

Effects of Enflurane and Epidural Anesthesia on Thyroid Hormone Changes with or without Liver Dysfunction

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Summary: The levels of thyroid hormones are well known to respond to anesthetics and surgical stresses. The conversion of T_4 to T_3 is also affected by liver function. The effects of enflurane and epidural anesthesia on the intraoperative plasma thyroid hormone levels were studied in 19 operative patients with or without liver dysfunction. This study demonstrates that the T_3 plasma levels decrease during surgery undergoing both epidural and enflurane anesthesia, but T_4 plasma levels increase during surgery. And the liver acts as hepatic thyroxine store and modifier of thyroid hormone metabolism.

Key Words: Thyroxine, Triiodothyronine, Anesthesia

Introduction

The levels of thyroid hormones (triiodothyronine, T_3 and thyroxine, T_4) are well known to respond to anesthetics and surgical stresses. It is generally agreed that surgery induces a decrease in circulating T_3 levels, but no consistent change in intraoperative T_4 levels²⁾. Since the peripheral conversion of T_4 to T_3 is also affected by liver function, it is not obvious whether the reported changes of T_3 and T_4 can be extrapolated to the patients with liver dysfunction. Liver dysfunction offers a possibility to manipulate the complex system of stress response by reducing thyroid hormones and thereby enabling investigation of hormonal interactions. Furthermore, anesthesia method itself can alter these complex and interdependent changes of thyroid hormones. It has been also well demonstrated that epidural anesthesia inhibits the endocrine-metabolic response to surgery¹⁾.

The purpose of the present study was to demonstrate the effects of enflurane and epidural anesthesia on the intraoperative plasma thyroid hormone levels in operative patients with or without liver dysfunction.

Patients and Methods

Clinical cases were summarized in Table 1. This study was approved by the institutional Board for Ethics Committee. Informed consent was obtained from 19 patients scheduled

for elective upper abdominal surgery that were in ASA physical status II or III. None of the patients had evidence of thyroid or other endocrine disease nor were they taking any drug, including hormonal preparations. All operations started at 9 am. to avoid daily variation of serum hormone concentration. Patients were allocated to four groups according to the anesthetic methods and liver function: Patients of group A (n = 6) underwent epidural anesthesia combined with nitrous oxide in oxygen and had normal liver function, patients of group B (n = 5) underwent epidural-nitrous oxide-oxygen anesthesia and had abnormal liver function, patients of group C (n = 4) underwent enflurane anesthesia combined with nitrous oxide in oxygen and had normal liver function, patients of group D (n = 4) underwent enflurane-nitrous oxide-oxygen anesthesia and had liver dysfunction. Liver dysfunction was determined with the use of preoperative Indocyanine green excretion test at 15 minutes. The level of less than 10% was designated as normal liver function group and more than 10% was as liver dysfunction group.

Table 1. Clinical cases

anesthetic method	group	liver function	number
Epidural	A	normal	6
	B	abnormal	5
Enflurane	C	normal	4
	D	abnormal	4

In epidural groups, at first, a catheter was inserted at the T_8 - T_9 or T_9 - T_{10} interspace, and mepivacaine 2% without adrenaline was injected to produce sensory blockade extending from T_1 to L_3 . And then, after endotracheal intubation was performed with 5mg/kg of thiomyal sodium and 1mg/kg of succinylcholine chloride, thereafter the anesthesia was maintained with oxygen and nitrous oxide. The epidural block was maintained during the operation with intermittent infusion of mepivacaine 2% 4-5ml every 45-60 minutes. In enflurane groups, the enflurane concentration was maintained between 1.0 and 2.5% after endotracheal intubation. Lactate Ringer's solution was administered i. v. during surgery at a rate of 10ml/kg/hr.

Blood samples for the measurements of T_3 and T_4 were obtained via the radial artery catheter at the following 7 time periods: before anesthetic induction (control), 30min after anesthetic induction, during the surgical procedure respectively 30min, 1 hour, 2 hours and 3 hours after surgical incision, and recovery room. T_3 and T_4 were analysed using radioimmunoassay.

Data were analyzed using unpaired t tests and analysis of variance. Statistical significance was set at $P < 0.05$. Data are presented as the mean \pm SE.

