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Glucose tolerance in elderly patients does not deteriorate during anesthesia and surgical stress

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Abstract: This study evaluated the glucose tolerance of elderly subjects compared with that of younger subjects under surgical stress. During surgery, glucose 0.1 g·kg^{-1} was administrated i.v. to the elderly group, aged 66–83 years (n = 11, mean 73.5 ± 5.9) and the control group, aged 19–64 years (n = 11, mean 50.9 ± 15.1), all of whom were scheduled for lower abdominal surgery and had a normal range of fasting blood sugar and glycosylated hemoglobin (HbA_{1C}). Between 3 and 90 min after glucose loading, the blood glucose levels of the control group increased more than those in the elderly group, and at 10 and 15 min those in the control group showed a significantly greater increase than those in the elderly group ($P < 0.05$). Serum insulin concentrations increased at 3 and 5 min, but no significant difference was observed between the two groups. Cortisol and catecholamines also showed no significant difference between groups. It was concluded that glucose tolerance in elderly subjects does not deteriorate during lower abdominal surgery.

Key words: Surgical stress, Glucose tolerance, Elderly patients, Stress hormones

Introduction

Recently, the elderly population has increased, with an accompanying increase in the number of surgical procedures performed in elderly patients. Although the progressive deterioration of glucose tolerance with age is well recognized [1,2], age-related changes in glucose tolerance under anesthesia and surgical stress have not been studied. The present study evaluated the differences in glucose tolerance between elderly and younger patients under anesthesia and surgical stress.

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Materials and methods

After informed consent and the University Ethics Committee's approval had been obtained, 22 patients with ASA physical status I and II, ranging in age from 19 to 83 years, who were undergoing elective surgery for lower abdominal lesions in Nippon Medical School Hospital, were assigned to two groups. The elderly group (n = 11) included patients aged over 65 years, while the patients in the control group (n = 11) were under 65 years. Exclusion criteria included those patients with any metabolic, endocrine, cardiac, renal, or hepatic disorders; those taking medications that influence carbohydrate metabolism; and obesity. The range of preoperative fasting blood glucose and glycosylated hemoglobin (HbA_{1C}) were within normal limits. Preanesthetic fasting started from 9 P.M. the day before surgery. Premedication consisted of atropine sulfate 0.5 mg and hydroxyzine pamoate 50 mg intramuscular injection 30 min before entering the operating room. After arrival in the operating room, an automated blood pressure cuff (BP-103i, Nippon Colin, Tokyo, Japan) was applied to monitor blood pressure at 5-min intervals. A lead II electrocardiograph (ECG; Life Scope 11, Nihon Koden, Tokyo, Japan) was continuously monitored. A pulse oximeter (Nellcor N-180, Nellcor Inc., CA, USA) was applied to monitor oxygen saturation. A Foley catheter (Bardex Foley Catheter, C.R. Bard Inc., Covington, GA, USA) was placed into the urinary bladder for monitoring body temperature. After insertion of an 18-gauge peripheral intravenous cannula on the dorsum of the right hand, lactated Ringer's solution was infused at a rate of 10 ml·kg^{-1}·h^{-1} for the 1st h, followed by 5 ml·kg^{-1}·h^{-1}. Anesthesia was induced with thiamylal 5 mg·kg^{-1} and vecuronium 0.15 mg·kg^{-1} to facilitate tracheal intubation. Subsequently, anesthesia was maintained by inhalation of nitrous oxide 70% in oxygen with 1%–2% isoflurane. End-tidal isoflurane concentration was measured by the

