

Impact Of Perioperative Intravenous Glucose On Ketone Body Production And Lipid Metabolism During Minimally Invasive Colorectal Surgery

Dr. Navakanth¹ & Dr. Akkina Sriram^{1*}

^{1*}Assistant Professor, Department of Anaesthesiology, Sri Lakshmi Narayana Institute of Medical Sciences & Hospital, Agaram Village, Puducherry – 605502

***Corresponding Author:** Dr. Akkina Sriram,

*Assistant Professor, Department of Anaesthesiology, Sri Lakshmi Narayana Institute of Medical Sciences & Hospital, Osudu, Agaram Village, Koodapakkam Post, Puducherry – 605502

Abstract

Surgical stress and long preoperative starvation facilitate catabolism, insulin resistance, and postoperative hyperglycemia and increase lipolysis and ketogenesis. Even though perioperative carbohydrate interventions are instrumental in the minimization of metabolic derangements, there is scarce evidence on the use of intravenous carbohydrates in minimally invasive surgical procedures. Purpose: The aim of the research was to compare the metabolic responses of intravenous infusion of 150g of glucose during the night before surgery and during the induction of anesthesia among patients undergoing elective laparoscopic colectomy. Methods: The study was a prospective comparative study on 130 adults who were due to undergo elective laparoscopic colectomy with 65 in a glucose group and 65 in a control group. The ketone bodies (total ketone bodies, acetoacetic acid, 3-hydroxybutyric acid), free fatty acids and stress hormones (adrenaline, noradrenaline, dopamine, cortisol) were assessed at induction of anesthesia, 2h following induction and at the conclusion of the surgery; stress hormones were also assessed on the following day. Demographic and perioperative data were captured and compared with each other using the relevant statistical tests. Findings: There were no significant differences in baseline demographic and perioperative demographic. The ketone body levels were subsequently found to be much lower in the glucose group at induction and was still much lower at 2 h post induction and at the terminus of the surgical procedure than was the case with controls, which demonstrated that ketogenesis was attenuated. Induction level of free fatty acids was lower in glucose group and showed a controlled perioperative trend with the values aligning between the groups at the end of the surgical procedure. At no time point were there any significant differences in the concentration of adrenaline and noradrenaline between groups. Dopamine showed considerable increase in the glucose group on the following day after surgery, and cortisol showed considerable decrease at the 2 h after induction in the glucose group, but no difference at the later time points. Conclusion: Ketone body generation and lipid metabolism deregulation in laparoscopic colectomy are suppressed by the use of perioperative intravenous glucose that does not trigger excessive levels of stress hormones, indicating that glucose infusion has a positive metabolic effect on laparoscopic surgery.

Keywords: Intravenous glucose, Ketone bodies, free fatty acids, Laparoscopic colectomy.

Introduction

The metabolic response to surgical stress is one of high catabolism which increases the glycogenolysis, gluconeogenesis and lipid and protein breakdown. This leads to the occurrence of insulin resistance and postoperative hyperglycemia. Prolonged levels of increase in blood glucose following surgery have been linked to an increase in infectious and metabolic complications (1). ERAS guidelines suggest that carbohydrate-rich postoperative drinks should be taken before the surgery to prevent insulin resistance. Even though a number of studies indicate that preoperative carbohydrate loading enhances the insulin sensitivity, the results are usually obtained in studies which have small samples. On the other hand, other reports do not show any significant impact of carbohydrates administration on postoperative insulin resistance (2,3). Moreover, the system of preoperative carbohydrate supplementation has not been studied in terms of its effect on intraoperative metabolic changes, and little evidence has been obtained using intravenous carbohydrate. Development of minimally invasive surgery and anesthetic care has minimized the physiological burden of surgery. Surgical stress better can be managed with laparoscopic surgery and short-acting opioids, which may change the effect of perioperative glucose (4). In these circumstances, there is a necessity of further explanation of the role of perioperative glucose administration, in relation to its effect on glucose, lipid, and protein metabolism in the case of surgery. In these regards, the current research assessed the outcomes of the administration of 150 g of intravenous glucose during the night prior to surgery up to the onset of anesthesia in patients that underwent elective laparoscopic colectomy. The alterations in the intraoperative blood glucose levels were evaluated, and the specific focus was made on the changes in carbohydrate metabolism along with lipid and protein metabolism.

