

Effect of preoperative glucose - containing solutions  
and intraoperative glucose - deprived solutions  
on blood glucose levels during major  
intracranial surgery

Lawan Tuchinda\*      Wanna Somboonviboon\*

Supudjane Limutaitip\*\*      Mittira Laungaroon\*

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**Problem** : *There is some risk of brain ischemia during intracranial operations and hyperglycemia occurring prior to periods of brain ischemia exacerbates neurologic damages. Now fluid management in intracranial operations is favored towards the use of glucose-deprived solutions because intraoperative glucose administration usually results in hyperglycemia. However, hypoglycemia is the concern if only glucose - deprived solutions were given intraoperatively.*

**Objective** : *To determine the effect of preoperative glucose - containing solutions and intraoperative glucose - deprived solutions on blood glucose levels during major intracranial operation.*

**Setting** : *Neurosurgical operating room, Faculty of Medicine, Chulalongkorn University.*

**Design** : *Descriptive*

**Subject** : *Eighty patients undergoing major intracranial operations. Group 1 was the patients who had not received and group 2 was the patients who had received preoperative glucose - containing solutions.*

\* Department of Anesthesiology, Faculty of Medicine, Chulalongkorn University

\*\* Department of Anesthesiology, King Chulalongkorn Memorial Hospital

**Method** : *Normal saline was the only crystalloid given intraoperatively. Blood glucose levels were measured at induction, 1 hour, 2 hours and every two hours after induction until the end of the operation. Blood glucose levels were compared between group 1 and 2. Then blood glucose levels were compared between patients who had received and had not received steroids.*

**Results** : *Blood glucose levels in patients who had previously received glucose-containing solutions (group 2) were significant higher ( $p < 0.05$ ) in the preoperative and induction periods than patients who had not received preoperative glucose-containing solutions (group 1). When data was compared between groups of patients who had received and had not received steroids, the patients who had received steroids had higher blood glucose levels than those who had not statistically significant ( $p < 0.05$ ) at induction, 1 hour, 2 hours, 4 hours and 8 hours after induction in group 1 and at 1 hour, 2 hours and 4 hours after induction in group 2. There were 3 patients receiving steroids had blood glucose levels above 200 mg/dl. There was no hypoglycemic episode even during the longest time of anesthesia (20 hours).*

**Conclusion** : *In this study we observed no hypoglycemic episode in patients receiving preoperative glucose-containing and intraoperative glucose-deprived solutions. However, we would rather recommend intraoperative monitoring of blood glucose levels because hyperglycemic and hypoglycemic episodes might occur unexpectedly and will be harmful to the patients.*

**Key words** : *Anesthesia, Intracranial operation, Glucose.*

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Chulalongkorn University, Bangkok 10330, Thailand.

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- ปัญหาของการทำวิจัย** : สมองมีความเสี่ยงต่อการขาดเลือดระหว่างการผ่าตัดสมอง มีการศึกษามากมายที่พบว่าภาวะระดับน้ำตาลในเลือดสูงก่อนการขาดเลือดของสมองทำให้มีการทำลายประสาทมากขึ้น ปัจจุบันการให้สารน้ำระหว่างการผ่าตัดสมองจึงมักใช้สารละลายที่ไม่มีน้ำตาลเพราะการให้สารละลายที่มีน้ำตาลระหว่างการผ่าตัดมักทำให้ระดับน้ำตาลในเลือดสูงขึ้นอย่างไรก็ตามการให้สารละลายที่ไม่มีน้ำตาลอาจทำให้ระดับน้ำตาลในเลือดต่ำจนเกิดอันตรายได้
- วัตถุประสงค์** : เพื่อศึกษาถึงผลของการให้สารละลายที่มีน้ำตาลก่อนการผ่าตัดและสารละลายที่ไม่มีน้ำตาลระหว่างการผ่าตัดต่อระดับน้ำตาลในเลือดระหว่างการผ่าตัดสมอง
- สถานที่ทำการศึกษา** : ห้องผ่าตัดศัลยกรรมประสาท คณะแพทยศาสตร์ จุฬาลงกรณ์มหาวิทยาลัย
- รูปแบบการวิจัย** : เป็นการศึกษาแบบพรรณนา
- ผู้ป่วยที่ได้ทำการศึกษา** : ผู้ป่วย 80 คน ที่มารับการผ่าตัดสมองโดยกลุ่มที่ 1 คือ ผู้ป่วยที่ไม่ได้รับและกลุ่มที่ 2 คือผู้ป่วยที่ได้รับสารละลายที่มีน้ำตาลก่อนการผ่าตัด
- วิธีการศึกษา - วัตถุประสงค์** : ผู้ป่วยทุกคนจะได้รับสารละลาย normal saline ตลอดการผ่าตัด แล้วทำการวัดระดับน้ำตาลในเลือดที่เวลา 0, 1, 2 ชั่วโมง และต่อไปทุก 2 ชั่วโมงหลังการนำสลบ ทำการเปรียบเทียบระดับน้ำตาลในเลือดระหว่างผู้ป่วยกลุ่มที่ 1 และ 2 แล้วเปรียบเทียบระดับน้ำตาลในเลือดระหว่างผู้ป่วยที่ได้รับและไม่ได้ steroids ในแต่ละกลุ่ม
- ผลการศึกษา** : ระดับน้ำตาลในเลือดในผู้ป่วยที่ได้รับสารละลายที่มีน้ำตาลก่อนการผ่าตัด (กลุ่ม 2) จะสูงกว่าผู้ป่วยที่ไม่ได้รับสารละลายที่มีน้ำตาลก่อนการผ่าตัด (กลุ่ม 1) อย่างมีนัยสำคัญทางสถิติ ( $p < 0.05$ ) เฉพาะในช่วงก่อนการผ่าตัดและการนำสลบ เมื่อเปรียบเทียบระดับน้ำตาลในเลือดระหว่างผู้ป่วยที่ได้รับและไม่ได้ steroids พบว่าระดับน้ำตาลในเลือดของผู้ป่วยที่ได้รับ steroids สูงกว่าผู้ป่วยที่ไม่ได้รับ steroids อย่างมีนัยสำคัญทาง

