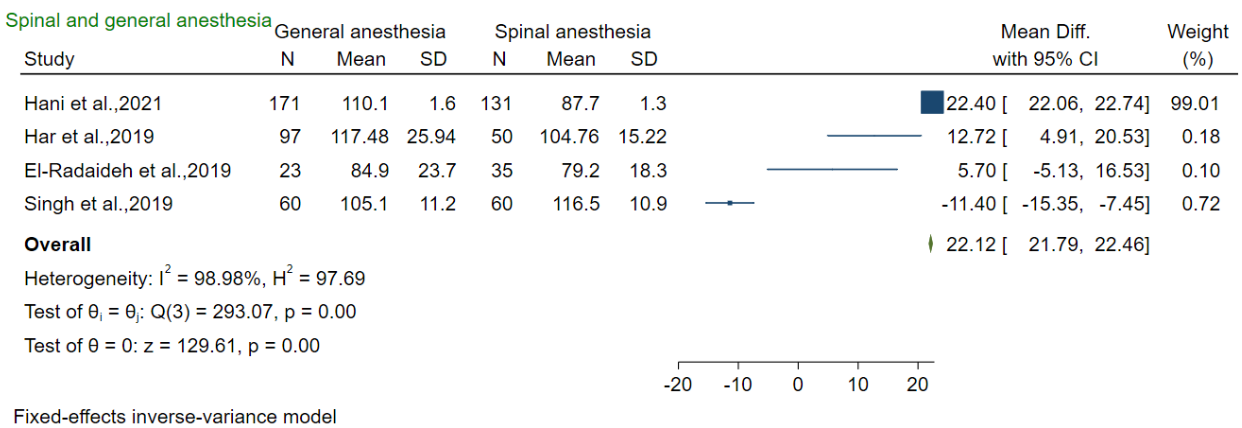

Figure2. Forest plot showed mean difference of post-operative blood glucose level between spinal and general anesthesia in non-diabetics patients

Spinal+ general and general anesthesia

Mean difference of post-operative blood glucose level between spinal+ general and general anesthesia in diabetics patients was 41.79 (MD, 41.79 95% CI 35.17, 48.41; p=0.00) among one study. There was statistically significant difference of post-operative blood glucose level between spinal+ general and general anesthesia in diabetics patients (Figure3). Mean difference of post-operative blood glucose level between spinal+ general and general anesthesia in non-diabetics patients was 3.00 (MD, 3.00 95% CI -9.91, 15.91; p=0.65) among one study. There was no statistically significant difference of post-operative blood glucose level between spinal+ general and general anesthesia in non-diabetics patients (Figure4).

Epidural and general anesthesia

Mean difference of post-operative blood glucose level between epidural and general anesthesia in non-diabetics patients was 6.22 (MD, 6.22 95% CI 1.73, 10.71; p=0.01) among two studies

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and heterogeneity found (I^2= 0.00%; P =0.83), there was statistically significant difference of post-operative blood glucose level between epidural and general anesthesia in non-diabetics patients (Figure5).

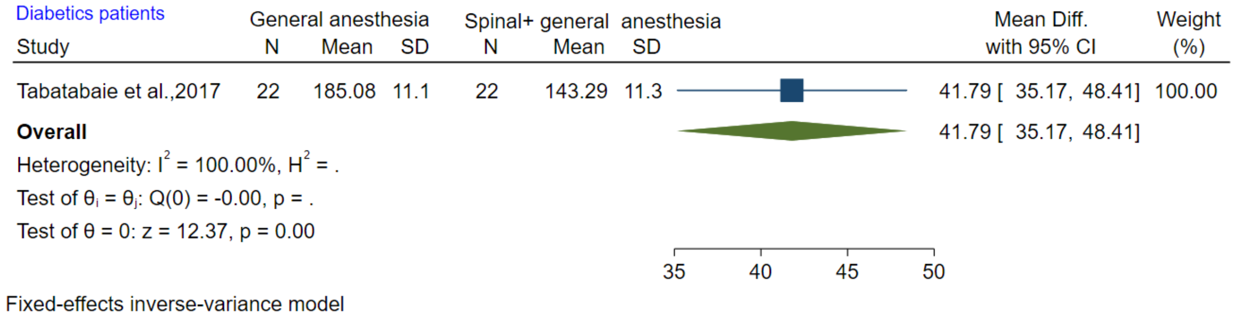

Figure3. Forest plot showed mean difference of post-operative blood glucose level between Spinal+ general and general anesthesia in diabetics patients