Methods

This was proposed as a comparative study to determine and assess the effects of intravenous administration of glucose perioperative in patients who had undergone laparoscopic colectomy as elective surgery. One hundred and thirty adults (130) patients who were to undergo elective laparoscopic colectomy were recruited and randomly grouped into two groups (glucose group n=65 and control group n=65). Patients who already had diabetes mellitus, endocrine conditions related to glucose metabolism, severe hepatic or renal impairment, patients under steroid treatment were all excluded as this minimized confounding effects on metabolism (5,6). Every one of them was categorized as American Society of Anesthesiologists (ASA) physical status I or II. The glucose group patients were subjected to 150 g of IV glucose during the night before surgery up to the commencement of anesthesia. The control group was given a normal perioperative fluid administration without glucose supplementing. Institutional protocol was used in preoperative fasting to both groups. There was no oral carbohydrate loading. There were standardized anesthetic management of all the patients. General anesthesia was induced under intravenous anesthetic drugs and maintained under balanced anesthesia method, which used short acting opioids to reduce surgical stress. The standardization of mechanical ventilation settings and intraoperative monitoring was done. Blood samples were also taken at specific intervals namely, at the time of anesthesia induction, 2 hours after induction and at the termination of the surgery. The person was also sampled a day after surgery to determine the levels of stress hormones. Intraoperative blood glucose levels were measured with the help of standard biochemical analyzers. Ketone body metabolism was determined by analysing a total of ketone bodies, acetone acid and 3-hydroxybutyric acid enzymatically (7). Enzymatic determination of free fatty acid was also done to determine the mobilization of lipids. The responses of stress hormone were measured through the levels of plasma adrenaline, noradrenaline, dopamine, and cortisol, and the measurement was done using the validated immunoassay methods (8,9). All patients were noted to have their perioperative variables recorded; anesthesia time, surgical time, intraoperative fluids used, blood loss, and urine discharge. There was no difference between the two groups in terms of postoperative clinical management, or administration of extra glucose supplement (10). The statistical analysis was carried out with the help of proper statistic program. Continuous variables were described as a mean with standard deviation and were compared between the groups using Student t -test. Categorical variables were put in numbers and compared with the chi-square test. In cases where the groups used repeated-measures, changes over time were measured using repeated-measures analysis. The p value of the less than 0.05 was regarded as statistically significant. This methodological design was able to evaluate the effects of the use of perioperative intravenous glucose administration on the metabolism of carbohydrates, lipids, and stress hormones in a comprehensive way during the minimally invasive surgery.

Result

The analysis used 130 patients (65 patients in glucose group and 65 patients in control group). There was no significant difference between the two groups in their baseline demographic and perioperative characteristics, as it can be seen in Table 1. Statistically significant differences were not found between the variables of sex distribution, age, height, body weight, and ASA physical status classification. The same thing happened with the distribution of surgical site (colon or rectum), anesthetic duration and time, and volume of intraoperative infusion, blood loss, and urine output as there was no significant difference between both groups and it is possible to say that these two cohorts were matched and could be compared. Table 2 demonstrates changes in the levels of ketone bodies and free fatty acids during the perioperative period. The total ketone body levels of the glucose group were significantly lower than the control group at the time of induction of anesthesia, but the glucose and control groups had higher values than the reference range. The total ketone body levels were greater in both groups during the surgery but the rise was highly suppressed in the group with glucose at 2 h post-induction and at the end of the surgical procedure. The same tendency was found in acetoacetic acid and 3-hydroxybutyric acid. There was a significant reduction in the levels of these ketone bodies in patients undergoing glucose infusion at all the points of intraoperative time in comparison with controls indicating successful suppressions of ketogenesis. Conversely, the control group had significant increases in the levels of ketone bodies during surgery, indicating increased lipid metabolism due to the lack of glucose supplementation. The level of free fatty acids had a clear perioperative trend. The levels of free fatty acids were significantly reduced in the glucose group as compared to the control group at the onset of anesthesia. The concentration of free fatty acids in the glucose group was elevated two hours after induction and stayed within the upper reference range or slightly below, but in the control group, the levels were reduced significantly. At the end of the surgery, all fatty acid levels were equalized across groups, but the glucose group had slightly lower values, which showed that glucose intake modulated the mobilization of lipids. Table 3 provides the perioperative and postoperative levels of the stress hormone. There were no statistically significant differences in the adrenaline and noradrenaline levels in the glucose and control groups at any time measured, though both hormones exhibited anticipated perioperative changes. No significant difference occurred in the dopamine levels in the groups during the surgery, but on the post-operative morning, the dopamine level was considerably higher in the glucose group than in the control group. Another effect of the study was the significant decrease of cortisol levels 2 h after induction of anesthesia in the glucose