infrared absorption method (Capnomac Ultima, ULT-Svi-31-04, Datex, Helsinki, Finland) for calculation of the total isoflurane dose, expressed as MAC·h. Supplemental doses of 0.02–0.04 mg·kg^{-1} vecuronium were administered as required. Ventilation was controlled to maintain an end-tidal carbon dioxide tension in the range of 30–40 mmHg. Before the surgical incision, a 22-gauge cannula was placed in the left radial artery to obtain blood samples. When the peritoneum appeared after median incision of the abdomen, glucose 0.1 g·kg^{-1} was injected from the right peripheral venous line within 30 s. Thereafter, arterial blood samples were obtained for blood glucose determination at 0 min (before glucose loading), 3, 5, 10, 15, 20, 25, 30, 40, 50, 60, 90, and 120 min after glucose injection, and for insulin radioimmunoassay (IRI) at 0, 3, 5, 10, 30, and 60 min. Triglycerides (TG), free fatty acids (FFA), catecholamines (adrenaline AD, noradrenaline NA, dopamine DP), cortisol (COR), and glucagon (GLU) were measured at 0, 30, and 60 min. Blood glucose concentration was measured by the hexokinase-G·6·P-dehydrogenase method; radioimmunoassay was used to determine IRI, COR, and GLU; enzyme assay, for FFA and TG; and high-pressure liquid chromatography (HPLC), for AD, NA, and DP. Urinary sugar levels were measured at 0, 30, and 60 min by the glucose oxidase method (automated glucose analyzer, Glucoroder-F, A&T, Tokyo, Japan). Parametric data were reported as mean ± SD. Statistical analysis was performed using one-way analysis of variance (ANOVA), and F-test and Fisher's PLSD test were used to assess statistical significance. A value of $P < 0.05$ was considered significant.

Results

Twenty-two patients scheduled for lower abdominal surgery were enrolled in the study. The elderly group was aged 66–83 years (mean 73.5 ± 5.9, $n = 11$, M:F = 4:7) and the control group was aged 19–64 years (mean 50.9 ± 15.1, $n = 11$, M:F = 5:6). Patients' data for age, gender distribution, body weight, body height, body mass index (BMI), MAC·h, urine output, and total urine glucose excretion are presented in Table 1. Except for age, there was no significant difference between the two groups.

Basal arterial glucose levels were similar in the elderly (99.2 ± 7 mg·dl^{-1}) and the control (97.5 ± 10 mg·dl^{-1}) group. Three minutes after glucose loading, arterial glucose levels rose to a peak value in the elderly (191.1 ± 27 mg·kg^{-1}) and control groups (208.2 ± 19 mg·kg^{-1}) and decreased thereafter (Fig. 1). Between 3 and 90 min, the blood glucose levels of the control group increased more than those in the elderly group, and at 10 and 15 min, there was a significant difference between the groups.

In both groups, the IRI increased significantly at 3 and 5 min, but there was no significant difference between the two groups (Table 2).

There was no change in GLU before and after glucose loading in either group, but values were higher in the elderly group at all time points compared to those in the control group. The IRI/GLU ratio (I/G) did not show any significant difference between the two groups throughout the study.

After glucose loading, there were increased COR values at 30 and 60 min but there was no significant difference between groups.

AD, ND, and DP did not change throughout the study, nor were there any significant differences between the two groups (Table 3).

Discussion

According to previous studies the decline in glucose tolerance begins in the third decade and appears to be continuous throughout the remainder of the adult life span [2]. Impaired glucose tolerance is determined by fasting blood glucose and the glucose loading test. The age effect on fasting blood glucose levels is small, approximately 1 mg·dl^{-1} per decade above 30 years of age [3–6]. In the 100-g oral glucose tolerance test for 1-h

Table 1. Patient characteristics

	Control group	Elderly group
Number of patients	11	11
Sex (male/female)	5:6	4:7
Age (years)	50.9 ± 15.1	73.5 ± 5.9*
Weight (kg)	57.5 ± 8	47.7 ± 10.5
Height (cm)	161.2 ± 9.4	153.4 ± 8.5
BMI (kg·m^{-2})	22 ± 2.0	20 ± 3.1
MAC·h	1.28 ± 0.34	1.24 ± 0.24
Urine output (ml)	289 ± 202	315 ± 289
TUGE (mg)	33.8 ± 23.6	31.3 ± 26.8

Values are expressed as mean ± SD.
BMI, body mass index; MAC·h, Mac × h during 2 h of measurement; TUGE, total urine glucose excretion during measurement.
*$P < 0.05$ *vs* control.

Table 2. Serum insulin concentration

Time (min)	Control group (μU·ml^{-1})	Elderly group (μU·ml^{-1})
0	2.18 ± 0.3	2.36 ± 1.2
3	8.54 ± 7.7	7.45 ± 6.0
5	6.45 ± 3.9	5.63 ± 3.2
10	4.36 ± 2.4	3.54 ± 1.5
30	5.45 ± 4.6	3.63 ± 1.8
60	6.27 ± 4.0	4.00 ± 1.8

Values are expressed as mean ± SD.

