The Ochsner Journal 14:175–178, 2014
© Academic Division of Ochsner Clinic Foundation

Intraoperative and Postoperative Blood Glucose Concentrations in Diabetic Surgical Patients Receiving Lactated Ringer's Versus Normal Saline: A Retrospective Review of Medical Records

Seth T. Billiodeaux, MD,[1] Christian G. Samuelson, MD,[1] Olga Willett, MD,[1] Sailesh Arulkumar, MD,[1] Drew Thomas, MD,[2] Craig S. Hamilton, MD,[1] Sushil K. Jain, PhD,[3] Chizoba Mosieri, MD,[1] Charles J. Fox, MD[1]

[1]*Department of Anesthesiology, Louisiana State University Health Sciences Center, Shreveport, LA*
[2]*School of Medicine, Louisiana State University Health Sciences Center, Shreveport, LA*
[3]*Department of Internal Medicine, Louisiana State University Health Sciences Center, Shreveport, LA*

ABSTRACT

Background: Hyperglycemia is associated with poor postoperative outcomes after carotid endarterectomy. This retrospective study examined the effect of lactated Ringer's and normal saline solutions on intraoperative blood glucose control in diabetic patients undergoing carotid endarterectomy.

Methods: The anesthetic and surgical records of type 2 diabetic patients who underwent carotid endarterectomy and received either lactated Ringer's solution or normal saline exclusively during the case were reviewed, and 20 patients were randomly selected from each group for further analysis. The outcome of interest was preoperative to postoperative change in blood glucose.

Results: The preoperative to postoperative mean changes in glucose for the normal saline and lactated Ringer's groups were 34.4 $\pm$ 70.32 mg/dL and 64.5 $\pm$ 61.38 mg/dL, respectively. This slight difference in the mean change in glucose between the 2 groups was not statistically significant (P=0.157).

Conclusion: Lactated Ringer's solution does not appear to cause a significant change in the mean blood glucose levels in diabetic patients undergoing carotid endarterectomy compared to patients receiving normal saline. Randomized controlled trials are needed to further determine whether lactated Ringer's solution adversely affects glucose control in diabetic surgical patients.

Address correspondence to
Chizoba Mosieri, MD
Department of Anesthesiology
Louisiana State University Health Sciences Center
1501 Kings Hwy.
Shreveport, LA 71130
Tel: (318) 675-4809
Email: cmosie@lsuhsc.edu

Keywords: Blood glucose, cardiovascular surgical procedures, diabetes mellitus, endarterectomy–carotid, hyperglycemia, Ringer's lactate

The authors have no financial or proprietary interest in the subject matter of this article.

INTRODUCTION

Numerous studies have established an increase in perioperative mortality and morbidity in diabetic surgical patients compared with nondiabetics. A 2010 study by Imran et al evaluated the impact of admission blood glucose levels on postoperative outcome in 2,856 coronary artery bypass graft patients and found an increased likelihood of adverse surgical outcomes in patients with an admission glucose level greater than 166 mg/dL.[1] A 2007 study by Gandhi et al analyzed 409 cardiac surgery patients and found that a 20 mg/dL increase in the mean intraoperative glucose level was associated with an increase in poor outcomes of more than 30%.[2] Similarly, Fish et al found that cardiac surgery patients with immediate postoperative glucose levels $<$200 mg/dL had a 13% risk of complications, whereas those with $\geq$200 and $\geq$250 mg/dL had a 36% and a 63% risk of complications, respectively.[3] As such, glucose control in the perioperative period should not be overlooked, especially in patients who have underlying problems with glucose regulation.

In 1978, Thomas and Alberti provided limited evidence that the use of Hartmann's solution—which is similar in composition to lactated Ringer's solution (LR)—causes transient elevation of blood glucose levels in diabetic patients and cautioned against the use of any lactate-containing intravenous (IV) fluid replacement for diabetic patients.[4] However, this theory has not been held to much further scrutiny. Lactate, a product of glycolysis, is converted into glucose via the Cori cycle. Lactate from LR infusion is hypothesized to convert into glucose in the same manner and contribute to hyperglycemia in diabetic surgical patients.[5]

In 1997, White and Goldhill conducted a survey of 82 British anesthesiologists to assess current bias towards LR and found that 21% of the surveyed physicians viewed LR as a source of IV glucose.[6] Yet, as our understanding of the negative impact of perioperative hyperglycemia has grown over the years, the use of LR has been infrequently mentioned in perioperative management guidelines for diabetic patients, causing confusion among many intensivists, anesthesiologists, and surgeons.