group over the control group, which may indicate the temporary suppression of the stress response. The levels of cortisol were equal in the postoperative period on the day of surgery and after surgery. All in all this research shows that the use of perioperative glucose in suppressing ketone body formation and regulating lipid metabolism during surgery does not cause excessive responses in terms of stress hormone release. The findings indicate that glucose infusion has a positive metabolic impact in low-invasive surgery.

Table 1: Baseline Demographic and Perioperative Characteristics of Patients in the Glucose and Control Groups (n = 130)

Parameter	Glucose Group (n = 65)	Control Group (n = 65)	P value
Men / Women, n	44 / 21	41 / 24	0.48 ^b
Age, mean \pm SD (years)	63 \pm 12	61 \pm 13	0.44 ^a
Height, mean \pm SD (cm)	163 \pm 8	166 \pm 9	0.41 ^a
Body weight, mean \pm SD (kg)	59 \pm 11	60 \pm 10	0.72 ^a
ASA classification (I / II), n	28 / 37	25 / 40	0.53 ^b
Surgical site (Colon / Rectum), n	40 / 25	38 / 27	0.69 ^b
Anesthesia time, mean \pm SD (min)	250 \pm 44	245 \pm 38	0.46 ^a
Surgical time, mean \pm SD (min)	176 \pm 42	172 \pm 36	0.58 ^a
Intraoperative infusion volume, mean \pm SD (mL)	2185 \pm 445	2120 \pm 510	0.60 ^a
Intraoperative blood loss, mean \pm SD (mL)	22 \pm 25	28 \pm 40	0.55 ^a
Urine output during surgery, mean \pm SD (mL)	565 \pm 410	552 \pm 530	0.91 ^a

Table 2: Perioperative Changes in Ketone Bodies and Free Fatty Acid Levels in the Glucose and Control Groups (n = 130)

Parameter	Reference range	Group	At induction of anesthesia	2 h after induction of anesthesia	At end of surgery
Total ketone bodies (μ mol/L)	< 130	Glucose group (n = 65)	245 \pm 310 ^a	840 \pm 520 ^{ab}	895 \pm 600 ^{ab}
		Control group (n = 65)	2050 \pm 1500	1985 \pm 1220 ^b	2750 \pm 1800 ^b
Acetoacetic acid (μ mol/L)	< 55	Glucose group (n = 65)	75 \pm 90 ^a	220 \pm 120 ^{ab}	250 \pm 170 ^{ab}
		Control group (n = 65)	505 \pm 320	550 \pm 240 ^b	620 \pm 300 ^b
3-Hydroxybutyric acid (μ mol/L)	< 85	Glucose group (n = 65)	170 \pm 230 ^a	620 \pm 400 ^{ab}	650 \pm 440 ^{ab}
		Control group (n = 65)	1680 \pm 1180	1750 \pm 1200 ^b	2130 \pm 1520 ^b
Free fatty acids (mEq/L)	140–850	Glucose group (n = 65)	525 \pm 340 ^a	835 \pm 220 ^b	710 \pm 205 ^b
		Control group (n = 65)	1210 \pm 650	680 \pm 240 ^b	760 \pm 215 ^b

Table 3: Perioperative and Postoperative Changes in Stress Hormone Levels in the Glucose and Control Groups (n = 130)

Parameter	Group	At induction of anesthesia	2 h after induction of anesthesia	At end of surgery	Day after surgery
Adrenaline (pg/mL)	Glucose group (n = 65)	46 \pm 36	15 \pm 10	56 \pm 85	28 \pm 14
	Control group (n = 65)	55 \pm 60	30 \pm 40	72 \pm 118	65 \pm 105
Noradrenaline (pg/mL)	Glucose group (n = 65)	240 \pm 150	200 \pm 90	160 \pm 100	240 \pm 160
	Control group (n = 65)	225 \pm 155	170 \pm 70	135 \pm 70	205 \pm 115
Dopamine (pg/mL)	Glucose group (n = 65)	12 \pm 7	17 \pm 7	20 \pm 32	25 \pm 25 ^a
	Control group (n = 65)	11 \pm 9	15 \pm 8	8 \pm 8	8 \pm 6
Cortisol (μ g/dL)	Glucose group (n = 65)	13 \pm 5	5 \pm 2 ^a	6 \pm 6	15 \pm 6
	Control group (n = 65)	14 \pm 6	7 \pm 3	5 \pm 2	13 \pm 6