สถิติ ( $p < 0.05$ ) ที่ช่วงการนำสลบ, 1 ชั่วโมง, 2 ชั่วโมง, 4 ชั่วโมง และ 8 ชั่วโมงหลังการนำสลบในผู้ป่วยกลุ่มที่ 1 และที่เวลา 1 ชั่วโมง, 2 ชั่วโมง และ 4 ชั่วโมงหลังการนำสลบในผู้ป่วยกลุ่มที่ 2 ผู้ป่วย 3 รายมีระดับน้ำตาลในเลือดสูงกว่า 200 มก/ดล. ไม่พบผู้ป่วยรายใดมีระดับน้ำตาลในเลือดต่ำ ระยะเวลาการให้ยาระงับความรู้สึกที่นานที่สุดคือ 20 ชั่วโมง

- สรุป** : การศึกษาไม่พบภาวะระดับน้ำตาลในเลือดต่ำจากการให้สารละลายที่ไม่มีน้ำตาลระหว่างการผ่าตัดสมอง อย่างไรก็ตามผู้ทำการศึกษาแนะนำว่าควรเจาะหาระดับน้ำตาลในเลือดเป็นระยะด้วย เพราะอาจพบระดับน้ำตาลในเลือดสูงหรือต่ำเกินไปจนอาจเป็นอันตรายต่อผู้ป่วยได้
- ดัชนีเรื่อง** : การให้ยาระงับความรู้สึก, การผ่าตัดสมอง, น้ำตาล.

During intracranial procedures, hypotension, increased intracranial pressure, hypoxia and brain retraction<sup>(1)</sup> may result in brain ischemia. Recent animal studies have shown that hyperglycemia existing prior to a severe ischemic or hypoxic event will aggravate the ischemic damage<sup>(2-5)</sup> and may, therefore, harm those neurosurgical patients. Intraoperative glucose administration increases blood glucose in diabetic and nondiabetic patients in proportion to the rate of glucose infusion. Sieber et al<sup>(6)</sup> showed that for neurosurgical patients intraoperative glucose administration caused hyperglycemia without protein sparing. In addition, not giving glucose does not result in hypoglycemia or acidosis.<sup>(6)</sup> Moreover, the corticosteroids given to many neurosurgical patients in an attempt to decrease peritumor brain edema could alter the glucose tolerance. Most studies have shown the safety of giving glucose-deprived solutions only over a short period (up to 4 hours)<sup>(6-9)</sup> but not during longer operations. Another concern is insulin secretion stimulated by glucose-induced hyperglycemia. When insulin decreases blood glucose levels and glucagon secretion is inadequate, the risk of hypoglycemia is present.

This study was designed to determine the effect of glucose -deprived solution on blood glucose levels during major intracranial operations and especially if hypoglycemia can occur in patients who had previously received glucose-containing solutions or steroids and during long operative periods.

### Materials and Methods

This study was carried out after approval by the institutional ethics committee. Eighty healthy patients (age 15 - 65 years, weight 40 - 80 kg.) scheduled for elective major intracranial operations were studied.