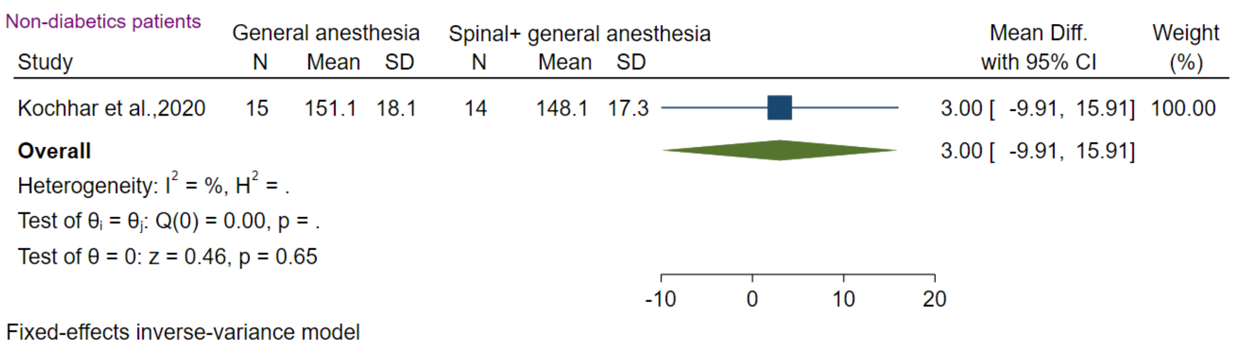

Figure4. Forest plot showed mean difference of post-operative blood glucose level between Spinal+ general and general anesthesia in non-diabetics patients

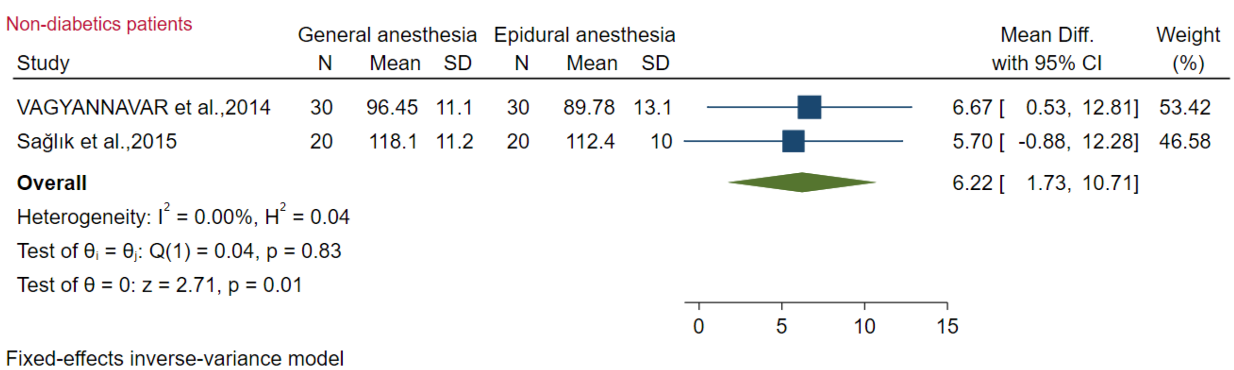

Figure5. Forest plot showed mean difference of post-operative blood glucose level between epidural and general anesthesia in non-diabetics patients

Epidural + general and general anesthesia

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Mean difference of post-operative blood glucose level between epidural + general and general anesthesia in non-diabetics patients was -1.50 (MD, -1.50 95% CI -8.92, 5.92; p=0.69) among one study, there was no statistically significant difference of post-operative blood glucose level between epidural + general and general anesthesia in non-diabetics patients (Figure 6).
Mean difference of post-operative blood glucose level between epidural + general and general anesthesia in diabetics patients was -4.30 (MD, -4.30 95% CI -15.63, 7.03; p=0.46) among one study. There was no statistically significant difference of post-operative blood glucose level between epidural + general and general anesthesia in diabetics patients (Figure7).

