Clinical Study of Glucose Metabolism during Partial Gastrectomy

– Comparison between Epidural and General Anesthesia –

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Plasma glucose, insulin, glucagon, growth hormone (GH) and cyclic-AMP (C-AMP) were measured in 14 patients undergoing partial gastrectomy under 5 g/hr glucose loading. Seven patients received general anesthesia (GOF; Group G) and the other seven, GO + epidural anesthesia (analgesia Th_4–L_1; Group E). Blood glucose increased in both groups, although it remained consistently lower in Group E than in Group G. Serum IRI and IRI/glucose ratio appeared consistently higher in Group E than in Group G and a significant difference was found between the two groups at the early period of surgery. The changes in plasma glucagon and GH were found independent of those in glucose. Cyclic-AMP was also consistently higher in Group G than in Group E and a significant difference was observed at the end of anesthesia. These results suggest that epidural anesthesia with 5 g/hr glucose loading may facilitate insulin release from the islet and peripheral blood uptake particularly during the early period of surgery while many other factors such as GH, cortisol and vagal stimulation seemed to be involved in the later period of surgery. (Key words: blood glucose, glucose loading, insulin, epidural anesthesia, upper abdominal surgery)

(Ogata M et al.: Clinical study of glucose metabolism during partial gastrectomy; comparison between epidural and general anesthesia. J Anesth 1:82–87, 1987)

It is well known that surgical stress elicits endocrine and metabolic changes characterized by the increase in the secretion of cortisol and catecolamine and subsequent glucose intolerance. The afferent neurologic blockade with epidural anesthesia has been reported to inhibit the hyperglycemic response following lower abdominal surgery[1,2].

However, there are still many discussions on insulin reponse to the plasma glucose during high level epidural anesthesia. In neck epidural anesthesia, it was reported that insulin response to the intraveous glucose is more elevated than in general anesthesia[3]. On the other hand, the basal insulin response is reported to be inhibited during high level spinal anesthesia[4] or epidural anesthesia[5,6].

However, as far as we know, only a few reports on the insulin response during upper abdominal surgery under continuous glucose loading have been reported[7]. The purpose of this investigation is, therefore, to compare the effects of epidural anesthesia on the hormonal response to the upper abdominal surgery under continuous glucose loading with those produced by general anesthesia.

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Patients and Methods

Fourteen patients undergoing elective surgery of gastrectomy starting at 9:00 AM were included in this study.

None of them had metabolic disturbance and received drugs known to affect blood glucose and IRI values.

Informed consent was obtained from all of the patients. Each patient was allowed to have normal diet on the day before surgery and premedicated diazepam 10 mg P.O. at 6:30 AM on the day of surgery. All patients were administered intravenous glucose continuously during surgery by a infusion pump from the time of first blood smapling in the preanesthetic period. The patients were divided into two groups of seven. The first group (group G) received general anesthesia (halothane-N_2O/O_2). The second group (group E) received epidural anesthesia with N_2O/O_2. In the group of E, the patients were placed in lateral position and epidural catheter was inserted at the $T_{6/7}$ or $T_{7/8}$. Epidural analgesia from T_4 to L_1 was obtained by using 10–15 ml of 2% mepivacaine and maintained during surgery with intermittent injection of mepivacaine through the epidural catheter. The patients were given pancuronium bromide 1 mg before endotracheal intubation to minimize fasciculation with S.C.C. Then, general anesthesia was induced with thiopental 4 mg/kg iv, and endotracheal intubation was performed following administration of S.C.C. 1 mg/kg iv and anesthesia was maintained with 30% N_2O–70% O_2. In the group of G, the patients were intubated as in the group of E. Anesthesia was maintained with 1–2% halothane in 30% O_2 and 70% N_2O. Surgery started between 9:00 AM and 9:30 AM. Blood pressure was adjusted primarily by an administration of the lactated Ringer (L/R) solution although persistent hypotension was corrected by intermittent administration of vasopressor drugs. The blood samples were taken from the peripheral veins opposite to the site of fluid and glucose administration. Samplings were made at the following periods; before induction, incision, 30, 90, and 150 min after skin incision, and the end of anesthesia. Blood glucose was measured by the standard glucose oxidase method, and IRI, glucagon, growth hormone (GH) and c-AMP were determined by radioimmunoassay. Statistical analysis was made by paired and unpaired student t-test. The value less than 0.05 was regarded as statistically significant.

