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Our Experience with Two Cardioplegic Solutions: Dextrose versus Non-Dextrose in Adult Cardiac Surgery

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Abstract: Intraoperative hyperglycemia has been observed to be associated with increased morbidity and mortality after cardiac surgery. Dextrose cardioplegia is used for its cardioprotective effects but may lead to intraoperative hyperglycemia and more postoperative complications. This was a retrospective observational study. Patient records (n = 2301) were accessed from a large database at a tertiary care facility. The two groups (dextrose vs. nondextrose) were then matched using preoperative variables of age, sex, body mass index, wound exposure time, preoperative HbA1c levels, renal failure, hypertension, and prior cerebrovascular disease. The following outcomes were recorded: 30-day mortality, sternal wound infection, stroke, and highest glucose level on cardiopulmonary bypass. The dextrose cardioplegia group showed statistically higher intraoperative glucose levels (272.76 ± 55.92 vs. 182.79 ± 45, p value = .0001). There was no difference in postoperative mortality, sternal wound infections or stroke incidence, nor in other secondary outcomes. The type of cardioplegia solution was shown to affect glucose levels; however, there was no effect on postoperative complication rates. **Keywords:** hyperglycemia, cardiac surgery, postoperative complications, stroke, cardiac anesthesia. *JECT. 2012;44:134–138*

The development of blood cardioplegia and retrograde delivery has improved the ability of surgeons to minimize myocardial ischemia and enhance postoperative myocardial function, yet there is considerable controversy regarding the most efficient solution to minimize damage to the myocardium during the ischemic period. Surgeons tend to consistently use a particular type and composition of cardioplegic solution based on personal preference (1).

Recently, an observational study using multivariate logistic regression analysis for diabetics undergoing cardiac surgery found that patients with better intraoperative glucose control were found to have less mortality and morbidity (2). Another study found that better control of hyperglycemia led to a reduction in sternal wound infection (3). Van den Berghe et al.'s 2001 study (4) showed a reduction in mortality, renal failure, and mechanical ventilation when intensive insulin therapy was used to control glucose concentration postoperatively. Conversely, two studies of tight glucose control, Gandhi et al. (5) (during cardiac surgery) and a second Van den Berghe et al. (6) (intensive care unit patients), resulted in slight increases in mortality.

The objective of this study was to examine the effects of two cardioplegia solutions (dextrose vs. nondextrose) on patient outcomes such as mortality, incidence of deep sternal wound infection, and cerebral vascular accidents as well as other clinical outcomes. The goal was to determine whether adverse outcomes were greater in either group.

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METHODS

Patient Selection

Adult cardiac surgery data from a large tertiary care facility operating in the New York metropolitan area were retrospectively analyzed. Facility data from both the New York State Cardiac Surgery Reporting System (CSRS) and the Society of Thoracic Surgeons (STS) database were used to compare key outcome variables between patients who received cardioplegia solution with dextrose (n = 540) vs. those who received cardioplegia solution without dextrose (n = 1761) (7,8). Specifically, the dextrose solution contained 670 cc of normal saline, 30 g of dextrose, 60 mEq of potassium chloride, and 100 mL of tromethamine .6 Molar. The nondextrose solution contained 500 mL of Isolyte-S, 22 mEq of sodium bicarbonate, 100 mg of lidocaine, and 30 mEq of potassium chloride. Both solutions were administered using a 4:1 blood-to-crystalloid ratio. Consecutive patients who underwent cardiac surgery with cardioplegia between May 2007 and December 2009 were selected for inclusion, yielding a total of 2301 individual cases. Patients undergoing cardiac surgery who did not receive a form of cardioplegia were excluded from the study. Patients who had procedures not using cardiopulmonary bypass were specifically excluded. This study was approved by the Institutional Review Board.

Preoperative Matching Variables

To enable direct comparison of the dextrose and nondextrose groups, propensity score matching was used (9). The following variables, partially chosen from the Euroscore risk assessment and the CSRS and STS databases, were used to equate the two groups: body mass index (BMI), HbA1c, pre-op creatine, ejection fraction, wound exposure time, diabetes mellitus, hypertension, chronic obstructive pulmonary disease, cerebrovascular disease, myocardial infarction, congestive heart failure, peripheral vascular disease, extensive aortic atherosclerosis, unstable shock, previous coronary artery bypass grafting (CABG) or other heart surgery, current CABG surgery, and current valve surgery.