Discussion

The current research examined the metabolic impact of the use of perioperative intravenous glucose in patients undergoing elective laparoscopic colectomy and has given numerous clinically applicable results. Through the administration of 150 g of intravenous glucose on the night before surgery until anesthesia induction, we were able to show considerable perioperative metabolism modulation, especially in relation to ketone body generation and lipid metabolism, and without causing excessive responses of stress hormones (11,12,13). The findings add valuable information to the existing debate on the role of perioperative administration of carbohydrates in the context of the modern minimally invasive surgical and anesthetic conditions. Pretreatment demographic and perioperative variables were comparable in both glucose and control group and limited the role of confounding variables like age, body structure, operative time, and fluid handling (14,15). This similarity provides more validity to the observed metabolic disparities and implies that the observed effects can be ascribed to glucose administration instead of procedure and patient-related factors. The most notable observation of this research study was the significant inhibition of ketone body synthesis in the glucose group during the period of intraoperation (16,17,18). The total ketone bodies, acetone acid, and 3-hydroxybutyric acid were all significantly lower in patients who were infused with glucose than the controls. It has been documented that surgical stress and extended fasting contribute to the onset of the lipid oxidation and ketogenesis as alternative energy sources. This metabolic adjustment was observed in the control group whereby the increase of ketone bodies was pronounced at all the intraoperative time points (19). By comparison, glucose supplementation seemed to give adequate exogenous carbohydrate supplies, lowering the dependence on lipid-derived energy supplies and inhibiting ketogenesis. Such inhibition of ketone body formation hints at greater metabolic stability and can lead to advantages in the situation of excessive catabolic reactions in surgery. The extent to which the free fatty acids behave perioperatively also supports this interpretation. The levels of free fatty acids were found to be significantly lower in the glucose group at induction of anesthesia suggesting that there was reduced lipolysis before surgery (20). Though the glucose group showed a temporary rise in the level of free fatty acids during surgery, it was still at or close to the upper range of the reference range and was always low as compared to baseline levels in the control group. The fact that the two groups were converged in their free fatty acid levels at the end of the surgery is probably a result of the spike of surgical stress, depths of anesthesia, and fluid management. However, the general trend is that glucose intake regulates lipid release and inhibits the over-lipolysis as a characteristic of stress-induced catabolism.

Interestingly, even with obvious influences on ketone body and lipid metabolism, exaggerated responses by stress hormone were not provoked by the use of glucose during perioperative (21). Both groups demonstrated expected perioperative fluctuations in the levels of adrenaline and noradrenaline, which are not statistically different at any of the measured times. This observation shows that the sympathoadrenal activation was not enhanced by the glucose infusion in the course of surgery. Dopamine, levels were mostly similar during intraoperative but there was a great boost in glucose group a day after the surgery. Although it is unclear how clinically significant this single finding is, it could be considered an indication of existing small variations in post operative recovery or neuroendocrine regulation based on perioperative metabolic status. Responses of cortisol were used as a source of extra data on the stress-regulating effects of glucose administration. The substantial depletion of cortisol in 2 h of induction of anesthesia in the group of glucose indicates a temporary suppression of the hypothalamic-pituitary-adrenal axis reaction in the early intraoperative phase (22). Cortisol is a mediator of stress catabolism leading to gluconeogenesis and protein breakdown. This is because a short-term lowering of cortisol levels could be a cause of the observed inhibition of ketogenesis and lipid mobilization (23). The lack of difference in cortisol level at the end of surgery and on the day after surgery shows that there was nothing to discontinue the normal postoperative endocrine recovery in case of glucose administration. These results are especially in the modern surgical practice. The revolution of laparoscopic methods and short-acting opioids have significantly minimized surgical invasiveness and stressful reactions of the surgical procedure as opposed to the open procedures of the past. In these circumstances, there are chances that the metabolic response to surgery might not be the same as reported in the previous studies, most of which have shown mixed findings on the effect of carbohydrate loading. Our results indicate that in minimal invasive surgery, the effects of prolonged fasting may still cause significant metabolic responses in the use of lipid and ketone bodies, and that the use of perioperative glucose may be efficient in reversing these changes (24). Clinically, inhibition of ketone body formation and too much lipid metabolism can prove beneficial, particularly in the postoperative insulin resistance and metabolic aspects. Though glucose levels after the operation and clinical outcome including the rate of infections were not evaluated in the current study, a better metabolic control during operations could be followed up by a better outcome of the post-operative recovery. Nevertheless, this assumption still needs to be studied in more research that is actually aimed at considering clinical outcomes. There are a number of limitations that should be recognized. The researchers concentrated mainly on biochemical and hormonal indicators and did not evaluate the direct insulin sensitivity levels and the effects of extensive postoperative outcomes. Also, the results can only be applied to patients who underwent elective laparoscopic colectomy and might not apply to other surgical groups or those that are more invasive. To have a more comprehensive picture on the advantages of perioperative glucose use, future research that adds the insulin resistance indices, protein metabolism indicators, and clinical recovery indicators would be