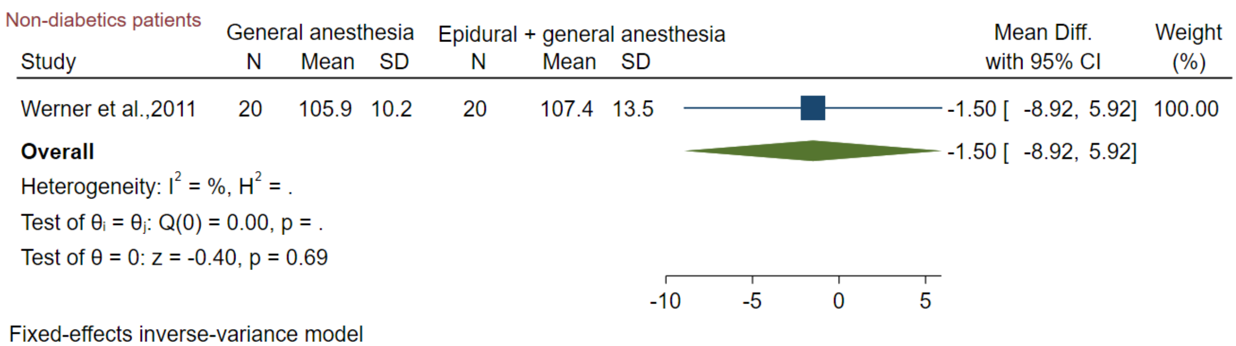

Figure6. Forest plot showed mean difference of post-operative blood glucose level between epidural + general and general anesthesia in non-diabetics patients

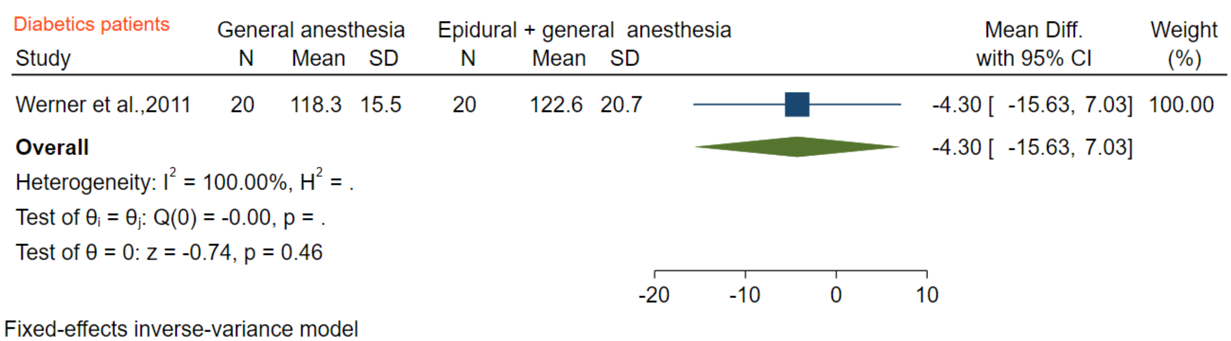

Figure7. Forest plot showed mean difference of post-operative blood glucose level between epidural + general and general anesthesia in diabetics patients

Spinal and general anesthesia in diabetics patients

Mean difference of post-operative blood glucose level between spinal and general anesthesia in diabetics patients was -11.30 (MD, -11.30 95% CI -18.74, -4.13; p=0.00) among one study, there was statistically significant difference of post-operative blood glucose level between spinal and general anesthesia in diabetics patients (Figure8).

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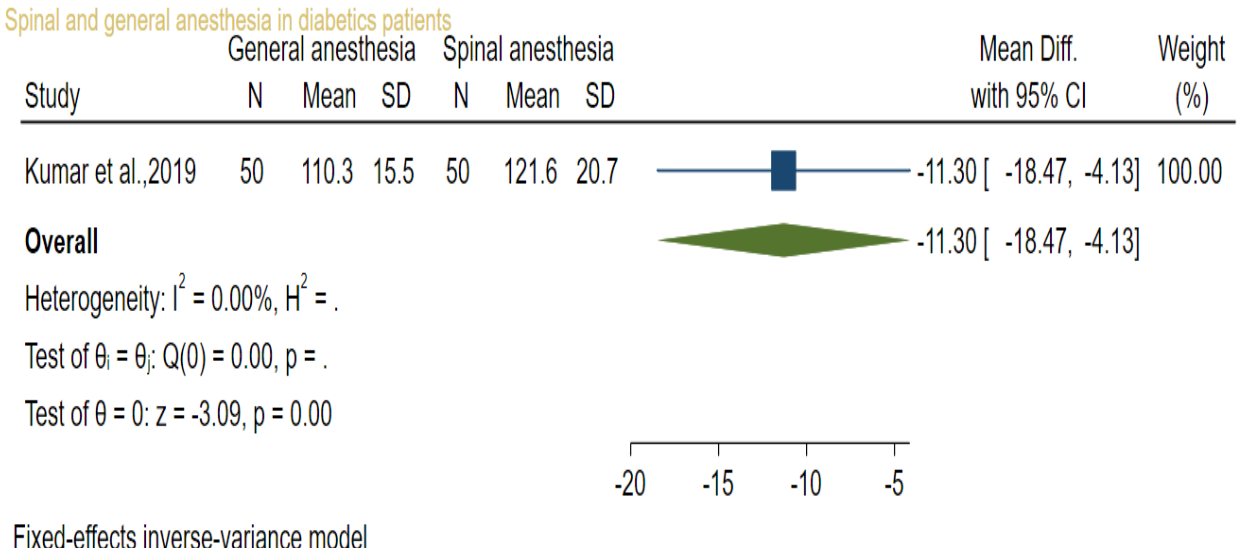

