

PROLACTIN RESPONSE TO STRESS IN MALE AND FEMALE CASES : A COMPARATIVE STUDY OF TOTAL INTRAVENOUS ANAESTHESIA (TIVA) AND INHALATION ANAESTHESIA

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SUMMARY : *In this study, we investigated the changes in serum prolactin (PRL) levels occurring in response to stress in male and female cases, applying two different anaesthetic techniques. Forty patients who underwent urethroplasty (ASA I-II) were divided into two equal groups according to their genders (M : Male, F : Female). Both groups were divided into two equal subgroups to apply two different anaesthetic techniques. M₁ and F₁ received total intravenous anaesthesia (TIVA) with propofol-alfentanil and oxygen-air mixture; M₂ and F₂ received inhalation anaesthesia (IA) with halothane 0.5-1 % and N₂O 66 % in oxygen. Serum PRL levels were measured before induction of anaesthesia (control), 30, 60 minutes after induction of anaesthesia, and 120 minutes after surgery. In all groups, there was an increase following induction of anaesthesia, and this was the highest at 30 minutes after induction in F₂. In the comparison made among the groups, it was established that there was not a difference in serum PRL levels between M₁ and F₁, while there were significant differences between M₂ and F₂ at 30 minutes and 60 minutes after induction ($p < 0.05$ for all comparisons). It was concluded that the increase in PRL response to stress was higher in females than that in males who received inhalation anaesthesia. In TIVA, there was not a difference in PRL levels related to gender suggesting that PRL response to stress could better be attenuated.*

Key Words : *Prolactin, TIVA, Inhalation Anaesthetics.*

INTRODUCTION

Prolactin (PRL) is released from the anterior pituitary gland and its secretion is controlled by dopaminergic mechanisms originating from the hypothalamus (6). This is one of the hormones, the serum levels of which change depending on anaesthesia and surgery, and normal values differ among males and females (7, 15, 16). In addition, PRL levels change during the sleep, different periods of life and depending on pituitary tumors like PRL-secre-

ting chromophobe adenomas.

This study was designed to investigate the changes in serum PRL in response to anaesthesia and surgery among male and female cases, applying total intravenous anaesthesia (TIVA) by propofol-alfentanil and air-oxygen or inhalation anaesthesia (IA) by halothane and N₂O-oxygen, as two different anaesthetic techniques.

MATERIALS AND METHODS

Patients

After obtaining Ethical Committee approval and written informed consent, we examined 40 patients (ASA physical status I-II) who underwent urethroplasty. Patients with known endocrine or neurological abnormalities and those with conditions likely to alter prolactin levels were excluded from the study.

Procedures

Patients were divided into two equal groups according to their genders (M : Male cases, F : Female cases). Both group were divided randomly into equal subgroups to apply two different anaesthetic techniques between 9.00-11.00 am. M_1 and F_1 received total intravenous anaesthesia (TIVA) with propofol-alfentanil and air-oxygen mixture. M_2 and F_2 received inhalation anaesthesia (IA) with halothane and N_2O -oxygen. All patients were premedicated with atropine 0.5 mg and diazepam 10 mg intramuscularly 45 minutes (min) before induction of anaesthesia.

Anaesthetic techniques

In TIVA groups : Alfentanil 25 $\mu\text{g}/\text{kg}$ in two minutes, propofol 2 mg/kg in 30 seconds, atracurium 0.5 mg/kg in 60 seconds were given iv for induction of anaesthesia. When the twitch depression reached 90 % (TOF-GUARD INMT), endotracheal intubation was performed. Ventilation was provided by the air-oxygen mixture, using a ventilator (Newport Breeze E-150) in such a way that the values would be ET_{CO_2} : 34 ± 4 mmHg and Fi_{O_2} : 0.3. Anaesthesia was maintained with alfentanil infusion 10 $\mu\text{g}/\text{kg}/\text{min}$ for 10 min and 0.5 $\mu\text{g}/\text{kg}/\text{min}$ thereafter plus propofol 10 $\text{mg}/\text{kg}/\text{hour}$ for the first 10 min, 8 $\text{mg}/\text{kg}/\text{hour}$ for the next 10 min and 6 $\text{mg}/\text{kg}/\text{hour}$ thereafter by two separate infusion pumps (IVAC 770). Atracurium administration was discontinued 20 min before the expected end of surgery. Cessation of alfentanil infusion was 15 min before the end, whereas propofol infusion was stopped during skin closure.