Table 1. Comparison of the two groups (each group; 7 patients)
No significant difference was found between the groups

	Go + Epidural	GOF
Age (years)	48.3±4.8	47.8±5.5
Weight (kg)	59.5±3.5	50.6±2.8
Fluid (ml/kg/min)	9.5±1.04	9.2±0.88
Blood loss (g)	491±104	425±86
Surgical duration (min)	230±11	207±24

(mean ± S.E.)

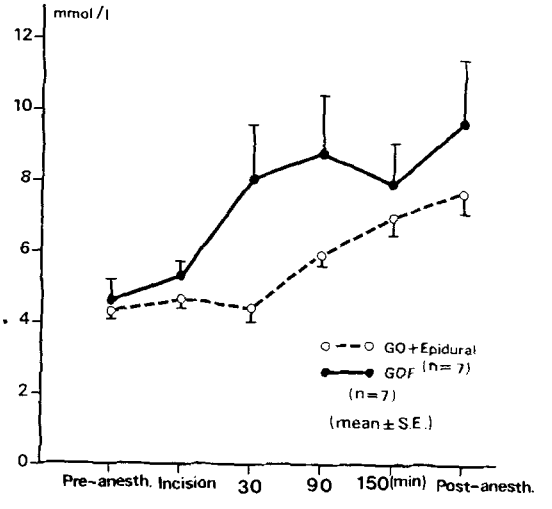

Fig. 1. The changes in blood glucose concentration in two groups under 5 g/hr glucose loading throughout the study. Although group G tended to be higher than group E, no significant difference was found between the groups.

Results

The details of the patients are shown in Table 1. No significant difference was found between two groups.

Blood glucose (fig. 1)

Blood glucose increased in both groups during surgery. However, the values in Group E were consistently lower than in Group G.

Serum IRI (fig. 2)

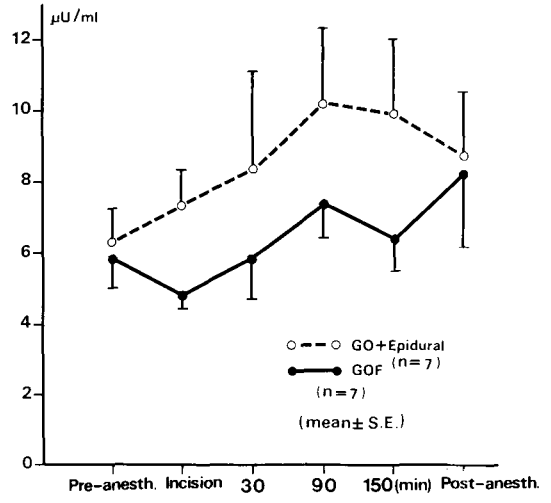

Fig. 2. Serum IRI response to partial gastrectomy with glucose loading (5 g/hr). Group G remained lower than group E (no significance).

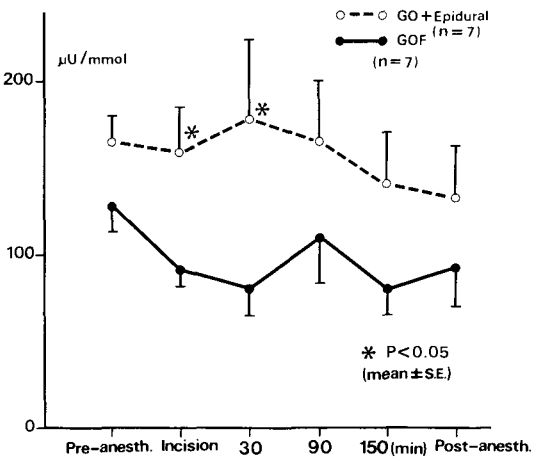

Fig. 3. The changes in the IRI/glucose ratio. Group E remained higher than group G throughout the study. A significant difference between two groups ($P<0.05$) was observed during the early period of surgery.

