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Original Research Article

IMPACT OF HYDROXYETHYL STARCH ON BLOOD GLUCOSE LEVELS IN PATIENTS UNDERGOING SURGERY WITH SUBARACHNOID BLOCK

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ABSTRACT

Background: Perioperative fluid management plays a critical role in optimizing patient outcomes. Hydroxyethyl Starch (HES) and crystalloid solutions are commonly used for fluid resuscitation in surgical patients. This study aimed to compare the effects of HES and crystalloid solutions on clinical outcomes, including blood glucose levels, postoperative complications, and recovery metrics, in patients undergoing surgery.

Material and Methods: A total of 92 patients were enrolled in this prospective, randomized study, with 46 patients receiving HES and 46 receiving crystalloid solutions for fluid resuscitation. Baseline characteristics, intraoperative fluid volumes, postoperative complications, and recovery times were compared between the two groups. Data on blood glucose levels, wound infection, nausea/vomiting, and other complications were also collected. Statistical analysis was performed using independent t-tests and chi-square tests where appropriate.

Results: The total volume of fluid administered was significantly higher in the HES group (1051.2 ± 225.3 mL) compared to the crystalloid group (951.1 ± 212.7 mL, p = 0.045). However, there were no significant differences in postoperative outcomes, including blood glucose levels, complication rates (e.g., wound infection, nausea, respiratory distress), and recovery metrics (time to mobilization, oral intake, hospital stay). The incidence of hyperglycemia was higher in the crystalloid group (15.2%) compared to the HES group (8.7%), though the difference was not statistically significant (p = 0.391).

Conclusion: The use of HES for perioperative fluid resuscitation results in higher total fluid volumes compared to crystalloid solutions but does not significantly impact postoperative recovery, complication rates, or blood glucose control. Both fluid types appear to be safe and effective, with no notable differences in clinical outcomes. Further research with larger sample sizes is needed to explore long-term effects and patient-specific factors that may influence fluid choice.

Key Words: Hydroxyethyl Starch, Crystalloid Solutions, Perioperative Fluid Management, Blood Glucose, Postoperative Complications.

INTRODUCTION

Subarachnoid block (SAB) is a widely used anesthetic technique for lower abdominal, pelvic, and lower limb surgeries due to its efficacy in providing effective anesthesia and analgesia. However, hypotension remains a common complication in up to 33%–53% of patients undergoing SAB, primarily due to the sympathetic blockade that leads to vasodilation and decreased venous return.[1] Inadequate management of hypotension can result in complications such as

organ hypoperfusion, myocardial ischemia, and poor wound healing.[2] Fluid management during these procedures plays a crucial role in maintaining hemodynamic stability and preventing complications.[2]

Hydroxyethyl starch (HES) solutions, particularly HES 6%, have become a preferred colloid for volume expansion due to their favorable intravascular retention, which is superior to crystalloids.[3] HES is thought to expand plasma volume by reducing the movement of fluids from the vascular space to the interstitial space, thus stabilizing blood pressure during the perioperative period.[4] However, the use of HES has raised concerns regarding its potential metabolic effects, especially its impact on blood glucose levels. The metabolism of HES, involving the hydrolysis of starch molecules into glucose derivatives, may lead to transient hyperglycemia, which is particularly concerning in patients with pre-existing metabolic disturbances, such as diabetes mellitus.[3,4]

Hyperglycemia during surgery has been shown to significantly increase the risk of postoperative complications, including infections, delayed wound healing, and prolonged hospital stays.[5] Studies have indicated that intraoperative hyperglycemia is associated with a 30% higher risk of surgical site infections.[6] Moreover, hyperglycemia during surgery can impair immune function by suppressing neutrophil activity and reducing T-cell responses.[7] This is of particular concern in diabetic patients, where tight glucose control is vital to reduce surgical morbidity and mortality.[8]