Figure8. Forest plot showed mean difference of post-operative blood glucose level between spinal and general anesthesia in diabetics patients

Subgroup meta-analysis

Subgroup meta-analysis of different types of anesthesia on intraoperative blood glucose levels in diabetics and non-diabetics patients was 21.89 (MD, 21.89 95% CI 21.56, 22.23; p=0.00) (Figure9).

Discussion

Diabetes is the most common metabolic condition worldwide and a major risk-factor for worse outcomes after surgery including mortality(20, 21). Present systematic review and meta-analysis showed general anesthesia causes higher blood glucose concentrations than spinalanesthesia in non-diabetics patients. Blood glucose level among the diabetic patients under general and spinalanesthesiawas found to be higher in post-surgery period when compared to the blood glucose level among the patients in pre surgery period. Combined general-epidural and general-spinalhad lower blood glucose levels. In a previous meta-analysis study conducted by Li et al., 2017 with the aim of assessing the impact of different anesthesia on intraoperative blood glucose levels of diabetes patients, the results showed thatcombined general-epidural anesthesia has a better glycemic control in intraoperative blood glucose levels(22).

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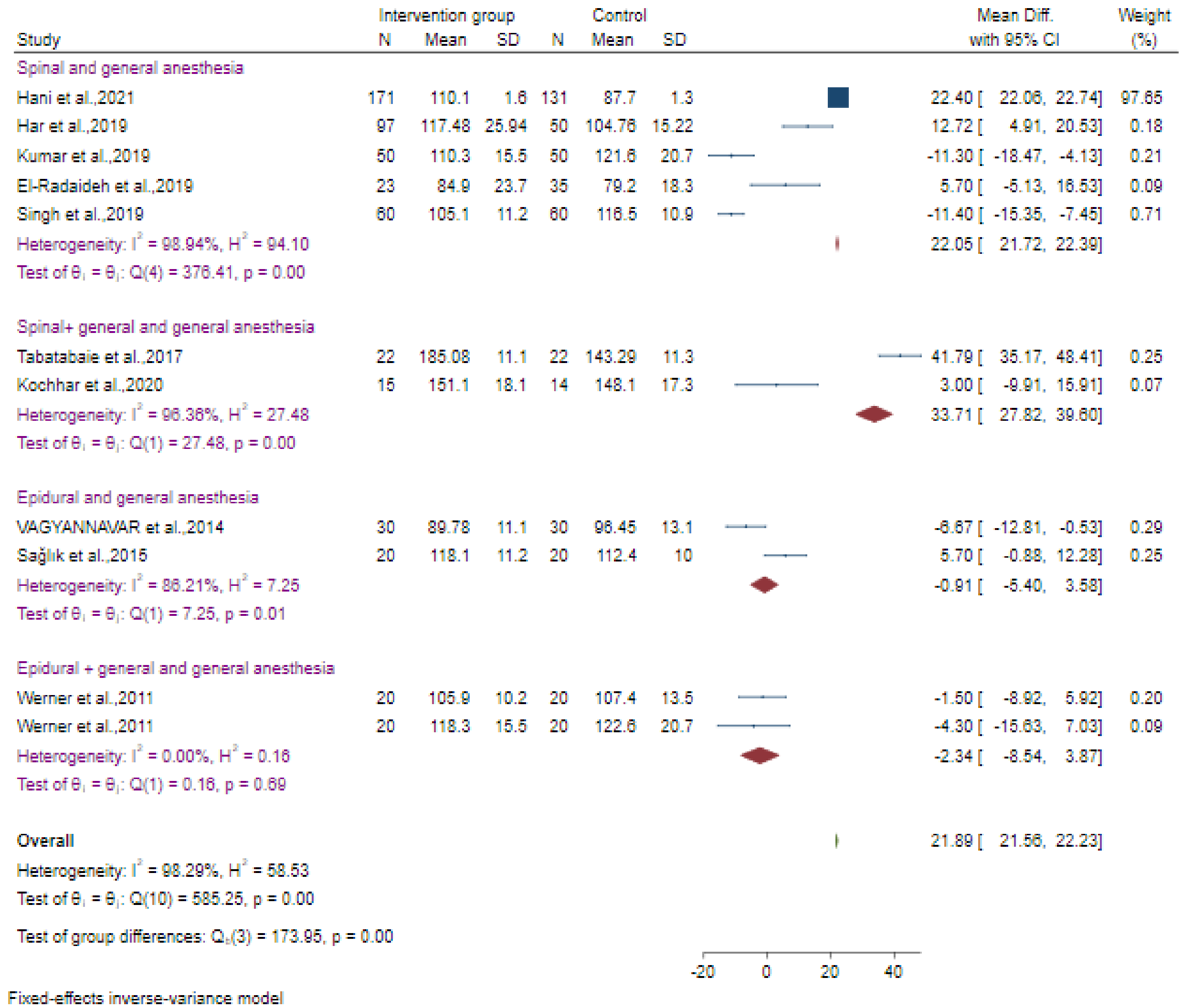