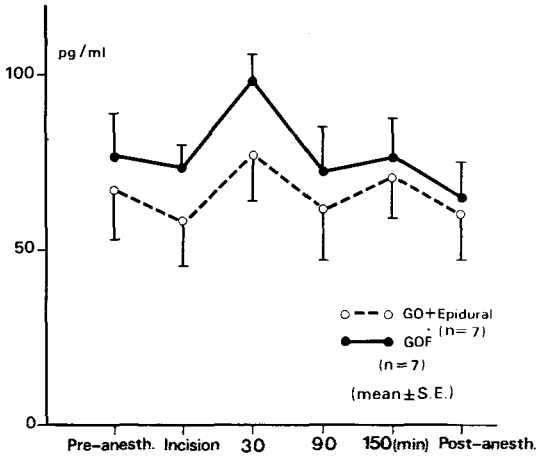

Fig. 4. The changes in plasma glucagon. No significant was found between the two groups.

The base-line level of serum IRI was slightly higher in group E than in group G, although the difference was not statistically significant. Serum IRI increased in both groups during surgery as blood glucose became elevated. However, the values in Group E were consistently higher than those in Group G. A significant difference was found between the groups at the time of skin incision ($p<0.05$).

I/G ratio (fig. 3)

The preanesthetic value of I/G ratio in group E was higher than in group G, although the difference was not significant. The I/G ratio in group E remained consistently higher than that in group G during surgery. There was a significant difference between the groups at both the time of incision and 30 min after incision.

Glucagon (fig. 4)

The level of serum glucagon was slightly higher in group G than in group E throughout the study although the difference was not statistically significant.

Growth hormone (GH) (fig. 5)

The preanesthetic level of serum GH was higher in group E than in group G and tended to increase after skin incision in both groups (no significance).

C-AMP (fig. 6)

In both groups, C-AMP increased during surgery. The increase in group E was smaller than that in group G. The difference between the groups at the end of anesthesia was found statistically significant. ($p<0.05$)

Discussion

It is well-known that glucose tolerance is

reduced and release of insulin is impaired by surgery under general anesthesia. In epidural anesthesia, however, there are many discussions on the insulin response. Our results demonstrate that epidural anesthesia, in contrast to general anesthesia, suppresses hyperglycemic response with an augmented insulin release especially during the early period of surgical procedure. These results are in contrast to those in other previous study performed during gastrectomy, where epidural anesthesia did not affect the insulin response[5]. We have no good explanations about this diference. However, it is suggested that this discrepancy may be attributed to the infusion of glucose during surgery. We employed an intra-operative infusion of glucose at a constant rate (5 g/hr) expecting its anti-ketogenic effect, while no glucose was administered in their study. Their patients were considered more susceptible to starvation than in our study. In addition, it has also been reported that the infusion of glucose (1 mmol/min) suppressed the splanchnic release of glucose during surgery (Stjernström et al.[8]). Our results may suggest that intraoperative infusion of glucose at a constant rate facilitates insulin release and suppresses the release of hepatic glucose during surgery. However, further studies will be needed in this regard.

Stimulation of the splanchnic sympathetic nerve is known to suppress insulin release by the α-adrenergic system. On the other hand, sympathetic blockade induced by high spinal anesthesia has been reported to decrease glucose tolerance and insulin release because the baseline adrenergic input is necessary to maintain the normal islet function[4]. In our present study, however, IRI/G ratio increased during surgery in epidural group and a significant difference was found between the two groups at the early period of surgery. Our results are consistent with those of Houghton who observed that epidural analgesia preserved glucose tolerance with an augmented insulin release[9]. Inhibition of the release of circulating catechcolamine by epidural anesthesia is suggested to facilitate insulin release and peripheral glucose utilization particulary in the early period of surgery.

Glucagon is known to elevate glucose in blood by gluconeogenesis and glycogenolysis. However,

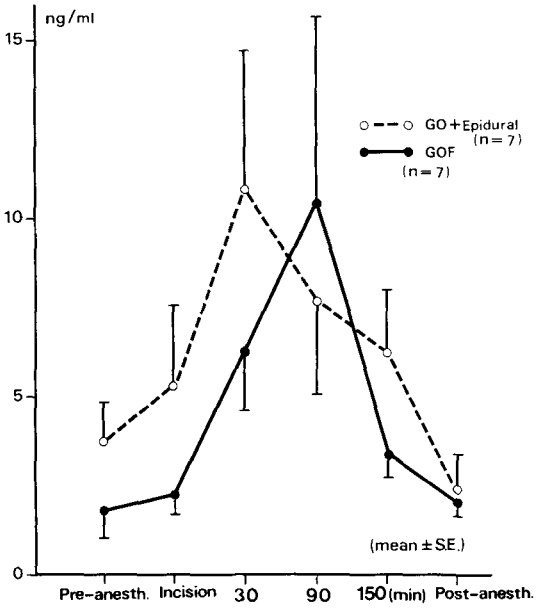

Fig. 5. Plasma growth hormone (GH). No significant difference was observed between the two groups.