Although convincing evidence exists that perioperative glycemic management improves postoperative morbidity and even mortality, the scientific basis is somewhat controversial. Elevated glucose is believed to play a role in abolishing ischemic preconditioning, amplifying ischemic reperfusion injury, and triggering coronary endothelial dysfunction and platelet dysfunction.[7]

Current recommendations regarding perioperative blood glucose control usually only address preoperative, intraoperative, and postoperative management strategies with respect to defined blood glucose ranges, antihyperglycemic medications, and continuous insulin infusions. Surprisingly few management protocols mention the appropriate choice of IV fluid products in diabetic patients.

With our growing understanding of the negative impact of hyperglycemia on postoperative infections and neurological, renal, and cardiovascular complications, every measure to prevent perioperative hyperglycemia should be taken, including the appropriate selection of IV fluids for diabetic patients. Therefore, the goal of this study was to compare the intraoperative use of LR to normal saline (NS) in diabetic patients undergoing carotid endarterectomy (CEA). The outcomes of interest were preoperative to postoperative change in glucose level and the mean difference in the change in glucose level between the 2 maintenance fluids. Our goal was to determine if the use of LR, compared to NS, placed diabetic patients at higher risk for postoperative hyperglycemia or increased the need for physician intervention.

METHODS

Prior to data collection, institutional review board permission was obtained. The design of the study was a retrospective analysis of all adult type 2 diabetic patients (International Classification of Diseases, Ninth Revision, Clinical Modification [ICD-9-CM] 250.02) who underwent CEA (Current Procedural Terminology [CPT] code 38.12) and for whom either LR or NS was exclusively used intraoperatively. Specific exclusion criteria included (1) any concurrent disease process other than carotid stenosis that could affect glucose utilization, such as ongoing infection, defined as elevated white blood cell count above 11,000 cells per microliter; (2) uncontrolled type 2 diabetes, defined as a preoperative blood glucose level greater than 300 mg/dL; (3) intraoperative insulin administration; or (4) in-house/home glucocorticoid treatment. CEA patients were selected because of the well-recognized impact of hyperglycemia upon perioperative morbidity in diabetic vascular surgery patients.[8,9] This subgroup of patients also offered the advantages of relatively standardized IV fluid use and short surgical times, our intent being to decrease the impact of these variables on our outcome.

A power analysis prior to the study determined that a sample size of 20 patients in each group would have 80% power to detect a significant mean difference in preoperative to postoperative glucose between LR and NS groups of 60 mg/dL, a clinically significant change in serum glucose that would require intervention in our group of patients. After obtaining and reviewing the patient records and applying inclusion and exclusion criteria, we used a computer-generated randomizer to select 20 patients for each group. The data extracted on each patient included age, sex, laterality of surgery, length of procedure, amount and type of IV fluid, and preoperative and postoperative glucose levels.

The NS and LR groups were compared for age, fluid administration per weight (mL/kg), preoperative glucose levels, and preoperative to postoperative change in glucose levels. Statistical significance was defined as $P<0.05$.

RESULTS

Twenty NS and 20 LR patients were isolated for each group. Demographic comparisons are displayed in Table 1. No significant difference was found between the 2 groups for age or fluid administration ($P>0.05$). In addition, both groups were well balanced for sex and laterality of surgery (right vs left). Preoperative glucose levels were significantly higher in the NS group.

The mean changes between preoperative and postoperative blood glucose levels in the NS and LR

Table 1. Demographic and Procedural Data for Patients Receiving Normal Saline vs Lactated Ringer's Solutions

	Normal Saline	Lactated Ringer's	*P* Value
Patients (n)	20	20	
Sex (male:female)	8:12	8:12	
Carotid Endarterectomy Laterality (right:left)	9:11	10:10	
Age (years)	65.85 ± 11.68	63.55 ± 9.05	0.49
Length of Procedure (hours)	4.36 ± 0.54	5.01 ± 3.57	0.142
Fluid (mL/kg)	20.63 ± 10.14	24.12 ± 11.02	0.319
Preoperative Glucose (mg/dL)	177.1 ± 71.23	136.80 ± 44.23	0.038[a]

Note: Continuous data are expressed as mean ± standard deviation.
[a]Statistically significant.

groups were 34.4 ± 70.32 mg/dL and 64.5 ± 61.38 mg/dL, respectively (Table 2). The difference in the mean change in glucose between the 2 groups was not statistically significant (P=0.157).