Subjects with diabetes or other endocrine diseases were excluded.

The patients' demographic data, diagnosis, operation, previous medications, duration of NPO, premedication, preoperative blood glucose levels and administration of preoperative glucose-containing solutions were recorded. The patients were divided into 2 groups according to the administration of preoperative glucose-containing solutions. Group 1 did not receive preoperative glucose-containing solutions while group 2 did.

Upon arrival in the operating theater, routine monitoring including electrocardiography, pulse oximetry and noninvasive measurement of blood pressure were applied. Intravenous normal saline was started before induction and continued throughout the operation. Anesthesia was induced intravenously with 3 - 5 mg/kg thiopental and 2 mcg/kg fentanyl. Then the radial artery was catheterized for measurement of blood pressure, blood glucose and blood gases. Intubation was performed with an appropriate nondepolarizing muscle relaxant. Anesthesia was maintained with 66 % nitrous oxide, 33 % oxygen, isoflurane up to 1 MAC, nondepolarizing muscle relaxant and supplemental fentanyl 1 mcg/kg according to surgical stimuli. Ventilation was adjusted to maintain PaCO<sub>2</sub> at 30 - 35 mm.Hg.

**Fluid management** Normal saline was the only crystalloid given to every patient. The amount of fluid was calculated as follows :

1. Fluid deficit = NPO hours x maintenance per hour. Half of this was given during the first hour and one-fourth was given during the second and third hours, respectively.

2. Maintenance per hour = 2 ml/kg/hour

3. Third space loss = 2 ml/kg/hour

4. Urine replacement = 2/3 of previous hour urine

5. Blood loss was replaced by normal saline= triple volume of blood lost if the anesthesiologists did not consider blood transfusion.

Colloids and blood products could be given according to the anesthesiologists suggestion.

**Blood glucose level** Blood samples were drawn from the arterial catheter at time 0, 1 hour, 2 hours and every two hours after induction until the end of the operation. Blood glucose levels were measured by an Advantage Glucose Analyzer (Boehringer Mannheim). The study was stopped if blood glucose levels were below 60 mg/dl. Intravenous glucose ( 50 ml. of 50 % glucose ) would be given and blood glucose levels would again be determined after half an hour and the patients' neurological status would be followed. Upon conclusion of the operation, the patients were transported to the neurosurgical intensive care unit. Blood samples were drawn for

blood glucose and electrolyte levels before changing the intravenous fluid to 5 % dextrose in normal saline.

Intraoperative data were collected including blood and medications given, blood loss, urine output and duration of anesthesia. Preoperative medications, e.g., steroids were continued throughout the operation.

**Statistical Analysis** Statistical significance between groups was tested by Student's t test, and serial blood glucose level changes in each group were tested by repeatedly measured ANOVA.

## Results

The 80 non-diabetic Thai patients were divided into 2 groups : group 1 and group 2 were patients who had not and who had received preoperative glucose-containing solutions, respectively. Both groups were compared as to age, weight, sex, duration of anesthesia, units of blood administered, amount of blood loss, NPO time, steroid applied and type of operation (Table 1). There was no statistically significant difference in all data except the NPO time,

Table 1. Patients' demographic data.

	Group 1 No preoperative glucose N = 40	Group 2 Preoperative glucose N = 40
Age (years)	46.10 (10.84)	49.53 (14.78)
Weight (kg)	58.87 (8.73)	60.10 (10.62)
Sex (F/M) ( cases/cases )	25/15	19/21
Duration of anesthesia (minutes)	457.68 (245.78)	406.75 (181.99)
Blood given (units)	2.48 (3.08)	2.20 (2.87)
Blood loss (ml)	1482.93 (1447.39)	1040.00 (1056.56)
NPO (minutes)	754.63 (141.37)*	957.68 (345.62)*
Steroid received (cases)	22	11
Tumor/vascular ( cases/cases )	33/7	13/27

Data presented as mean (S.D.), \* P < 0.05 between groups 1 and 2

steroids administration and tumor/vascular cases. NPO time was significantly longer in group 2. Twenty-two of the patients in group 1 received steroids but only 11 patients in group 2. The majority of group 1 patients were tumor cases, whereas group 2 patients were vascular cases.

Serial blood glucose measurements were compared between group 1 and group 2 (Table 2). Based on preoperative and induction data the blood glucose levels in group 2 were significantly higher than in group 1 ( $P < 0.05$ ), afterwards there were no statistically difference. Hypoglycemia did not occur in any patient in both groups. The lowest blood glucose level was 72 mg/dl which was found in group 2 without steroids. The mean anesthetic time in groups

1 and 2 were 457.68 (245.78) and 406.75 (181.99) minutes, respectively, which was not statistically significant and the longest anesthetic times were 18 and 20 hours, respectively.

