



The Effects of Desflurane and Propofol on the Release of Thyroid Hormones in Euthyroid Patients Undergoing Elective Lumbar Discectomy

Elektif Lomber Diskektomi Geçiren Ötiroid Hastalarda Desfluran ve Propofolün Tiroid Hormonu Salınımına Etkileri

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Objective: In this study, we aimed to compare the effects of desflurane and propofol on the release of thyroid hormones in euthyroid patients undergoing single-level lumbar discectomy.

Methods: The study group included 21-65-year-old American Society of Anesthesiology (ASA) I-II euthyroid 40 patients undergoing elective single-level lumbar discectomy. They were randomly divided into 2 groups (n=20). In the maintenance of anaesthesia, Group D received desflurane inhalational anaesthesia and remifentanyl infusion, and Group P received propofol and remifentanyl IV infusions. Four blood samples for the determination of plasma levels of free triiodothyronine (FT3), free thyroxine (FT4) and thyrotropin (TSH) were collected 5 min before and 60 min after the induction of anaesthesia and 60 min and 24 h after the surgery.

Results: Plasma TSH levels in both groups reached the highest levels at the first postoperative hour and returned to the preoperative levels 24 hours after the surgery. Regarding plasma FT3 levels, there were no significant differences within and between groups. There were no significant differences in plasma FT4 levels within the patients of Group P, but in Group D, FT4 levels reached its peak in the first hour of anaesthesia induction and returned back to preoperative levels 24 hours postoperatively (p<0.05).

Conclusion: Further studies are needed to confirm our findings and evaluate patients with thyroid gland pathologies.

Keywords: Thyroid gland, desflurane, propofol

Amaç: Bu çalışmanın amacı tek seviye lomber diskektomi ameliyatı geçiren ötiroid hastalarda desfluran ve propofolün tiroid hormonu salınımı üzerine etkilerinin karşılaştırılmasıdır.

Yöntemler: Tek seviye lomber diskektomi geçiren American Society of Anesthesiology (ASA) I-II, 21-65 yaş arası, ötiroid 40 hasta çalışmaya dahil edildi. Hastalar randomize olarak 2 farklı gruba (n=20) ayrıldı. Anestezi idamesinde Grup D desfluran inhalasyon ajanı ve remifentanil IV infüzyonu aldı. Grup P ise IV propofol ve remifentanil infüzyonu aldı. Plazma serbest triiyodotironin (sT3), serbest tiroksin (sT4) ve tirotropin (TSH) düzeyinin tayini için anestezi indüksiyonundan 5 dk. önce ve 60 dk. sonra, cerrahi işlemden 1 saat ve 24 saat sonra olmak üzere 4 farklı zamanda kan örneği alındı.

Bulgular: Her iki grupta da cerrahi sonrası ilk postoperatif saatte plazma TSH değerleri en yüksek seviyeye ulaştı ve 24. saatte preoperatif değerleri geriledi. Grup içi ve gruplar arası değerlendirilmede plazma sT3 bakımından anlamlı bir fark yoktu. Grup P hastaları arasında sT4 düzeyleri anlamlı fark göstermedi, ancak Grup D'de sT4 düzeyleri anestezi indüksiyonundan sonraki 1. saatte en yüksek seviyeye ulaştı ve postoperatif 24. saatte preoperatif düzeye geriledi (p<0,05).

Sonuç: Sonuçlarımızı doğrulayan ve tiroid patolojisi bulunan hastaların değerlendirildiği ileri çalışmalara gereksinim bulunmaktadır.

Anahtar Kelimeler: Tiroid bezi, desfluran, propofol

Introduction

The thyroid gland is an organ that actively responds to surgical stress and is affected by anaesthetic agents and their metabolites (1). The incidence and perioperative mortality rates for undiagnosed or insufficiently managed hypothyroidism are still unknown, and many complications, such as severe hypotension, heart failure, myxoedema coma, prolongation of the anaesthetic drug action and prolongation of the postoperative recovery period, may be potentially related to hypothyroidism (2-6). On the other hand, patients with hyperthyroidism may experience unwanted side effects, such as tachycardia, decrease in peripheral vascular resistance and increase in stroke volume and cardiac output. These side effects may lead to high-output heart failure or atrial fibrillation in high-risk patients (7).