Postoperative Outcome Variables

The primary outcome variables in this study were: mortality, deep sternal wound infection, cerebral vascular accident intraoperative up to 24 hours, and postoperative cerebral vascular accident greater than 24 hours. Mortality was defined as 30-day mortality; this term included patients who died after discharge from the hospital but within 30 days of surgery and patients who died in the hospital after 30 days. Deep sternal wound infection was defined as drainage of purulent material from the sternotomy wound and instability of the sternum within 6 months of surgery. Cerebral vascular accident was identified as a new focal neurologic deficit not including a transient ischemic attack.

Secondary outcome variables were: 30-day renal failure rate, leg infection, sepsis, transient ischemic attack, prolonged ventilation, reoperation for bleeding, dialysis, and mean peak glucose on bypass. Mean peak glucose on bypass was determined every 30 minutes on cardiopulmonary bypass sampling from the pump, both arterial and venous, samples and measured in mg/dL.

Intraoperative Management

Intraoperative management differed only with respect to the cardioplegia solution that was given. Mean arterial pressure (MAP) was targeted for most patients on bypass between 50 and 80 mmHg. Higher MAP was targeted for patients with pre-existing neurologic disease and advanced age (older than 80 years). Neurologic disease was defined as a history of stroke or angiographic evidence or a 50% narrowing in a major cerebral or carotid artery (common or internal) or previous surgery for such disease. Blood hematocrits were maintained above 21% on bypass. Patients were put on insulin infusions (250 units in 250 mL of normal saline) if blood glucose rose above 180 mg/dL at any time during the procedure. Blood glucoses were targeted for maintenance between 120 mg/dL and 160 mg/dL in all patients. Blood glucoses that fell below that range resulted in termination of the insulin infusion. Anesthetic management of the patient varied depending on the anesthesia practitioner. In general, a mixture of sufentanil and versed and volatile anesthetic was used. Isoflurane was used on pump. Some practitioners preferred a continuous propofol infusion in lieu or in addition to the volatile agent.

Statistical Methods

Because this was a nonrandomized retrospective cohort study, it was necessary to match patients who received cardioplegia solution with dextrose to those who did not. This was accomplished using propensity score matching used by statisticians who were not aware of the hypothesis. This method enabled direct comparison of the dextrose and nondextrose groups by simultaneously matching on a number of confounding variables.

Comparability of the two groups before and after matching was evaluated using the two-sample t test for continuous variables and the chi-square test or Fisher's exact test, as deemed appropriate, for categorical variables. Summary statistics in Table 1 are reported as mean, standard deviation, and median (first quartile, third quartile) in their original units after matching.

Four hundred eighty-six matched pairs were identified from the original database (a total of 972 patients). It should be noted that propensity score matching yielded matches for 90% of patients.

A result was considered statistically significant at the $p < .05$ level. However, to adjust for multiple testing, a primary outcomes result was considered significant only if $p < .0125$

Table 1. Comparability of the groups after matching.

Variable	Unexposed (nondextrose) (n = 486)	Exposed (dextrose) (n = 486)	*p* Value
Age (years)*	66.77 ± 12.50 68.00 (59.00, 76.00)	67.39 ± 13.49 69.00 (59.00, 79.00)	.4551
BMI (kg/m^2)*	28.50 ± 5.57 27.57 (24.93, 31.30)	28.05 ± 5.32 27.47 (24.39, 31.16)	.1973
HbA1c (%)*	6.29 ± 1.40 6.00 (5.50, 6.60)	6.24 ± 1.26 5.90 (5.50, 6.50)	.5593
HbA1c < 7	285 (58.64%)	302 (62.14%)	.7378
Preoperative creatinine (mg/dL)*	1.30 ± 1.06 1.10 (.90, 1.30)	1.35 ± 1.28 1.00 (.90, 1.30)	.4743
EF (%)*	49.69 ± 13.81 55.00 (40.00, 60.00)	50.40 ± 12.51 53.00 (45.00, 60.00)	.3998
Wound exposure time (in minutes)*	312.93 ± 96.09 292.50 (244.00, 370.00)	311.49 ± 90.57 298.00 (243.00, 364.00)	.8100
Gender (% male)	342 (70.37%)	332 (68.31%)	.4866
Race (% white)	380 (78.19%)	373 (76.75%)	.5234
DM	168 (34.57%)	154 (31.69%)	.3401
HTN	382 (78.60%)	375 (77.16%)	.5885
COPD	144 (29.63%)	153 (31.48%)	.5309
CVD	65 (13.37%)	73 (15.02%)	.4622
MI within 1–7 days	44 (27.16%)	45 (29.41%)	.4229
Current CHF	161 (33.13%)	166 (34.16%)	.7343
PVD	66 (13.58%)	61 (12.55%)	.6342
Extensive aortic atherosclerosis	55 (11.32%)	52 (10.70%)	.7585
Unstable shock	13 (2.67%)	11 (2.26%)	.6793
Previous CABG	22 (4.53%)	25 (5.14%)	.6537
Any other previous surgery	13 (2.67%)	13 (2.67%)	1.0000
Current CABG surgery	307 (63.17%)	300 (61.73%)	.6429
Current valve surgery	282 (58.02%)	254 (52.26%)	.0710