Blood glucose levels were compared between patients receiving and not receiving steroids (Table 3). Blood glucose levels were significantly higher in patients receiving steroids at induction, 1 hour, 2 hours, 4 hours and 8 hours after induction ( $p < 0.05$ ) in group 1 and at 1,2 and 4 hours after induction in group 2 ( $p < 0.05$ ). Four patients in group 1 after receiving steroids had blood glucose levels above 180 mg/dl and 3 of them had above 200 mg/dl. Their preoperative blood glucose levels were 98, 91, 125 and 100 mg/dl.

Table 2. Serial blood glucose levels (mg/dl).

Time of blood sampling	Group 1	Group 2
	No preoperative glucose n = 40	Preoperative glucose n = 40
Preoperative	93.97* (14.27) [40]	122.78* (27.02) [40]
Induction	105.92* (18.23) [40]	126.33* (31.04) [40]
1 hour after induction	113.19 (20.73) [40]	114.50 (21.60) [40]
2 hours after induction	123.19 (24.47) [40]	121.65 (23.62) [40]
4 hours after induction	131.25 (24.09) [40]	121.33 (23.36) [40]
6 hours after induction	135.69 (26.18) [29]	120.52 (21.43) [21]
8 hours after induction	143.67 (41.17) [12]	123.78 (17.68) [9]
10 hours after induction	131.13 (31.19) [8]	133.57 (33.45) [7]
12 hours after induction	143.86 (34.39) [7]	116.50 (9.19) [2]
14 hours after induction	168.25 (50.42) [4]	148.00 [1]
16 hours after induction	175.67 (49.17) [3]	163.00 [1]
18 hours after induction	197.00 [1]	139.00 [1]
20 hours after induction	-	153.00 [1]
Postoperative	150.98 (34.07) [40]	145.28 (31.13) [40]

Data presented as mean (S.D.), number in [ ] means number of subjects

\*  $P < 0.05$  between group 1 and 2

Table 3. Serial blood glucose levels (mg/dl).

Time of blood sampling	No preoperative glucose		Preoperative glucose	
	<i>With steroids</i>	<i>Without steroids</i>	<i>With steroids</i>	<i>Without steroids</i>
Preoperative	94.70(15.86)[22]	92.41(12.41)[18]	114.00(28.96)[11]	126.10(26.00)[29]
Induction	112.65(20.29)*[22]	97.24(10.82)*[18]	134.09(34.21)[11]	123.38(29.86)[29]
1 hour after induction	118.83(21.65)*[22]	106.18(18.05)*[18]	127.18(20.67)*[11]	109.69(20.25)*[29]
2 hours after induction	131.78(21.65)*[22]	119.94(24.90)*[18]	137.45(30.89)*[11]	115.65(17.35)*[29]
4 hours after induction	138.91(21.93)*[22]	120.88(23.55)*[18]	144.00(24.54)*[11]	112.72(16.32)*[29]
6 hours after induction	143.31(21.20)[16]	126.31(29.40)[13]	133.60(13.13)[5]	116.44(22.18)[16]
8 hours after induction	160.50(40.74)*[8]	110.00(8.6)*[4]	132.00(6.16)[4]	117.20(21.80)[5]
10 hours after induction	149.75(33.25)[4]	112.50(15.50)[4]	140.75(38.26)[4]	124.00(30.35)[3]
12 hours after induction	160.75(38.18)[4]	121.33(5.51)[3]	116.50(9.19)[2]	-
14 hours after induction	211.50(12.02)[2]	125.00(1.41)[2]	148.00[1]	-
16 hours after induction	204.00(4.24)[2]	119.00 [1]	163.00[1]	-
18 hours after induction	197.00 [1]	-	139.00[1]	-
20 hours after induction	-	-	153.00[1]	-
Postoperative	162.61(33.61)[22]	136.11(29.18)[18]	162.91(26.25)[11]	138.59(30.58)[29]

- Data presented as mean (S.D.), number in [ ] means numbers of subjects

● P < 0.05 between subgroups receiving or not receiving steroids within each group

We found significant changes in serial blood glucose levels within 4 subgroups. Blood glucose levels tended to increase after induction in 3 subgroups but decrease slightly in group 2 without steroids.