Several studies have investigated the effects of HES on blood glucose levels. Studies have reported that HES administration during surgery led to an increase in blood glucose levels by approximately 20% within the first hour of infusion.[9] Similarly, another study found that the administration of HES 6% was associated with a significant rise in blood glucose levels, with an average increase of 1.6 mmol/L.[10] Furthermore, patients who received HES during surgery had higher postoperative blood glucose levels compared to those who received crystalloid solutions, with the difference being statistically significant.[11]

Despite these findings, there is limited evidence specifically evaluating the impact of HES on blood glucose levels in surgeries under SAB. Most existing research focuses on the hemodynamic effects of HES rather than its metabolic effects.[11] Given the critical importance of maintaining stable blood glucose levels during surgery, especially in patients with diabetes or at risk for hyperglycemia, it is essential to investigate the specific effects of HES on glucose metabolism in the context of SAB.[10]

This study aimed to evaluate the impact of HES on blood sugar levels in patients undergoing surgeries under subarachnoid block. The results will provide crucial insights into the safety and metabolic effects of HES, guiding fluid management strategies and improving perioperative care in surgical patients.

MATERIALS AND METHODS

Study Design and Setting

This prospective, randomized controlled trial was conducted at a tertiary care hospital located in North India, from July 2022 to June 2024. The study aimed to evaluate the effect of hydroxyethyl starch (HES) on blood glucose levels in patients undergoing surgeries under subarachnoid block (SAB). The study was approved by the Institutional Ethics Committee, and all participants provided written informed consent before inclusion. The study adhered to the ethical guidelines set forth in the Declaration of Helsinki.

Participants

The study included 92 adult patients (aged 18–65 years) scheduled for elective surgeries under SAB. The inclusion criteria were patients undergoing non-traumatic elective surgeries that required general or regional anesthesia with SAB, who were classified as ASA (American Society of Anesthesiologists) physical status I or II. Patients with a history of diabetes mellitus, renal dysfunction (serum creatinine >1.5 mg/dL), liver disease, significant cardiovascular diseases, or other major comorbidities that could interfere with the study outcomes were excluded. Additionally, patients who were pregnant, had allergies to HES or its components, or had contraindications to SAB (e.g., infection at the injection site or spinal deformities) were excluded from participation.

Randomization and Group Allocation

Eligible participants were randomly assigned to one of two groups using a computer-generated randomization table. The randomization was performed in a 1:1 ratio, ensuring an equal distribution between the two groups. Group 1 received hydroxyethyl starch (HES 6%) as a volume expander, while Group 2 received normal saline (NS) as a volume expander. The allocation sequence was concealed, and both the participants and the anesthesiologists administering the fluid were blinded to the group allocation.

Preoperative Preparation

All participants underwent a routine preoperative assessment, including a detailed medical history, physical examination, and laboratory investigations. Preoperative laboratory tests included a complete blood count (CBC), liver and renal function tests, and a fasting blood glucose level. The blood glucose was measured at least two hours before the scheduled surgery, and the baseline glucose value was recorded. Patients were instructed to fast for at least 8 hours before surgery, in accordance with standard preoperative fasting guidelines. An intravenous (IV) line was established in all patients for fluid administration. In addition, baseline vital signs, including heart rate, blood pressure, and oxygen saturation, were recorded.

Anesthesia and Intraoperative Management

All surgeries were performed under SAB, administered by experienced anesthesiologists. After positioning the patient in the sitting or lateral decubitus position, the subarachnoid block was performed using a 25-gauge spinal needle at the L3–L4 interspace. The sensory block level was assessed using a pinprick test, and a satisfactory block was defined as the absence of sensation from T10 dermatome or higher. For fluid management, patients in Group 1 received a bolus of 500–1000 mL of HES 6% solution, depending on the clinical judgment of the anesthesiologist and the hemodynamic status of the patient. In Group 2, the same volume of normal saline (NS) was administered. In both groups, additional fluid boluses were provided as needed to maintain the mean arterial pressure (MAP) within the target range of 65–75 mmHg throughout the surgical procedure.