Results

T_3 ; The control values of respective groups were follows, A group 105 ± 10.8 ng/dl, B 93.6 ± 34.0 , C 105 ± 24.8 , D 110 ± 22.8 . T_3 plasma levels had tendency to decrease gradually during operating procedure and got the least levels at recovery room in all groups. Especially in A group, T_3 concentration significantly decreased by 18% at 1 hour after skin incision and this level was maintained during surgery and recovery room. In D group, T_3 concentration significantly decreased by 20% at 3 hours after skin incision. This result may show that the conversion rate of T_4 to T_3 is decreased in abnormal liver. (Fig. 1, 2)

T_4 ; The control values of respective groups were follows, A group 9.30 ± 1.04 μ g/dl, B 11.1 ± 2.09 , C 9.83 ± 3.17 , D 8.40 ± 2.39 . In C group, T_4 concentration increased by 31% after 30 minutes anesthesia induction and this level was maintained during surgery. This elevation returned to the preoperative control value at recovery room. In A group, T_4 concentration also increased by 16% after 30 minutes anesthesia induction. But this elevation is less than that of C group. Although no significant differences was observed between A group and C group, this result may show that enflurane is responsible for T_4 increase. The maximum T_4 elevation is about 40% in C group, but about 30% in D group. This result may show that the amount of T_4 hepatic store in abnormal liver is less than that of normal liver. (Fig. 3, 4, 5)

Discussion

Tissue injury, hemorrhage and surgical stress can cause a multidimensional body response to trauma. This response is thought to be mainly mediated by afferent neurogenic impulses from the area of injury. Therefore abolition of sensory as well as autonomic afferent stimuli by neurogenic blockade such as epidural anesthesia may help in reducing the endocrine and metabolic response to surgery^{6,10}. A major liver function is regulation of intermediary metabolism. The liver acts as an amplifier or modifier of hormone action. However little is known about the relationship of severity of liver disease to anesthetic

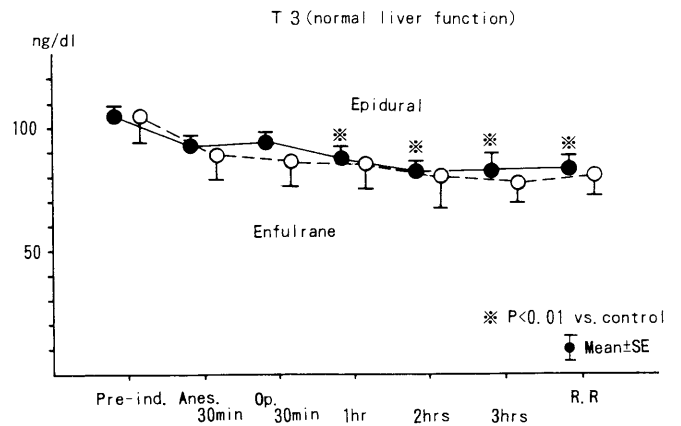


Fig. 1. The changes of T_3 in patients with normal liver function under epidural anesthesia (●—●, group A) or enflurane anesthesia (○—○, group B). Data are presented mean \pm SE.

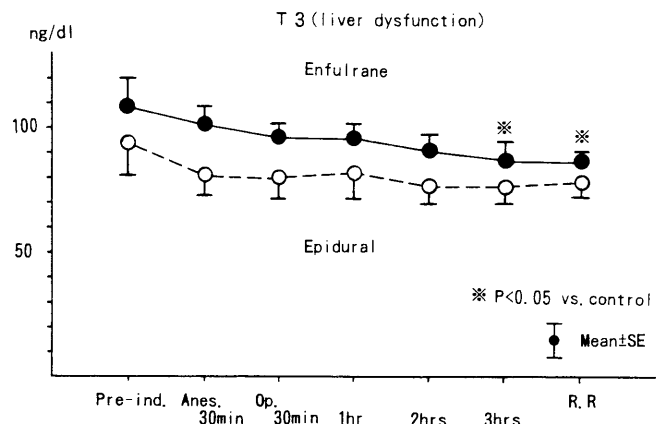


Fig. 2. The changes of T_3 in patients with liver dysfunction under enflurane anesthesia (●—●, group D) or epidural anesthesia (○—○, group B). Data are presented mean \pm SE.

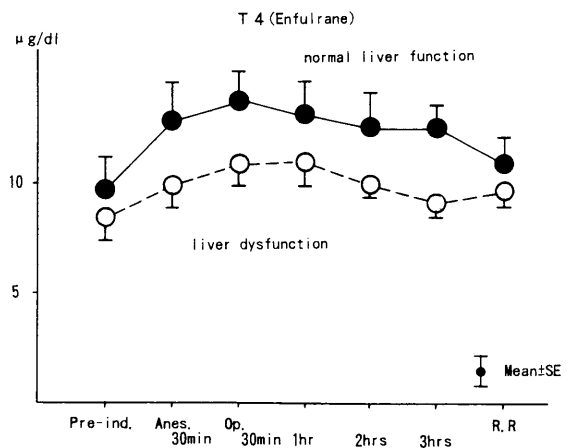


Fig. 3. The changes of T_4 in patients with normal liver function (●—●, group C) or with liver dysfunction (○—○, group D) under enflurane anesthesia. Data are presented mean \pm SE.