In IA groups : Anaesthesia was induced with thiopentone 6 mg/kg and atracurium 0.5 mg/kg . Anaesthesia was maintained with 66 % $\text{ET}_{\text{N}_2\text{O}-\text{O}_2}$ and ET_{AA} (halothane) 0.5-1 %.

In all groups, ventilation was mechanically conducted with IPPV in such a way that the values would be ET_{CO_2} : 34 ± 4 mmHg and Fi_{O_2} : 0.3. All patients received a bolus of 0.5 mg/kg to facilitate the endotracheal intubation and infusion of 0.4 $\text{mg}/\text{kg}/\text{h}$ atracurium for the neuromuscular block. The adequacy of anaesthesia was evaluated according to the presence of significant variations in systolic, diastolic and mean arterial pressures and the heart rate and to the presence of the autonomic nervous system stimulations such as sweating and salivation. Neostigmin 0.07 mg/kg and glycopyrolate 0.01 mg/kg were administered iv to the patients with continuing neuromuscular blockage. If spontaneous ventilation was still inefficient ($\text{ET}_{\text{CO}_2} \geq 45$ mmHg), nalorphine 10 mg IV was given iv. In both groups, the patients received meperidine hydrochloride 50 mg intramuscularly for postoperative analgesia, if needed. Postoperative analgesia was evaluated by VAS (Visual analogue scale : 0-10).

Monitorization

Blood pressure (systolic, diastolic, mean) and heart rates, SpO_2 , Fi_{O_2} , ET_{CO_2} , $\text{ET}_{\text{N}_2\text{O}}$, ET_{AA} (AA : Anaesthetic agent-halothane), and temperature were determined by two monitores (Datascope passport and Datex capnomac ultima).

Blood sampling

Serum PRL levels were measured in venous blood samples at 10 min before induction (BI) (control), 30, 60 min after induction (AI) and 120 minutes after surgery (AS) by the radioimmunoassay kit for the immunoradiometric determination of PRL in serum (IRMA-mat Prolactin Byk-Sangtec Diagnostica GmbH & Co. KG) (Normal values : Male; 35-350 mIU/L, female; 40-470 mIU/L; assay range : 0-8000 mIU/L).

Data analysis

The means and the standard deviations were calculated. In the comparison of patients' characteristics, the duration of anaesthesia, and serum PRL concentrations between the groups, Student's *t* test was applied. PRL levels were statistically evaluated in the same group with analysis of variance test. All statistical analyses were performed by the statistical package for social sciences for Windows V5.01 (SPSS INC., 1989-1992). $p < 0.05$ was considered significant.

RESULTS

There were no significant differences between the groups in terms of patients' characteristics and duration of anaesthesia (Table 1). The changes in haemodynamic variables were within acceptable limits during this study.

Although there were no significant differences, all PRL values of F₁ and F₂ were higher than those of M₁ and M₂. In all groups, it was observed that there was an increase at 30, 60 min after induction and 120 min after surgery, compared with the control values ($p < 0.05$). This was the highest at 30 min in F₂ (4202.2 ± 776.3 mIU/L). In the comparison made among the groups, there was not a difference between group M₁ and group F₁, whereas there were significant differences between group M₂ and group F₂ at 30 and 60 min after induction ($p < 0.05$) (Fig. 1). There were no significant differences between group M₁ and group M₂, group F₁ and group F₂ (Table 2).

DISCUSSION

PRL is a 21500 Dalton single-chain polypeptide neurohormone that is secreted in response to stress and with regulatory effects on the immune system, released in a pulsatile fashion (1).