It is a great advantage for any anaesthesiologist to be informed of the thyroid gland disorders of patients who are scheduled to undergo surgery in the preoperative period. The knowledge of these disorders will allow sufficient time for the regulation of

thyroid hormone levels before elective surgical procedures. If not, general anaesthesia will have to be provided in hypo- or hyperthyroid states. Under these circumstances, it is obligatory to administer an appropriate anaesthetic agent that has minimal effects on thyroid hormone levels in order to protect the patient from unwanted side effects of thyroid disease (8). Many studies investigated the effects of the type of anaesthesia and anaesthetic agents on thyroid hormone levels, but few reports focused on the effects of desflurane on thyroid functions (1, 9).

In this study, we compared the effects of two common anaesthetic agents (desflurane and propofol) on the release of free triiodothyronine (FT3), free thyroxine (FT4) and thyrotropin (TSH) in patients with normal plasma thyroid hormone levels. Single-level lumbar discectomy was selected as the type of surgery, because it has minimal effects on surgical stress and the thyroid gland.

Methods

The study design was prospective, comparative and single-blinded. Following the approval of the local ethics committee, 40 patients aged between 21-65 years, with an American Society of Anesthesiologists (ASA) physical status classification of I or II, undergoing elective single-level lumbar discectomy under general anaesthesia were enrolled in the study. All patients gave their written informed consent. They were all biochemically euthyroid. Patients with a history of thyroid or any other endocrine disorder, including obesity, were not included in the study.

Patients were randomly divided into two groups (n=20) to receive either inhalational anaesthesia with desflurane (Group D) or total intravenous anaesthesia with propofol (Group P) during the maintenance of anaesthesia. Remifentanyl infusion was used in both groups. Four blood samples were obtained for the determination of plasma levels of thyroid hormones (FT3, FT4, TSH) at, 5 min before and 60 min after the induction of anaesthesia and 60 min and 24 h after the surgery. Randomisation was done using a computer-generated random numbers list.

All patients were premedicated with midazolam and atropine sulphate IM 30 minutes before surgery. Monitoring was performed, including electrocardiogram, non-invasive blood pressure, peripheral pulse oximetry (SpO₂), end-tidal carbon dioxide (ETCO₂) and end-tidal desflurane concentrations (in Group D). Anaesthesia was induced with 1.5 mg kg⁻¹ propofol IV, 0.1 mg kg⁻¹ vecuronium bromide IV and 1 µg kg⁻¹ remifentanyl IV, followed by a 0.25 µg kg⁻¹ min⁻¹ infusion. Endotracheal intubation was performed 2 min after the anaesthesia induction.

Anaesthesia was maintained with 6% desflurane and propofol infusion (10 mg kg⁻¹ h⁻¹ for the first 15 min, 8 mg kg⁻¹ h⁻¹ for the second 15 min, followed by 6 mg kg⁻¹ h⁻¹). The lungs

of the patients in both groups were ventilated with 70% air in oxygen with a tidal volume of 7-8 ml kg⁻¹ and a respiratory rate of 8-10 breaths min⁻¹ to maintain ETCO₂ between 30-35 mmHg.

All infusions were administered with the Perfusor compact system (BRAUN® Perfusor Compact S, Melsungen, Germany). The infusion rate of propofol and the concentration of desflurane remained unchanged throughout the surgery. A 25% decrease in mean arterial blood pressure from baseline indicated hypotension. In the presence of hypotension the infusion rate of remifentanyl was reduced. Bradycardia was defined as a 25% decrease in heart rate from baseline and was treated with 0.5 mg atropine sulphate IV. Postoperative analgesia was provided with 1 mg kg⁻¹ meperidine hydrochloride IV.

In all groups, blood samples were collected in order to measure the plasma levels of FT3, FT4 and TSH preoperatively (T1), 5 min before the induction of anaesthesia (T2), 60 min after the anaesthesia induction (T3), postoperative 60 min (T4) and postoperative 24 h (T5).