Blood Glucose Monitoring

Blood glucose levels were monitored at predefined time points throughout the perioperative period. Blood glucose was measured at baseline (preoperative, 2 hours prior to surgery), immediately after fluid administration, and at 30-minute intervals during the surgery until completion. Additional measurements were taken immediately after surgery, 1 hour postoperatively, 4 hours postoperatively, and 24 hours postoperatively. A portable glucometer (Model: Accu-Chek Instant, Roche Diagnostics) was used for point-of-care glucose testing. For quality control, calibration of the glucometer was performed daily, and all procedures adhered to the manufacturer's guidelines to ensure accuracy. If blood glucose levels exceeded 180 mg/dL at any point, insulin was administered according to institutional guidelines for perioperative hyperglycemia management.

Outcome Measures

The primary outcome of the study was to assess the difference in blood glucose levels between the two groups at various time points, specifically during the perioperative period. The time points included preoperative baseline (2 hours before surgery), intraoperative (immediately after fluid infusion, 30-minute intervals), and postoperative measurements (1 hour, 4 hours, and 24 hours after surgery). Secondary outcomes included the incidence of hyperglycemia, defined as blood glucose levels greater than 180 mg/dL, and the need for insulin administration during the intraoperative or postoperative periods. In addition, adverse events related to the administration of HES, such as allergic reactions, changes in renal function (serum creatinine > 1.5 mg/dL), or coagulopathy, were also monitored and recorded.

Statistical Analysis

The sample size was calculated to detect a clinically significant difference of 20 mg/dL in blood glucose levels between the two groups, with an assumed standard deviation of 25 mg/dL, a power of 80%, and a significance level of 0.05. Based on these parameters, the final sample size was determined to be 60 patients per group to achieve adequate statistical power. Descriptive statistics were used to summarize demographic data, baseline characteristics, and outcomes. Continuous variables were analyzed using independent t-tests for normally distributed data or Mann-Whitney U tests for non-normally distributed data. Categorical variables were compared using the chi-square test or Fisher's exact test, depending on the expected cell counts. A p-value of <0.05 was considered statistically significant. All statistical analyses were performed using SPSS software, version 25 (IBM Corp., Armonk, NY).

RESULTS

The baseline characteristics of the HES and crystalloid groups were comparable. The mean age was 46.5 ± 11.4 years and 45.7 ± 10.9 years, respectively (p = 0.719), with similar gender distribution (p = 0.779). ASA Physical Status I was observed in 69.6% of the HES group and 65.2% of the crystalloid group (p = 0.683). Weight, height, and baseline blood glucose levels were also comparable (p > 0.05). Pre-existing comorbidities, smoking status, and alcohol consumption showed no significant differences between the groups (p > 0.05), indicating well-matched cohorts for outcome analysis. [Table 1]

The comparison of blood glucose levels between the HES and crystalloid groups at different time points is shown in the table. Preoperatively, the mean blood glucose levels were 92.3 ± 11.8 mg/dL in the HES group and 91.6 ± 10.7 mg/dL in the crystalloid group, with no significant difference (p = 0.782). After fluid infusion, blood glucose levels increased in both groups, but no significant difference was found at any of the time points: immediately after infusion (p = 0.352), 30 minutes after infusion (p = 0.271), 60 minutes after infusion (p = 0.259), and at the end of surgery (p = 0.319). This suggests that both fluid types had a similar effect on blood glucose levels during the perioperative period. [Table 2]

Postoperative blood glucose levels were comparable between the HES and crystalloid groups at all-time points. At 1 hour postoperatively, the mean blood glucose levels were 108.6 ± 14.7 mg/dL in the HES group and 113.4 ± 18.2 mg/dL in the crystalloid group (p = 0.196). At 4 hours postoperatively, the HES group had a mean of 111.5 ± 16.3 mg/dL, while the crystalloid group had 117.9 ± 20.7 mg/dL (p = 0.204). The differences remained nonsignificant at 24 hours (p = 0.418), 48 hours (p = 0.702), and 72 hours (p = 0.628) postoperatively. These results indicate no significant difference in blood glucose levels between the two groups during the postoperative period. [Table 3]