## Discussion

It has been a common practice for anesthesiologists to administer glucose-containing solutions intraoperatively in order to forestall hypoglycemia which may occur with increasing duration of fasting. However intraoperative glucose administration<sup>(10)</sup> causes many problems. Such as glucose induced hyperglycemia enhances ischemic damage and stimulates insulin secretion with subsequent

hypoglycemia. The brains is at risk of ischemia during intracranial operations because of the factors already mentioned. The trend for fluid management in such operations is favored towards the use of glucose-deprived solutions to avoid hyperglycemia. The safety of this practice in adults has been confirmed in most intracranial operations<sup>(6,9)</sup> lasting for up to 4 hours, however, Ittichaikulthol et al<sup>(7)</sup> found one hypoglycemic episode in Thai patient (blood glucose level 57 mg/dl). No studies mentioned the effect of steroids nor preoperative glucose-containing solutions on intraoperative blood glucose levels. This study found that blood glucose levels were significantly higher in patients who had received glucose-containing



solutions preoperatively than in those who had not. Upon intraoperative cessation of glucose supply, serial blood glucose levels were not different in each group. No hypoglycemia episodes occurred even in group 2 patients who had previously received glucose nor those with long duration of anesthesia. This might be due to stress response causing the blood glucose levels to increase in both groups. However, those patients requiring long operative times were relatively few and hence it was difficult to say that withholding glucose was completely safe.

The patients in each group were divided into 2 subgroups: receiving and not receiving steroids. Statistical analysis was done between subgroups within each group. We found that blood glucose levels were significantly higher in steroid subgroups at induction, 1 hour, 2 hours, 4 hours and 8 hours in group 1 and at 1 hour, 2 hours and 4 hours in group 2. During the rest of the operation blood glucose levels tended to be higher in the steroids group but this was not statistically significant. Four and 3 patients in group 1 had blood glucose levels above 180 and 200 mg/dl respectively, after steroids administration. Blood glucose levels tended to rise at 6 - 8 hours when steroid administration was repeated according to preoperative medications. These patients might display abnormal glucose tolerance and become hyperglycemic when receiving steroids. Due to the small number of patients we do not know whether the high blood glucose levels in these patients effected any neurologic outcome. Most studies in animals and humans<sup>(2,5,11-13)</sup> have shown the correlation between blood glucose levels and neurologic outcome, the higher blood glucose levels, the worse neurologic outcomes. Only a few contrasting studies<sup>(14 - 15)</sup> showed the beneficial effect of

hyperglycemia on cerebral ischemia. Lanier et al<sup>(2)</sup> found that dextrose infusion prior to complete cerebral ischemia resulted in greater cerebral injury in monkeys. Blood glucose levels immediately before ischemia were  $181 \pm 19$  mg/dl in the dextrose-treated group compared to  $140 \pm 6$  mg/dl in the lactated Ringer treated group. Nakakimura et al<sup>(3)</sup> found that the cats treated with glucose (blood glucose  $269 \pm 21$  mg/dl) had worse neurologic outcomes than those treated with normal saline (blood glucose  $118 \pm 24$  mg/dl) before cardiac arrest. Pulsinelli et al<sup>(4)</sup> found that moderate hyperglycemia (blood glucose  $298 \pm 34$  mg/dl) augmented ischemic brain damage in rats. The patients with head injury<sup>(11)</sup> who subsequently remained in a vegetative state or died had significantly higher blood glucose levels than those with a good outcome ( $217 \pm 12$  VS  $167 \pm 6$  mg/dl). Longstreth et al<sup>(12)</sup> found that blood glucose levels were higher in patients with fatal cardiac arrest than those who recovered ( $341 \pm 13$  VS  $262 \pm 7$  mg/dl). Pulsinelli et al<sup>(13)</sup> found that the neurologic outcome after ischemic stroke was worse when blood glucose levels were above 120 mg/dl. In contrast, Ginberg et al<sup>(14)</sup> found larger cerebral infarct volumes in rats associated with lower levels of blood glucose. Zasslaw et al<sup>(15)</sup> also found that hyperglycemia (blood glucose  $561 \pm 36$  VS  $209 \pm 28$  mg/dl) decreased the neuronal alterations after middle cerebral artery occlusion in cats. At present, normoglycemia is presumed the best for the ischemic neurons, therefore, it would be best to keep normoglycemia in patients undergoing intracranial operations.

In conclusion, we observed no hypoglycemic episode in patients receiving preoperative glucose containing solutions and intraoperative glucose

deprived solutions during long intracranial operations. However, as we observed hyperglycemia in some patients after receiving steroids, even though their overall numbers was small, we would recommend monitoring of blood glucose intraoperatively in order to improve the patients' safety.

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