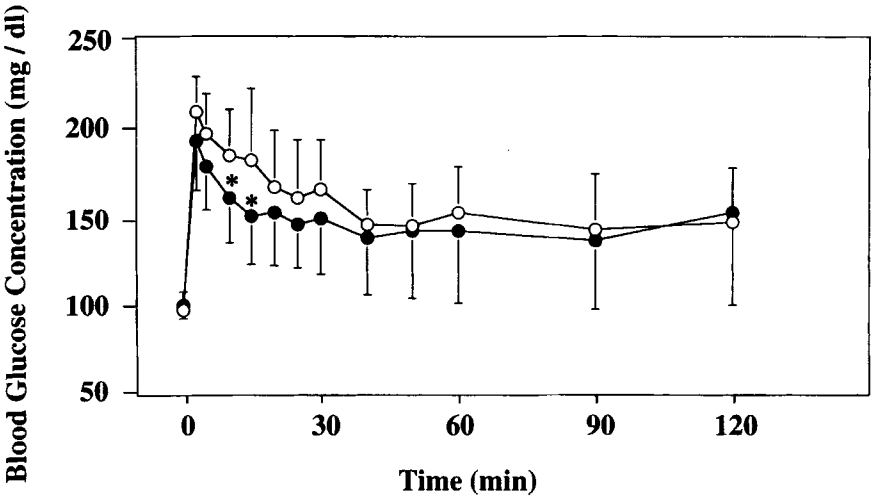

Fig. 1. Time course of changes in blood glucose concentration. At 10 and 15 min, the blood glucose concentration in the control group (*open circles*) increased significantly compared to that in the elderly group (*solid circles*). Each group: n = 11. All values are expressed as mean ± SD

Table 3. Parametric data

	Group	0 min	30 min	60 min
GLU ($pg \cdot ml^{-1}$)	Elderly	75.2 ± 33.9	83.9 ± 24.1	81.5 ± 29.5
	Control	47.7 ± 20.9	58.6 ± 21.9	60.0 ± 21.1
DP ($pg \cdot ml^{-1}$)	Elderly	35.0 ± 8.0	71.4 ± 32.8	62.5 ± 25.4
	Control	20.0 ± 15.5	58.4 ± 43.3	57.4 ± 49.1
NA ($pg \cdot ml^{-1}$)	Elderly	487.3 ± 116	450.1 ± 126	400 ± 119
	Control	352.8 ± 160	356.1 ± 121	344 ± 135
AD ($pg \cdot ml^{-1}$)	Elderly	72.1 ± 53	98.1 ± 60	70.8 ± 82
	Control	69.4 ± 74	122 ± 78	114 ± 69
COR ($\mu g \cdot dl^{-1}$)	Elderly	11.2 ± 3.8	19.1 ± 2.2	20.2 ± 4.0
	Control	9.0 ± 3.7	20.1 ± 1.0	21.6 ± 4.1
TG ($mg \cdot dl^{-1}$)	Elderly	116.4 ± 77.4	97.0 ± 68.3	93.9 ± 66.7
	Control	85.7 ± 45.1	71.0 ± 36.5	69.7 ± 35.1
FFA ($mEq \cdot l^{-1}$)	Elderly	0.70 ± 0.2	0.93 ± 0.2	0.87 ± 0.2
	Control	0.69 ± 0.2	0.92 ± 0.2	0.77 ± 0.3
I/G ratio	Elderly	0.03 ± 0	0.10 ± 0.1	0.08 ± 0
	Control	0.05 ± 0	0.18 ± 0.2	0.12 ± 0.1
US ($g \cdot dl^{-1}$)	Elderly	0.01 ± 2.1	0.01 ± 0	0.01 ± 0
	Control	0.01 ± 2.1	0.01 ± 0	0.02 ± 0

All data are expressed as mean ± SD.
GLU, glucagon; DP, dopamine, NA, noradrenaline; AD, adrenaline; COR, cortisol; TG, triglycerides; FFA, free fatty acids; I/G, insulin radioimmunoassay/glucagon; US, urine sugar.

values, these range from 4 to 14 $mg \cdot dl^{-1}$ per decade with a mean of 9.5. For 2-h values, the range is from 1 to 11 $mg \cdot dl^{-1}$ per decade with a mean of 5.3 [1]. The intravenous glucose tolerance test shows an age-related decline in the glucose disappearance rate, which averages approximately 0.15%–0.20% min^{-1} per decade of life [1,2]. The same results have been observed with the tolbutamide tolerance test [4,5,7] and the cortisone-oral glucose tolerance test [1].