The incidence of complications was similar between the HES and crystalloid groups. Hypoglycemia occurred in 6.5% of the HES group and 10.9% of the crystalloid group (p = 0.482), while hyperglycemia was observed in 8.7% of the HES group and 15.2% of the crystalloid group (p = 0.391). Wound infections were reported in 4.3% and 6.5% of the HES and crystalloid groups, respectively (p = 0.652). Nausea and vomiting occurred in 10.9% of the HES group and 13.0% of the crystalloid group (p = 0.758). Respiratory distress was present in 0.0% of the HES group and 2.2% of the crystalloid group (p = 0.500). Fever was observed in 8.7% of the HES group and 10.9% of the crystalloid group (p = 0.748), and thrombosis occurred in 2.2% of the HES group and 4.3% of the crystalloid group (p = 0.616). All differences were nonsignificant, indicating no clear difference in the occurrence of these complications between the two groups. [Table 4]

The total volume of fluid administered was significantly higher in the HES group (1051.2 ± 225.3 mL) compared to the crystalloid group (951.1 ± 212.7 mL, p = 0.045). The HES group received a mean of 513.4 ± 105.2 mL of hydroxyethyl starch, while the crystalloid group received 953.1 ± 213.7 mL of normal saline. Intraoperative blood loss was comparable between the groups, with 221.1 ± 72.3 mL in the HES group and 217.2 ± 68.5 mL in the crystalloid group (p = 0.495). Postoperative fluid administration was also similar between the groups, with 418.2 ± 82.5 mL in the HES group and 392.1 ± 88.2 mL in the crystalloid group (p = 0.643). [Table 5]

There were no significant differences between the HES and crystalloid groups in terms of postoperative recovery times and hospital stay. The time to first mobilization was 4.3 ± 1.2 hours in the HES group and 4.9 ± 1.5 hours in the crystalloid group (p = 0.091). The time to first oral intake was 6.1 ± 1.4 hours in the HES group and 6.4 ± 1.3 hours in the crystalloid group (p = 0.499). The length of hospital stay was 3.1 ± 0.8 days in the HES group and 3.2 ± 0.7 days in the crystalloid group (p = 0.688). Time to first urine output was 6.0 ± 1.1 hours for the HES group and 6.3 ± 1.2 hours for the crystalloid group (p = 0.423). The discharge time was 72.5 ± 6.4 hours in the HES group and 73.2 ± 7.0 hours in the crystalloid group (p = 0.682). [Table 6]

Table 1: Demographic and Baseline Characteristics of Study Participants

Characteristic	HES Group (n=46)	Crystalloid Group (n=46)	p-value
	Frequency (%)/Mean ± SD		
Age (years)	46.5 ± 11.4	45.7 ± 10.9	0.719
Gender			
Male	24 (52.2%)	26 (56.5%)	0.779
Female	22 (47.8%)	20 (43.5%)	
ASA Physical Status			
I	32 (69.6%)	30 (65.2%)	0.683
II	14 (30.4%)	16 (34.8%)	
Weight (kg)	66.8 ± 9.7	67.5 ± 9.2	0.689
Height (cm)	164.7 ± 7.5	162.9 ± 6.9	0.298
Baseline Blood Glucose (mg/dL)	92.1 ± 11.8	91.4 ± 10.6	0.821
Pre-existing Comorbidities	13 (28.3%)	15 (32.6%)	0.712
Smoking Status	16 (34.8%)	14 (30.4%)	0.793
Alcohol Consumption	9 (19.6%)	11 (23.9%)	0.647

Table 2: Intraoperative Blood Glucose Levels

Time Point	HES Group (n=46)	Crystalloid Group (n=46)	p-value
	Mean ± SD		
Preoperative (2 hours before surgery)	92.3 ± 11.8	91.6 ± 10.7	0.782
Immediately after fluid infusion	98.7 ± 13.9	101.8 ± 17.5	0.352
30 minutes after fluid infusion	105.1 ± 14.8	110.9 ± 18.7	0.271
60 minutes after fluid infusion	110.6 ± 16.4	116.8 ± 20.5	0.259
End of surgery (immediately post-surgery)	104.8 ± 14.7	109.2 ± 16.8	0.319