*Data are reported as mean, standard deviation, and median (first quartile, third quartile), and are analyzed using the two-sample *t* test.
BMI, body mass index; EF, ejection fraction; DM, diabetes mellitus; HTN, hypertension; COPD, chronic obstructive pulmonary disease; CVD, cerebrovascular disease; MI, myocardial infarction; CHF, congestive heart failure; PVD, peripheral vascular disease.

(Bonferroni adjustment, .0125 = .05/4). No adjustments were made for secondary outcomes. The widths of the confidence intervals for differences in rates (Table 2) are provided for insights into the precision of the results.

RESULTS

All rates were in the average range as reported by the New York State Department of Health (NYSDOH) during

Table 2. Matched pairs analyses of primary and secondary outcomes.

	n	Unexposed (nondextrose)	Exposed (dextrose)	Difference and 95% Confidence Interval for Difference	*p* Value
Mortality (30-day)	486	24 (4.94%)	19 (3.91%)	1.03 (–1.47 to 3.53)	.5114
Sternal wound infection	486	6 (1.23%)	4 (.82%)	.41 (–.89 to 1.71)	.7539
Renal failure	486	19 (3.91%)	14 (2.88%)	1.03 (–1.26 to 3.32)	.4731
Leg infection that requires excision of tissue, positive blood cultures, or treatment with antibiotics	486	5 (1.03%)	3 (.62%)	.41 (–.75 to 1.58)	.7266
Sepsis	486	8 (1.65%)	12 (2.47%)	–.82 (–2.66 to 1.02)	.5034
Transient ischemic attack	486	2 (.41%)	1 (1.21%)	.21 (–.51 to .92)	1.0000
Cerebral vascular accident (CVA) intraoperative less than 24 hours	486	4 (.82%)	2 (.41%)	.41 (–.60 to 1.42)	.6875
CVA greater than 24 hours	486	5 (1.03%)	5 (1.03%)	.00 (–1.30 to 1.30)	1.0000
Prolonged ventilation	486	75 (15.43%)	70 (14.40%)	1.03 (–3.42 to 5.48)	.7117
Reoperation for bleeding	486	15 (3.09%)	8 (1.65%)	1.44 (–.53 to 3.41)	.2100
New dialysis	486	18 (3.70%)	11 (2.26%)	1.44 (–.70 to 3.58)	.2478
Postoperative Day #1, 6 AM glucose (mg/dL)†	361	125.38 ± 27.69	123.62 ± 26.19	–1.76 (–5.60 to 2.08)	.2817*
Postoperative Day #2, 6 AM glucose (mg/dL)‡	351	130.22 ± 28.22	129.78 ± 26.56	–.44 (–4.53 to 3.64)	.7681*
Highest glucose on bypass (mg/dL)§	485	182.79 ± 45.98	272.76 ± 55.92	89.98 (83.65 to 96.30)	<.0001*

*Data were analyzed using the paired *t* test.
†Standard deviation (SD) of the mean difference for the paired analysis = 37.13.
‡SD of the mean difference for the paired analysis = 38.94.
§D of the mean difference for the paired analysis = 70.91.