It is known that females have greater PRL responses to anaesthesia and surgery compared with

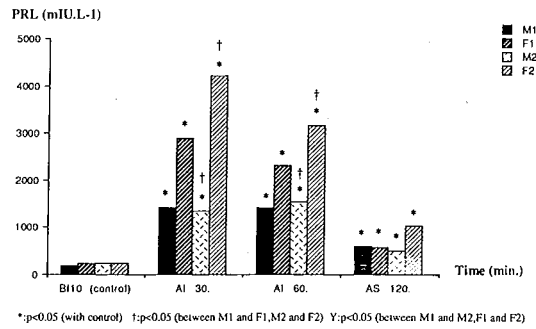


Fig - 1 : Serum PRL levels (values : mean).
M₁: Male-TIVA, F₁: Female-TIVA, M₂: Male-IA, F₂: Female-IA, BI : Before induction, AI : After induction, AS : After surgery.

males (7). It has also been demonstrated that PRL levels are higher in girls than in boys during puberty, due to the higher serum estrogen levels (4). The physiologic role of estrogen in modulating PRL secretion in females has been reported to be unclear because PRL concentrations remain stable throughout the menstrual cycle (9). It has also been reported that the administration of opioid receptor agonists is one of the factors increasing serum PRL levels in males and females, and that opioid regulation of PRL secretion in humans is unclear (4, 5).

	M ₁ (n:10)	F ₁ (n:10)	M ₂ (n:10)	F ₂ (n:10)
age (yr)	49.2 ± 11.8	40.3 ± 14.0	47.7 ± 13.9	43.2 ± 12.9
weight (kg)	68.8 ± 4.4	70.7 ± 14.5	67.5 ± 2.7	68.3 ± 12.1
duration of anaesth. (min)	67.0 ± 4.5	65.7 ± 3.3	66.3 ± 4.6	67.2 ± 3.8

Table 1 : Patients' characteristics and duration of anaesthesia (mean ± SD) (No significant differences).

Time (min)	M ₁ (n:10)	F ₁ (n:10)	M ₂ (n:10)	F ₂ (n:10)
BI 10 (control)	199.7 ± 84.0	241.6 ± 91.7	231.1 ± 112.1	238.7 ± 114.5
AI 30.	1423.5 ± 568.0*	2888.6 ± 2132.9*	1334.5 ± 848.5*†	4202.2 ± 776.3*‡
AI 60.	1411.8 ± 667.8*	2299.0 ± 1391.4*	1545.3 ± 741.0*†	3149.8 ± 1181.4*‡
AS 120.	594.6 ± 210.4*	586.7 ± 430.6*	515.1 ± 308.7*	1034.6 ± 581.5*

* : $p < 0.05$ (significantly higher than their respective control values), † : $p < 0.05$ (between M₁ and F₁, M₂ and F₂).

BI : before induction, AI : After induction, AS : After surgery.

Table 2 : Serum PRL concentrations (mIU/L, mean ± SD).

There are five types of opioid receptors (μ , κ , σ , δ and ϵ). Epsilon receptors show hormonal effect when they are stimulated by β -endorphins. Cairo et al. (2) have suggested modulation by opioids of the GABA-ergic inhibitory action and the involvement of a GABA-ergic mechanism in the regulation of PRL responses. It has been shown that the endogenous opioid peptides are essential in initiating and maintaining daily PRL and their effects are performed by decreasing tuberoinfundibular dopamine neuronal activity (12). According to our findings, the PRL levels were lower in TIVA group receiving alfentanil, which is an opioid, probably because alfentanil was not used in high doses during this study.

Preoperative baseline serum PRL levels were reported to be higher in patients who had their preoperative blood samples taken after inhalation induction as compared to patients who had their preoperative blood samples taken before inhalation induction (13). It has been reported that serum PRL levels increased in both TIVA with propofol-fentanyl or alfentanil and inhalational anaesthesia with isoflurane-nitrous oxide, but this increase in PRL was lower in TIVA (3, 10). This fact could be explained by the effects of inhalation anaesthetic agents (such as halothane and isoflurane) which may increase serum PRL concentrations (8, 13). In our study, PRL levels were higher than those in TIVA, in the groups receiving inhalation anaesthesia.

In conclusion, the increase in PRL levels occurring in response to anaesthesia and surgical stress was higher in females receiving inhalation anaesthesia than that in males receiving inhalation anaesthesia. In TIVA, there was not a difference related to gender in PRL levels. Our opinion is that PRL response depending on stress could be attenuated by TIVA and that TIVA should be preferred especially in hyperprolactinemic female cases.

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