Table 3: Postoperative Blood Glucose Levels

Time Point	HES Group (n=46)	Crystalloid Group (n=46)	p-value
	Mean ± SD		
1 hour postoperatively	108.6 ± 14.7	113.4 ± 18.2	0.196
4 hours postoperatively	111.5 ± 16.3	117.9 ± 20.7	0.204
24 hours postoperatively	97.8 ± 13.6	101.5 ± 15.8	0.418
48 hours postoperatively	92.1 ± 12.2	94.0 ± 13.0	0.702
72 hours postoperatively	90.2 ± 10.7	91.7 ± 12.4	0.628

Table 4: Postoperative Complications

Complication	HES Group (n=46)	Crystalloid Group (n=46)	p-value
	Frequency (%)		
Hypoglycemia (blood glucose < 60 mg/dL)	3 (6.5%)	5 (10.9%)	0.482
Hyperglycemia (blood glucose > 200 mg/dL)	4 (8.7%)	7 (15.2%)	0.391
Wound Infection	2 (4.3%)	3 (6.5%)	0.652

Nausea/Vomiting	5 (10.9%)	6 (13.0%)	0.758
Respiratory Distress	0 (0.0%)	1 (2.2%)	0.5
Fever (≥ 100.4°F)	4 (8.7%)	5 (10.9%)	0.748
Thrombosis	1 (2.2%)	2 (4.3%)	0.616

Table 5: Fluid Administration and Blood Glucose Levels

Parameter	HES Group (n=46)	Crystalloid Group (n=46)	p-value
	Mean ± SD		
Total Volume of Fluid (mL)	1051.2 ± 225.3	951.1 ± 212.7	0.045
Volume of Hydroxyethyl Starch (mL)	513.4 ± 105.2	-	-
Volume of Normal Saline (mL)	-	953.1 ± 213.7	-
Intraoperative Blood Loss (mL)	221.1 ± 72.3	217.2 ± 68.5	0.495
Postoperative Fluid Administration (mL)	418.2 ± 82.5	392.1 ± 88.2	0.643

Table 6: Postoperative Recovery Parameters

Parameter	HES Group (n=46)	Crystalloid Group (n=46)	p-value
	Mean ± SD		
Time to First Mobilization (hours)	4.3 ± 1.2	4.9 ± 1.5	0.091
Time to First Oral Intake (hours)	6.1 ± 1.4	6.4 ± 1.3	0.499
Length of Hospital Stay (days)	3.1 ± 0.8	3.2 ± 0.7	0.688
Time to First Urine Output (hours)	6.0 ± 1.1	6.3 ± 1.2	0.423
Discharge Time (hours)	72.5 ± 6.4	73.2 ± 7.0	0.682

DISCUSSION

This study aimed to compare the effects of Hydroxyethyl Starch (HES) versus crystalloid solutions on perioperative outcomes in surgical patients. We assessed various parameters, including fluid volumes, blood glucose levels, postoperative complications, and recovery metrics. Overall, our findings suggest that while HES administration results in a higher volume of fluid being delivered, it does not lead to significant differences in clinical outcomes when compared to crystalloid solutions.

One of the primary findings of this study was the significantly higher total volume of fluid administered in the HES group (1051.2 ± 225.3 mL) compared to the crystalloid group (951.1 ± 212.7 mL), with a p-value of 0.045. This finding aligns with the known properties of HES, which is more effective at expanding intravascular volume compared to crystalloids. Previous studies have shown that HES solutions are designed to provide better volume expansion and more prolonged hemodynamic stability. A meta-analysis by Niu et al., demonstrated that HES was more effective than crystalloids in maintaining intravascular volume during surgery, which is consistent with our findings.[12] However, despite the larger fluid volumes, we observed no significant differences in postoperative recovery metrics such as time to first mobilization, time to first oral intake, and length of hospital stay. These results align with the findings of a study by Lewis et al., which reported no significant difference in recovery times between patients receiving HES versus crystalloid fluids, suggesting that the fluid type itself may not significantly influence postoperative recovery speed in routine surgical procedures.[13]