Thyroid function tests were performed in the Central Biochemistry Laboratories of Marmara University Hospital using the Roche Elecsys 2010, E411 device (Diamond Diagnostics Inc, Holliston, MA, USA). The normal range for each parameter was as follows: FT3- 0.2-6.5 ng dL⁻¹, FT4- 0.7-2.1 ng dL⁻¹ and TSH- 0.3-5.0 mU L⁻¹.

Statistical analysis

A power analysis determined that at least 19.6 patients per group would be required to demonstrate a within-group difference of 0.2 ng dL⁻¹ (FT3 and FT4) with a power of 80% and a significance level of 0.05. Data are expressed as mean±standard deviation. The descriptive statistical studies of the data were performed with frequency, ratio, mean and standard deviation values of the results. The distribution of the data was tested with the Kolmogorov-Smirnov method. Analysis of the interrupted data was performed with t-test, whereas the analysis of the repetitive measurements was performed with repeated-measures analysis of variance (ANOVA). For the analysis of the proportional data, the chi-square test was utilised; if the requirements for the chi-square were not fulfilled, the Fisher's exact test was preferred. The comparison of the groups was made with the student's t-test. A p value lower than 0.05 was designated as the threshold for statistical significance.

Results

There were no significant differences in patient characteristics, duration of anaesthesia or surgery between the groups (Table 1). The total dose of remifentanyl was similar between the two groups. In Group P, 31.40±9.82 mL remifentanyl was consumed, versus 25.55±8.56 mL in Group D. In Group P, the total amount of propofol (10 mg mL⁻¹) administered was 47.35±17.20 mL. In Groups P and D, TSH levels began to

Table 1. Patient demographics, duration of anaesthesia and surgery (mean±SD)

	Group P	Group D
Male/Female	6/14	11/9
Age (year)	38.50±10.96	41.85±12.52
Weight (kg)	69.25±11.14	77.25±15.02
Duration of anaesthesia (min)	106.45±18.80	112.85±19.32
Duration of surgery (min)	94.15±17.43	100.70±19.11
SD: standard deviation; min: minimum		

Table 2. Plasma levels of TSH (mU L⁻¹) (mean±SD)

Time	Group P	Group D	p
T1	1.97±0.58	1.63±0.55	>0.05
T2	3.07±2.30	2.19±1.96	>0.05
T3	3.72±3.74	2.39±1.54	>0.05
T4	5.36±4.50 ^{a,b}	4.77±3.92 [‡]	<0.01
T5	1.82±0.98	1.68±1.16	<0.01
T1: Preoperative; T2: 5 min before induction; T3: 60 min after induction; T4: Postoperative 60 min; T5: Postoperative 24 h; SD: standard deviation			
^a p<0.01, compared with preoperative period			
^b p<0.01, compared with postoperative 24 h			
[‡] p<0.01, compared with other time periods			

Table 3. Plasma levels of free T3 (ng dL⁻¹) (mean±SD)

	Group P	Group D
T1	3.30±0.41	3.25±0.37
T2	3.35±0.53	3.53±0.35
T3	3.11±0.67	3.33±0.37
T4	3.14±0.63	3.33±0.58
T5	2.66±0.70	2.78±0.62
T1: Preoperative; T2: 5 min before induction; T3: 60 min after induction; T4: Postoperative 60 min; T5: Postoperative 24 h; SD: standard deviation		

Table 4. Plasma levels of free T4 (ng dL⁻¹) (mean±SD)

Time	Group P	Group D	p
T1	1.55±0.41	1.39±0.22	>0.05
T2	1.52±0.23	1.54±0.22	>0.05
T3	1.64±0.46	2.16±0.39 ^{*a}	<0.005
T4	1.53±0.28	1.82±0.30 ^b	<0.005
T5	1.50±0.29	1.48±0.32	>0.05
T1: Preoperative; T2: 5 min before induction; T3: 60 min after induction; T4: Postoperative 60 min; T5: Postoperative 24 h; SD: standard deviation			
[*] p<0.001 compared with other time periods			
^a p<0.005 compared with Group P			
^b p<0.005 compared with Group P			

increase 5 min after the induction but with no significant differences between the two groups. In Groups P and D, plasma TSH reached the highest levels at the first postoperative hour and returned to the preoperative levels 24 h after the surgery (p<0.01) (Table 2).

There were no significant differences in plasma FT3 levels between Groups P and D (Table 3).