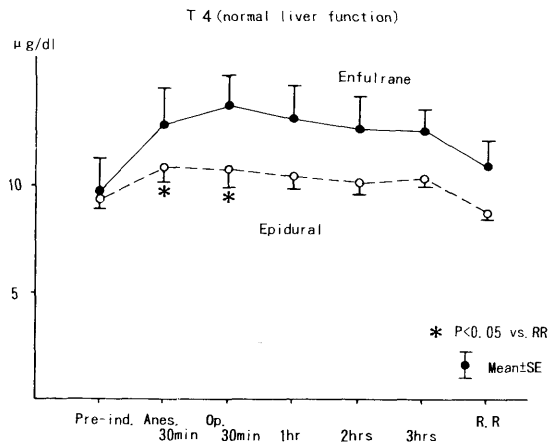


Fig. 4. The changes of T₄ in patients with normal liver function under enflurane anesthesia (●—●, group C) or epidural anesthesia (○—○, group A). Data are presented mean ± SE.

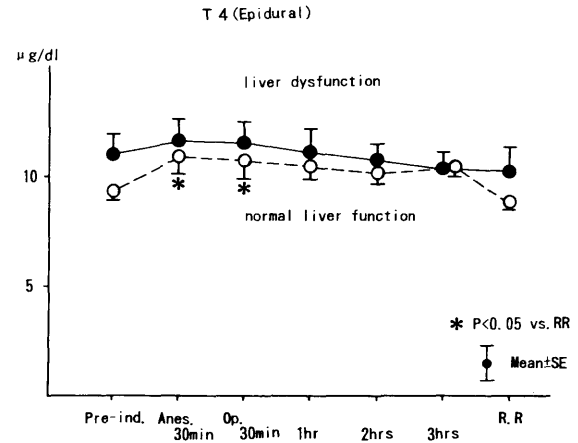


Fig. 5. The changes of T₄ in patients with liver dysfunction (●—●, group B) or with normal liver function (○—○, group A) under epidural anesthesia. Data are presented mean ± SE.

methods or to changes of thyroid hormones during surgery.

The results of the present investigation showed that T₃ plasma levels decrease consistently during surgery undergoing both epidural and enflurane anesthesia. This is in line with other reports⁹. Although the mechanism for the surgery-induced decrease in T₃ remains obscure, the suggestion that it is due to decreased peripheral conversion of T₄ to T₃ is likely to be correct⁹, because in D group, which is the liver dysfunction group, T₃ decrease is not significant. It is well known that the liver is the major organ responsible for peripheral conversion of T₄ to T₃, and liver disease, such as liver cirrhosis, might be expected to result in decreased hormonal and metabolic response in the liver. This is indeed suggested by the glucose tolerance studies of Johnston et al.⁷ and diminished tolerance to carbohydrate loads was noted in hepatic cirrhosis. So these our results may show that the liver is also responsible for the intraoperative T₃ decrease. On the molar basis, T₃ is several times more potent than T₄¹². Therefore, peripheral conversion of T₄ to T₃ may be a form of hormone activation. Under general anesthesia, metabolic rate in man decreases, therefore we may do not need more potent T₃.

Intraoperative increase in T₄ concentration were also observed in the present study, although it is not statistically significant⁹. There are some reports suggesting halothane release T₄ from hepatic stores⁹. Harland et al.⁴ labelled thyroxine with radio-iodine and clearly showed that concomitant with the increase in protein binding iodine, thyroxine radioactivity in the liver decreased progressively, while plasma radioactivity increased. And they suggested this effect was reversible. Therefore the rise in T₄ may be due to displacement, probably from the liver into the plasma. We think enflurane as well as halothane has that same effect, and if liver function is abnormal, hepatic T₄ store may decrease. In liver dysfunction groups, T₄ increase was reduced than that of normal liver function groups, although it was not statistically significant (Fig. 3). The

effect of epidural anesthesia on thyroid hormone changes during surgery has been still controversial^{10,11}. The T₄ increase in epidural anesthesia groups was less than that of enflurane anesthesia group (Fig. 4). Therefore, thyroid hormone changes during surgery can be modified by epidural anesthesia to block afferent neurogenic impulses from surgical sites.

The present study confirms the results that by Oyama et al.⁹ that surgery causes a decrease in circulating T₃ concentrations and the small rise in intraoperative T₄ concentrations. And stress-induced changes of thyroid hormones seems to be influenced by afferent neurogenic blockade by epidural anesthesia. Furthermore, the thyroid hormone changes during surgery seems dependent of the liver function as the thyroid hormones store and metabolic modifier. The mechanism behind this intraoperative changes in thyroid hormone metabolism remains to be discovered but it might be speculated that afferent neurogenic blockade and liver function play very important roles during surgery.

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