Although the pathophysiological mechanisms of glucose intolerance in older individuals remain unclear, a defect in insulin secretion, decreased peripheral tissue responsiveness to insulin (either a receptor or postreceptor defect), augmented basal hepatic glucose production, impaired suppression of hepatic glucose production, and impaired hepatic glucose uptake [6] are considered to be the main intrinsic factors. Extrinsic factors include a change in body composition with decreased lean body mass [8], decreased physical activity [9] (which contributes to diminished insulin sensitivity), altered dietary intake [10] (an age-related decline in total caloric intake will result in impaired glucose tolerance), drug effects, and stress stimulation. The decreased lean body mass in older subjects may contribute to the impaired disposal of glucose because there is less tissue in which to store the carbohydrate [8]. In addition, the diminution in lean body mass leads to a corresponding increase in percent adiposity. This means that for a given weight, an older individual has more fat, and is therefore more obese than a younger subject [11].

In our study, intravenous glucose loading under anesthesia and surgical stress showed that the elderly group had a significantly lower glucose concentration than the control group. In general, drug tolerance should be assessed from the relationship between the amount of drug administered and disposed of or the relationship between the amount of drug administered and its certain side effects. Since a metabolized amount of glucose given exogenously is very difficult to determine in human studies, we evaluated glucose tolerance from an average of the glucose loaded, that retained in the blood, and that excreted in urine in this study. The total urine glucose excretion was not significantly different between the two groups during the study period. Under the stress of anesthesia and surgery, we hypothesize that glucose tolerance was well maintained even in elderly subjects, and that glucose metabolism in the elderly may be different from that in younger people.

Other parameters such as IRI, GLU, I/G ratio, TG, CO, AD, NA, and DP did not show any significant difference between groups. Within these parameters, there was no evidence that could explain these results, which differ from those of previous papers. However, unlike others, this study was performed with intravenous glucose loading under conditions of anesthesia and surgical stress. In a constant state of circulation, anesthesia alone has no great effect on the endocrine system. However, even if modified by anesthesia, surgery produces a stress response as a function of the degree of trauma. Surgical stress in humans produces a neuroendocrine response that includes increased sympathetic nervous system activity, as can be assessed by elevated circulating levels of catecholamines [12,13]. Catecholamine administration can have major effects on carbohydrate metabolism [14–16]. Therefore, increased adrenergic activity could have contributed to the hyperglycemia and impaired insulin release that have been observed during surgical stress in humans [17–19]. However, additional factors occurring during surgical stress that could influence carbohydrate metabolism include the administration of multiple drugs for anesthesia [20], the secretion of other stress hormones such as cortisol and growth hormone [21,22], and the release of vasoactive substances from the site of tissue trauma.

In the aging process, the adrenal gland undergoes fibrotic, hemorrhagic, and cystic changes [23]. It is reported that during either stress-free or surgical stress conditions, the cortisol levels showed no significant difference between younger and elderly subjects [24]. In our study, there were no significant differences in cortisol and catecholamines levels between the two groups. This means that there was no difference in response to stress between elderly and younger subjects. Previous investigators have suggested a decreased sensitivity of peripheral receptors to stress hormones in elderly subjects [25]. Cortisol acts on muscle and adipose tissue to decrease insulin sensitivity, and adrenaline inhibits peripheral glucose uptake, inducing hyperglycemia. It is considered that the blood glucose of elderly subjects under surgical stress would be suppressed if cortisol and adrenaline were not transmitted to receptors in peripheral tissue.

In conclusion, our study showed that glucose tolerance did not deteriorate in elderly subjects compared with younger subjects during lower abdominal surgery.

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