DISCUSSION

In 1983, Walsh et al conducted a small randomized study comparing an infusion of Hartmann's solution to normal saline in otherwise healthy patients undergoing cholecystectomy and found no significant difference in the intraoperative glycemic response between the groups.[10] However, given that this study only analyzed nondiabetic patients who would be expected to better compensate for alterations in blood glucose, the results cannot be generalized to the diabetic population. Van Zyl et al compared the use of LR and NS for fluid resuscitation in patients presenting with diabetic ketoacidosis and found the average time to decrease blood glucose levels to <14 mmol/L (252 mg/dL) was significantly greater in the LR group.[11] These data raise further speculation regarding the use of LR in diabetic patients.

Although the initial findings published by Thomas and Alberti[4] might suggest that LR should be avoided in all diabetic patients to help control perioperative hyperglycemia, alternative IV fluid options are not entirely benign either. Large volumes of NS have been shown to cause hyperchloremic metabolic acidosis and acute kidney injury in intensive care unit patients. While solutions such as Plasma-Lyte (Baxter Healthcare Corporation) and Normosol (Hospira, Inc.) are at a more physiologic pH and electrolyte concentration than NS, these solutions are generally more costly.[12] Because of the cost and risk of alternative IV fluids, LR is often used in the perioperative setting despite its potential adverse impact on glycemic control.

The results from our study indicate that LR does not significantly increase blood glucose concentration compared to NS in type 2 diabetic patients undergoing CEA. One possible explanation for the minimal change in blood glucose level after LR infusion has been briefly discussed in an editorial by Simpson et al.[13] The article suggests that the 29 mmol/L of lactate from Hartmann's solution (or 28 mmol/L from LR) could yield 14.5 mmol of glucose at most, which converts to an approximate increase of 261 mg/dL in blood glucose. While this number is clinically significant, after accounting for extracellular redistribution, this number is considerably reduced to approximately 1 mmol/L or 18 mg/dL, which is clinically insignificant. Another potential explanation for the minimal change in blood glucose level is that the lactate is converted to glycogen rather than to glucose by the liver in a process known as the glucose paradox. Radioisotope tracer studies have revealed that lactate is also directly oxidized as a fuel source in the heart and active skeletal muscles.[13] In fact, Didwania et al performed substrate-specific electrode analysis of 24 healthy volunteers who were infused with 1 L of LR, NS, 5% dextrose in LR, or 5% dextrose in water and found that LR and NS did not increase lactate concentrations over an infusion period of 240 minutes.[14]

Table 2. Preoperative to Postoperative Change in Blood Glucose in Normal Saline and Lactated Ringer's Groups

	Normal Saline	Lactated Ringer's	*P* Value
Change in Glucose (mg/dL)	34.4 ± 70.32	64.5 ± 61.38	0.157
Mean Difference (95% confidence interval)	−30.1 (−71.01 to +10.81)		

Note: Continuous data are expressed as mean ± standard deviation.

According to most perioperative diabetic guidelines, blood glucose treatment is reserved for patients with values greater than 200 mg/dL, and, in most cases, insulin dose adjustments are only recommended for changes from baseline of 50 mg/dL or more. Therefore, a 30.1 mg/dL difference between LR and NS in the mean change in blood glucose level (as seen in our study) would, at most, only result in a change of 1 degree of insulin sliding scale or basal rate adjustment and is therefore clinically insignificant.

We must, however, point out the limitations of this study. We had a large variance between preoperative and postoperative blood glucose levels within both groups, as well as a significant difference in preoperative glucose levels between our NS and LR groups. This large variance could be secondary to many factors, including poor preoperative blood glucose control, intraoperative stress, or variations in length of actual time between preoperative and postoperative blood glucose measurements. These factors could be better controlled by a prospective study that used each test subject as a control, infusing both NS and LR on separate occasions, or by increasing the power of the study. Although this study has limitations inherent to any retrospective review, it provides an indication of the size of study that will likely be required to demonstrate a difference between LR and NS fluid regimens for CEA, if a difference indeed exists. As such, our study has use as a model on which to base future prospective efforts.