Figure9. Forest plot showed Subgroup meta-analysis

Study showed the post-operative readings were significantly higher in the general anesthesia group with a mean sugar level of 110.1 mg/dL and a mean sugar level in the spinal anesthesia group of 87.7 mg/dL (P = 0.00)(11).Other study showed there wasstatistically significant differenceof post-operative plasma glucose among non-diabetics patients who received general and spinal anesthesia(13). El-Radaideh et al., compared the blood glucose concentration with spinal anesthesia or general anesthesia in patients undergoing elective cesarean section surgery, the result showed much lower increase in blood glucose concentration under spinal anesthesia than under general anesthesia(14). One study reported spinal anesthesia with general anesthesia can control the blood sugar of diabetic patients and reduce the need for insulin in them, as well as control blood pressure and heart rate to improve the quality of anesthesia, improve theoutcome of analgesia and quality of life in diabetic patients undergoing coronary artery bypass graft surgery andplay an important role(16).In some studies, it has been suggested that hypoglycemia in patients undergoing neuraxial anesthesia with general anesthesia is due to decreased gluconeogenesis, and increased environmental consumption in this area is less important due to decreased insulin during the stress response. The role of thoracic epidural block in inhibiting the stress response seems to be greater than mere anesthesia because the use of systemic analgesia by opioid drugs or epidural block by these drugs has not been able to inhibit the stress response as well as local anesthetics(23).It seems that in addition to the control effects of spinal anesthesia with general on the control of blood sugar in diabetic patients, according to the general application mentioned for spinal anesthesia in cases such as reduction of deep vein thrombosis, pulmonary embolism, reduced urgency Blood transfusion, lower risk of pneumonia and respiratory depression, and reduction of myocardial ischemia and infarction, promote this method to have positive effects on improving the quality of anesthesia, analgesia and quality of life of the patient. It is also recommended to emphasize the use of this method in anesthesia training courses so that by encouraging specialists to consider it in their decisions, it will be a suitable solution in dealing with special patients (16, 24).It should be noted that elevated postoperative blood glucose levels also increase the risk of infection, which easily leads to a variety of complications and higher surgical risks. Therefore, the choice of anesthesia was an important method to ensure stable blood glucose levels.One of the limitations of the present study was the high heterogeneity between the studies and one of the strengths of the present study was the high quality of the studies. It is suggested that more RCT studies be performed in this area.High sample size and follow-up period can help to report better evidence. Also should pay attention to the advantages and disadvantages of different types of anesthesia and physicians should choose a more appropriate anesthesia according to the conditions and preferences of patients.

Conclusion

The results of meta-analysis in the present study show that compared to different types of anesthesia in diabetic and non-diabetic populations, general anesthesia has better control of glycemic in postoperative blood glucose levels.

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