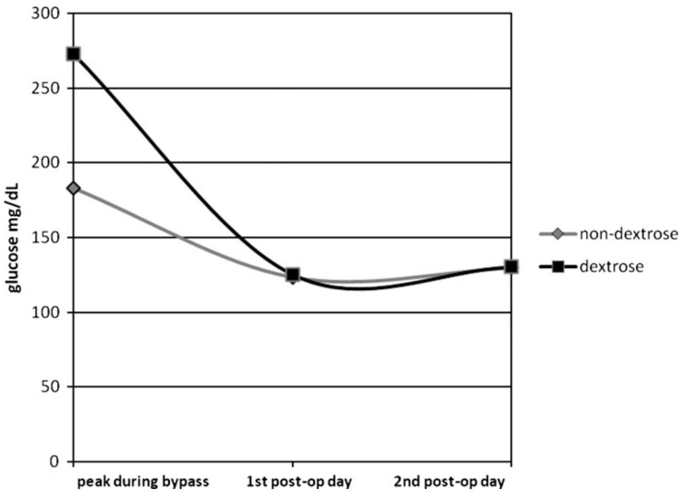

Figure 1. Glucose (mg/dL) during bypass and first and second days after bypass.

this time period (10). No significant differences were found between groups for any outcomes of this study. Specifically:

- The postoperative deep sternal wound infection rate was 1.23% in the nondextrose group and .82% in the dextrose group.
- The cerebral vascular accident rates within 24 hours of surgery were .82% in the nondextrose group and .41% in the dextrose group.
- The cerebral vascular accident rates after 24 hours were 1.03% in each of the two groups.
- Mortality was 4.94% in the nondextrose group and 3.91% in the dextrose group.
- The postoperative new dialysis rate, defined as a patient who had never been dialyzed preoperatively or dialyzed once but required dialysis postoperatively, was 3.70% in the nondextrose group vs. 2.26% in the dextrose group.

As may be expected, the highest peak glucose on bypass was significantly higher in the dextrose group (272.76 ± 55.92 vs. 182.79 ± 45, p value = .0001). However, on the first postoperative day (POD #1 6 AM), dextrose levels were similar in both groups (125.38 ± 27.69 vs. 123.62 ± 26.19). On the second postoperative day (POD #2 6 AM), dextrose levels were also similar (130.22 ± 28.22 vs. 129.78 ± 26.56; Figure 1). The well-controlled postoperative glucoses reflect an intensive insulin protocol in which all patients are placed on arrival to the cardiothoracic intensive care unit.

DISCUSSION

The aim of this study was to observe outcomes for patients receiving cardioplegic solutions with and without dextrose. This study did not find a significant difference in cerebral vascular accident rate between those patients who received dextrose cardioplegia and those who did not. Because we controlled for a number of key variables that would potentially impact the cerebrovascular accident rate, we had expected the higher glucose group to have a higher rate. Nevertheless, the rate did not differ between the groups. Other studies have found results similar to the results reported herein (11,12).

In this study, both groups exhibited a rather low deep sternal wound infection rate. The authors were surprised by this finding, because the dextrose group had higher glucose levels on bypass. Prior research has shown an increase in deep sternal wound infections when blood glucose was above 200 mg/dL through POD 2 (3,13). A contributing factor to the low deep sternal wound infection rates may be that the average BMI was relatively low (28 kg/m^2) in each cohort. Aggressive insulin management postoperatively may also have contributed to the low incidence in both groups.

Postoperative ventilation and mortality were not statistically different between the groups. This finding is not consistent with prior research done by Doenst et al. (2) and Ouattara et al. (14), which show that peak glucose levels on bypass was independently associated with increased mortality and morbidity in both diabetics and nondiabetics. Aggressive management in the cardiothoracic unit may have prevented complications. Long-term control of glucose levels or elevated preoperative HbA1c levels may be more important for morbidity and mortality after cardiac surgery rather than short-term hyperglycemia (15).

Strengths and Limitations

Although this study used a well-designed quasi-experimental approach, all factors that might affect the blood glucose level intraoperatively could not be controlled for. Hypothermia, for example, may account for variance in insulin resistance and, hence, glucose levels (16).

It should also be acknowledged that implementation of an appropriate randomized trial would be impractical given surgeon preferences with respect to the cardioplegia used.

A strength of this study was the use of a validated database: New York State CSRS data are validated internally before submission to the NYSDOH. In addition, records are randomly audited by the NYSDOH.

Finally, sample size and statistical approach was a strength of the study. The use of propensity score matching of various preoperative risk factors did indeed achieve uniformity in the two groups.

CONCLUSION

This study suggests that the use of dextrose cardioplegia is not detrimental on key outcome variables such as deep sternal would infection, cerebral vascular accident rate, and mortality in conjunction with aggressive insulin management, intra- and postoperatively, and good blood glucose control. A large randomized clinical trial may confirm or refute this conclusion.

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