CONCLUSION

The findings published by Thomas and Alberti[4] have not been reliably replicated. We have a theoretical basis to caution the use of lactated fluid replacement therapy in diabetic patients. However, as our understanding of biochemistry has expanded, we now appreciate that lactate does not contribute significantly to glucose load. Based on the results of the current study, LR does not appear to cause a significant change in mean blood glucose levels of controlled type 2 diabetic patients undergoing CEA. However, randomized controlled trials are needed to conclusively determine whether LR adversely affects glucose control in diabetic surgical patients.

REFERENCES

1. Imran SA, Ransom TP, Buth KJ, et al. Impact of admission serum glucose level on in-hospital outcomes following coronary artery bypass grafting surgery. *Can J Cardiol*. 2010 Mar;26(3):151-154.
2. Gandhi GY, Nuttall GA, Abel MD, et al. Intensive intraoperative insulin therapy versus conventional glucose management during cardiac surgery: a randomized trial. *Ann Intern Med*. 2007 Feb 20;146(4):233-243.
3. Fish LH, Weaver TW, Moore AL, Steel LG. Value of postoperative blood glucose in predicting complications and length of stay after coronary artery bypass grafting. *Am J Cardiol*. 2003 Jul 1;92(1):74-76.
4. Thomas DJ, Alberti KG. Hyperglycaemic effects of Hartmann's solution during surgery in patients with maturity onset diabetes. *Br J Anaesth*. 1978 Feb;50(2):185-188.
5. Brooks GA, Fahey TD. *Fundamentals of Human Performance*. New York, NY: McMillan; 1987: 46-47.
6. White SA, Goldhill DR. Is Hartmann's the solution? *Anaesthesia*. 1997 May;52(5):422-427.
7. Kovalaske MA, Gandhi GY. Glycemic control in the medical intensive care unit. *J Diabetes Sci Technol*. 2009 Nov 1;3(6):1330-1341.
8. McGirt MJ, Woodworth GF, Brooke BS, et al. Hyperglycemia independently increases the risk of perioperative stroke, myocardial infarction, and death after carotid endarterectomy. *Neurosurgery*. 2006 Jun;58(6):1066-1073; discussion 1066-1073.
9. Debing E, Aerden D, Van den Brande P. Diabetes mellitus is a predictor for early adverse outcome after carotid endarterectomy. *Vasc Endovascular Surg*. 2011 Jan;45(1):28-32. Epub 2010 Dec 13.
10. Walsh ES, Traynor C, Paterson JL, Hall GM. Effect of different intraoperative fluid regimens on circulating metabolites and insulin during abdominal surgery. *Br J Anaesth*. 1983 Feb;55(2):135-140.
11. Van Zyl DG, Rheeder P, Delport E. Fluid management in diabetic-acidosis—Ringer's lactate versus normal saline: a randomized controlled trial. *QJM*. 2012 Apr;105(4):337-343. Epub 2011 Nov 22.
12. Yunos NM, Bellomo R, Hegarty C, Story D, Ho L, Bailey M. Association between a chloride-liberal vs chloride-restrictive intravenous fluid administration strategy and kidney injury in critically ill adults. *JAMA*. 2012 Oct 17;308(15):1566-1572.
13. Simpson AK, Levy N, Hall GM. Peri-operative i.v. fluids in diabetic patients—don't forget the salt. *Anaesthesia*. 2008 Oct;63(10):1043-1045.
14. Didwania A, Miller J, Kassel D, Jackson EV Jr, Chernow B. Effect of intravenous lactated Ringer's solution infusion on the circulating lactate concentration: Part 3. Results of a prospective, randomized, double-blind, placebo-controlled trial. *Crit Care Med*. 1997 Nov;25(11):1851-1854.

This article meets the Accreditation Council for Graduate Medical Education and the American Board of Medical Specialties Maintenance of Certification competencies for Patient Care, Medical Knowledge, Systems-Based Practice, and Practice-Based Learning and Improvement.