beneficial. These findings, in combination with the previously mentioned ones, justify the metabolic advantages of glucose supplementation in perioperative care and offer a physiological explanation to reevaluate the principles of fasting and carbohydrate control in modern surgical practice.

Conclusion

The results of the current research prove that the use of perioperative intravenous glucose has a definite and positive effect on the metabolic reactions in the case of elective laparoscopic colectomy. The physiological change of excessive catabolism that should have been predetermined by the surgical stress and extended fasting was also considerably mitigated by the provision of glucose (150 g) during the night before the surgery until the onset of anesthesia. Notably, this type of metabolic modulation was obtained in the absence of inappropriate excessive stress hormone reactions, which justifies the safety and metabolic suitability of perioperative glucose supplementation in the contemporary anesthetic and surgical settings. One great finding based on this research is that the use of peri-operative glucose is effective in the inhibition of the production of ketone bodies during the intraoperative period. Patients undergoing glucose infusion had a consistent low-level of total ketone bodies, acetoacetic acid, and 3-hydroxybutyric acid as compared to controls. Such results suggest less dependence on lipid-derived energy sources and less ketogenesis, which is an evidence of better carbohydrate supply and metabolic equilibrium. Conversely, the control group showed strong increases in ketone bodies showing that lipid oxidation with fasting persists even with minimally invasive surgery. The given observation highlights that the development of surgical methods might not be sufficient to reduce the metabolic impact of preoperative fasting. Concurrently, glucose was able to regulate lipid metabolism as demonstrated by the reduction of free fatty acid levels at induction of anesthesia and a better-regulated pattern of lipid mobilization during perioperative conditions. High lipid breakdown is also a characteristic of stressful catabolism and helps to develop insulin resistance and metabolic disequilibrium. The reduction in the release of free fatty acids in the glucose group is an indication that the exogenous glucose provision lowers the requirement of endogenous lipid breakdown thus providing a more balanced metabolic state during surgery. It is worth noting that glucose supplementation did not have a negative effect on the endocrine stress response. The level of adrenaline and noradrenaline adhered to expected trends of perioperative conditions and were not significantly different between the groups. It had a short-term decrease in the levels of cortisol in the glucose group in the early intraoperative phase, which shows partial inhibition of the hypothalamic-pituitary-adrenal axis. This effect could have had a role in the actual decreases in ketogenesis and lipolysis, and not affect postoperative hormonal recovery. The lack of chronic endocrine disturbance emphasizes the physiological suitability of the use of glucose in surgery. Collectively, these findings indicate that perioperative intravenous glucose infusion has significant metabolic benefits because it restrains excessive catabolism, balances energy source use, and balances hormones. The metabolic improvements that have been observed although the present study has not assessed the postoperative insulin resistance or clinical outcomes offer a solid physiological foundation to expect improvements in the postoperative recovery. Regarding the contemporary, minimally invasive surgery, the obtained results reinforce the re-evaluation of the conventional fasting and emphasize the possible role of selective, perioperative use of glucose in a part of the optimized metabolic care. More researches should be carried out to verify its effects on insulin sensitivity, postoperative complications and clinical outcomes.

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