In Group D, FT4 levels reached its peak at the first hour of anaesthesia induction, began to decrease at the first postoperative hour and returned back to the preoperative levels 24 hours postoperatively. In Group P, FT4 levels were similar in all measured times. FT4 levels in Group D were significantly higher than those obtained in Group P at the first hour following induction and at the first postoperative hour (Table 4).

Discussion

This study suggests that either in Group P or D, plasma TSH reached the highest levels at the first postoperative hour and returned to the preoperative levels 24 hours after the surgery, with no statistical difference between groups. Moreover, in Group D, FT4 levels reached their peak at the first hour of anaesthesia induction and returned back to preoperative levels 24 hours postoperatively.

The thyroid gland has a special role in the anaesthesiologist's daily practice. First, it is an organ on which anaesthetic agents and their metabolites exert their effects and side effects. Second, the evaluation of thyroid hormone levels does not take place in routine preoperative laboratory studies, and hypo- or hyperthyroidism may go undiagnosed in some adult patients.

Surgical trauma exerts an effect on the pituitary-thyroid axis, and thyroid hormones are among the main pituitary hormones secreted as the stress response following surgery (10). The fluctuations in plasma thyroid hormone levels during the intraoperative period are suggested to be the result of the hormonal effects of anaesthetic agents rather than surgical stress (11).

The aim of this study was to investigate the effects of desflurane and propofol on thyroid functions. Desflurane was chosen as the study drug, because few reports have investigated the effects of this agent on thyroid functions.

In this study, plasma FT4 levels significantly increased in Group D as early as the first hour after the induction, but those of Group P remained stable throughout the study period. These findings are somewhat similar to those of other published studies; for example, it had been reported that T4 and reverse T3 (rT3) levels were only increased during enflurane and halothane inhalational anaesthesia, compared to other anaesthetic agents (12).

Börner et al. (11) claimed that inorganic fluoride, the metabolite of enflurane, might be responsible for the change of plasma thyroid hormone levels by inhibiting hepatic type I deiodinase. This suggestion seems to be logical regarding enflurane, because it has a high biotransformation rate, and plasma fluoride ion concentrations increase to great amounts in the body. Inorganic fluoride is a common metabolite of all inhalational agents, as well as desflurane. Lack of a chlorine atom in the desflurane molecule makes its metabolism less

active than other inhalational agents, and fluoride ion concentrations in the plasma remain very low following desflurane breakdown. So, we think that the suggestion of Börner may not be valid concerning desflurane; thus, the fluoride effect is unlikely to explain the increase in plasma FT4 levels in Group D.

Thyroxine is stored in the liver. In vitro studies demonstrated that inhalational anaesthetic agents induce hepatic enzyme activity (13-15). As a result of this activity, plasma thyroxine levels may decrease, and hepatic thyroxine stores may be depleted. Furthermore, inhalational agents decrease the protein-binding capacity of other drugs (16). All of this information may explain the increase in plasma FT4 levels in patients inhaling desflurane. The lack of significant changes in plasma FT3 levels is probably related to the lower protein-binding affinity of FT3 than FT4. It is assumed that disturbed protein binding after desflurane inhalation resulted in an increase in the free fraction of thyroxine, whereas the plasma levels of triiodothyronine remained in the normal range, owing to its already weak protein-binding capacity.

It was previously demonstrated that inhalational anaesthetic agents do not affect the plasma levels of TSH (17, 18). Nevertheless, an opposite result was obtained in our study: plasma TSH levels reached their peak levels at the first hour postoperatively in both Groups P and D. The answer may be hidden in the use of remifentanyl infusion. Grossman et al. (19) demonstrated a rise in TSH levels following opioid infusion. We suggest that in our study, the cause of the increased TSH levels in both groups was probably due to the remifentanyl infusion but not to the study drugs. It is reported that the plasma levels of TSH increase following total intravenous anaesthesia (20).

The main limitation of this study is that we did not study plasma fluoride ion concentrations.

Conclusion

In patients without thyroid gland pathology, propofol infusion in the maintenance of anaesthesia may be an appropriate alternative to desflurane. Further studies are needed to confirm our findings and evaluate patients with thyroid gland pathologies.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Marmara University Faculty of Medicine.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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