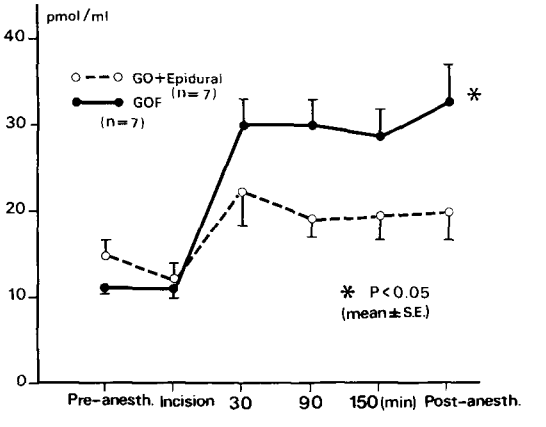

Fig. 6. The changes in plasma c-AMP. A significant difference was observed between the groups at the end of anesthesia.

there are also many discussions on the changes of serum glucagon during surgery. Brandt et al demonstrated that serum glucagon remained unchanged in both epidural and general anesthesia during hysterectomy[2], while other studies showed that plasma glucagon increased in surgical patients under general anesthesia[10] as well as in burned patients[11]. In this respect, our findings are considered to favor the results of Brandt et al. The results of these latter two studies suggest that

plasma glucagon plays only a minor role in controlling the blood glucose level during surgery.

An increase in plasma growth hormone during surgery has been reported under general anesthesia. However, epidural anesthesia was shown to suppress the elevation of the plasma growth hormone[2]. In our study, it was demonstrated that serum GH increases after skin incision in both general and epidural groups. These our observations indicate that activation of hypothalamic-anterior pituitary axis is responsible for the increase of growth hormone because our previous studies[12] demonstrated that epidural anesthesia could not suppress the elevation of ACTH, cortisol as well as GH in upper abdominal surgery.

The plasma concentration of cyclic AMP, known as the common intracellular second messenger for hormones, increased during surgery and a good correlation was found between the changes in plasma adrenaline and cyclic AMP[13]. In our present study, a significant difference in plasma c-AMP appeared between the two groups at the end of surgery, which was considered consistent with the results of Nistrap et al.[14] They observed that blockade of the afferent nerve impulse from the site of surgical trauma reduces the catabolic response to surgery.

Hyperglycemic and impaired glucose tolerance during surgery are also well-documented. The following mechanisms for intraoperative hyperglycemia have been reported[15]: 1) increased glucose production from the liver secondary to the increased secretion of CA and glucagon, 2) enhanced glucose production by direct sympathetic simulation of the liver, 3) inhibition of the insulin secretion by the increased CA. 4) impaired glucose utilization by CA, GH and cortisol which act as insulin antagonist. In epidural anesthesia, however, serum glucose has been reported to be suppressed during surgery despite of reduction of the insulin release[2,5,6]. In regard to this finding, the following mechanisms are considered; 1) suppression of the hepatic glucose release, 2) increased peripheral uptake of glucose. Our findings in our current study, however, indicate that epidural anesthesia with constnat infusion of glucose facilitates insulin release particularly during the early period of surgery. As for its mechanisms, we consider that epidural anesthesia inhibits the sympathetic impulse to the pancreas, which might be playing a predominant role in inhibiting the insulin secretion. In the late period of surgery, however, there were no significant differences between the two groups on IRI, IRI/G in our present study. For the explanation of these results on IRI and IRI/G, it was considered that increased GH and cortisol in the late period of surgery may have reduced the insulin responses. And secondary hyperglycemia following this reduced insulin response may have induced the insulin secretion in both groups by vagal stimulation[16], which could not be blocked even by epidural anesthesia.

In conclusion, epidural anesthesia was considered to facilitate not only glucose utilization but also insulin response to glucose in the early period of surgery. However, it was also suggested that many other factors such as GH and cortisol, related to the insulin sensitivity, and vagal involvement with the release of insulin are all to be investigated further in the future.

(Received Nov. 28, 1986, accepted for publication Nov. 28, 1986)

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