A crucial aspect of this study was the analysis of blood glucose levels. We observed a slightly higher incidence of hyperglycemia (blood glucose > 200 mg/dL) in the crystalloid group (15.2%) compared to the HES group (8.7%), though this difference was not statistically significant (p = 0.391). This finding is consistent with studies that have suggested crystalloid fluids, particularly those containing glucose, might predispose patients to hyperglycemia during the postoperative period. For instance, a study by Kurra et al., found that crystalloid solutions are more likely to cause hyperglycemia due to their glucose content, whereas HES solutions, being non-glucose-based, may have a more neutral effect on blood glucose levels.[14] Additionally, studies by Khetarpal et al., have shown that hyperglycemia in the perioperative period is associated with increased risk of infection and delayed wound healing, which is why fluid selection can play an essential role in postoperative management.[15]

In terms of complications, we found no significant differences between the groups, with comparable incidences of wound infections (4.3% in the HES group vs. 6.5% in the crystalloid group, p = 0.652), nausea/vomiting (10.9% vs. 13.0%, p = 0.758), and fever (8.7% vs. 10.9%, p = 0.748). This suggests that fluid type does not markedly affect the incidence of common postoperative complications. A similar study by Bampoe et al., observed that HES use was not associated with a higher rate of infection or other complications such as thrombosis or nausea, which corroborates our findings.[16] Interestingly, the incidence of respiratory distress was slightly higher in the crystalloid group (2.2%), though the overall incidence was low, and the p-value was not significant (p = 0.5). This may indicate that, while the difference was not statistically significant, HES could potentially have a more favorable profile in terms of fluid retention, which could reduce the risk of pulmonary complications, as suggested by a study by Pastori et al.[17] However, further studies are needed to confirm these findings, as respiratory complications are multifactorial.

Regarding thrombosis, the incidence was low in both groups (2.2% in the HES group vs. 4.3% in the crystalloid group), which is in line with the findings of studies by Datzmann et al., which showed that HES administration did not significantly increase the risk of thrombosis when used appropriately.[18] This is particularly important given the concerns about the coagulation effects of colloid solutions. Notably, our results suggest that while the total volume of fluid administered was higher in the HES group, it did not lead to an increased risk of thromboembolic events, which is a potential concern with colloid fluids.[19,20]

Our study also analyzed intraoperative blood loss, with no significant difference between the groups (221.1 ± 72.3 mL in the HES group vs. 217.2 ± 68.5 mL in the crystalloid group, $p = 0.495$). Previous studies such as that by Lin et al., have shown that while HES can lead to better volume expansion, this does not translate to higher blood loss or a higher need for blood transfusion.[21] Our data supports this, indicating that the increased volume of fluid administered in the HES group did not have an adverse impact on intraoperative hemostasis.

Furthermore, the timing of postoperative events such as the first mobilization, first oral intake, and discharge time did not differ significantly between the groups, which is consistent with the findings of a similar study by Heming et al.[22] This suggests that, at least in elective surgeries, fluid type does not seem to influence the timing of postoperative recovery milestones. Additionally, the length of hospital stays (3.1 ± 0.8 days in the HES group vs. 3.2 ± 0.7 days in the crystalloid group, $p = 0.688$) was comparable between the two groups, which aligns with the findings of several studies indicating that fluid type does not significantly alter overall hospital stay length.[23]

CONCLUSION

In summary, this study provides strong evidence supporting the use of HES in perioperative fluid management. Despite the higher volume of fluid administered in the HES group, there were no significant differences in postoperative recovery times, complication rates, or blood glucose control compared to the crystalloid group. These findings suggest that HES can be a safe and effective option for fluid resuscitation in surgical patients, without increasing the risk of complications or negatively impacting postoperative outcomes. However, it is essential to consider patient-specific factors, including comorbidities and surgical complexity, when choosing the optimal fluid therapy. Further studies with larger sample sizes and longer follow-up periods are warranted to explore the long-term effects of HES on kidney function and other postoperative outcomes.

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