Originals

M. I. Ramos[1]
M. J. Cardoso[1]
F. Vaz[1]
M. D. Torres[2]
F. García[3]
G. Blanco[3]
E. M. González[4]

Influence of the grade of anxiety and level of cortisol on post-surgical recovery

[1] Departamento de Farmacología y Psiquiatría
[2] Departamento de Fisiología
 Facultad de Medicina
 UEx
 Badajoz. Spain

[3] Servicio de Cirugía del Hospital Universitario Infanta Cristina
 SES
 Badajoz. Spain
[4] Centro de Salud Ciudad Jardín
 SES
 Badajoz. Spain

Introduction. The objective is to analyze the influence of several biological and/or psychological factors on post-surgery recovery.

Method. Our sample was made up of 42 inpatients waiting for surgery. The day before the intervention, they filled out Spielbergers' State/Trait Anxiety Inventory (STAI) and a sample of saliva was collected at 8:00 in order to determine cortisol concentration. Recovery was codified as «good» or «poor» using the Moix criteria (1995).

Results. Patients with higher scores on the STAI had higher levels of salivary cortisol and their recovery was worse compared with patients with low anxiety.

Conclusions. Our results confirm the relationship between specific psychological variables, cortisol levels and the characteristics of the surgery recovery process of the patients.

Key words:
Anxiety. Cortisol. Stress. Psychobiology. Surgical recovery.

Influencia del grado de ansiedad y el nivel de cortisol sobre la recuperación posquirúrgica

Introducción. El objetivo es analizar la influencia de diversos factores psicológicos y/o biológicos en la recuperación postoperatoria.

Método. La muestra estuvo compuesta por 42 pacientes hospitalizados para someterse a una intervención quirúrgica. El día previo a la intervención se administró el Test de Ansiedad Estado/Rasgo de Spielberger (STAI) y se tomó una muestra de saliva a las 8:00 para determinar el nivel de cortisol. La variable de recuperación se codificó como «buena» o «mala» en base a los criterios descritos por Moix (1995).

Resultados. Los sujetos que puntuaban de forma elevada en el STAI presentaban un mayor nivel de cortisol en saliva y su recuperación fue peor en comparación con otros pacientes con baja ansiedad.

Conclusiones. Nuestros datos confirman la relación existente entre determinadas variables psicológicas, los valores de cortisol y el proceso de recuperación quirúrgica del paciente.

Palabras clave:
Ansiedad. Cortisol. Estrés. Psicobiología. Recuperación posquirúrgica.

INTRODUCTION

The role of elevated pre-operative anxiety is sufficiently documented by research to be considered as a symptom in all surgical procedures. Thus, its possible influence in different patients and in different surgery protocols must be considered. Pre-operative anxiety has been an intensely studied theme in recent decades[1,2]. Another feature related with pre-operative anxiety is the providing of information to the patient. It has been verified that the visit to the anesthesiologist is more effective than barbituric medication in reducing peri-operative anxiety and post-surgical analgesic requirements[3].

All surgical procedures entail a generalized challenge for the body and acute stress. When faced with stressful situations, the human being mobilizes his/her physiological resources in order to respond to these situations as a reaction or response to stress[4] in which the CNS, endocrine system and immunological system participate. It has been seen that the body releases corticotropin (CRH), inducing the pituitary gland to secrete adrenal corticotropic hormone (ACTH) into circulation when there is a stressful situation. This acts on the level of the cortical area of the adrenal glands, causing glucocorticoid secretion, which has known immuno-suppressant effects[5]. Thus, the response to stress depresses the immune system through hyperactivation of the hypo-

Correspondence:
María Jesús Cardoso Moreno
Departamento de Farmacología y Psiquiatría
Facultad de Medicina de Badajoz
Universidad de Extremadura
Avenida de Elvas, s/n
06071 Badajoz (Spain)
E-mail: Cardoso@us.es

thalamo-pituitary axis, increasing vulnerability to diseases[6] and, consequently, increasing the risk of post-surgical complications. In this context, the general objective of the present work was to identify possible psychobiological factors that could negatively influence the subsequent surgical recovery.

Therefore, this study attempts to evaluate possible psychobiological risk factors that influence the course of the post-operative period by means of a medical intervention protocol to measure it. It is attempted to define the factors that could predict poor post-operative course in regards to days of hospital stay, post-surgery anxiety and complications.

METHOD

Subjects

In this work, patients who were hospitalized and waiting for surgery in the Surgery Department between October 2005 and June 2006 participated voluntarily. The sample was made up of 42 patients (38.10% men and 61.90 women), divided into two age groups based on the Erikson criteria[7]. The first group was called «young», and included subjects whose ages range from 25 to 49 years (45.24%) and the second age group was called «mature», including those patients whose ages range from 50 to 70 years (54.76%). The Mini Mental State Exam[8] was used to verify that none of them had cognitive disorders and it was checked to assure that they had not been previously operated on for the same disease. A total of 52.39% of the patients were operated on for cholecystitis and 46.61% for the resection of a colon or breast tumor. It was also assured that the healthcare team was the same for each disease and that the patients had sufficient information on the surgical procedure.

Evaluation

Anxiety

The anxiety level of the study subjects was evaluated using the State-Trait Anxiety Inventory (STAI)[9]. This is considered to be a useful instrument to study anxiety via means of self-evaluation of two independent concepts of it. The function of this questionnaire is to evaluate Anxiety-State on Anxiety-Trait both in the normal population and in patients from different clinical groups. Anxiety-State (A/E) is defined as a transitory emotional condition characterized by tension, apprehension and hyperactivation of the Autonomic Nervous System. This may vary in intensity and fluctuate over time. The subject answers each item, evaluating it between 0 and 3 according to how he/she feels at the moment. The instructions clarify that some answers are not any more correct than others. The Anxiety-Trait (A/R) is characterized by a stable anxious tendency due to the ten-

dency of the subject to perceive daily situations as threatening. This leads to an increase in the grade of anxiety. In this case, the subject answers each item, scoring them between 0 and 3 according to how he/she feels in general. There are different studies that have verified the reliability and validity of this questionnaire[10,11].

Cortisol

The Coat-A-Count Cortisol Kit was used for the radioimmunoassay of the cortisol levels in saliva. This is a test designed to make a quantitative measurement of the cortisol levels (hydrocortisone, Compound F). The Coat-A-Count procedure is a solid-phase radioimmunoassay in which the I[125] radioactively labeled cortisol competes for the antibody binding sites with the cortisol in the patient's sample during a specific time period. As the antibody was immobilized to the wall of a polypropylene tube, when the supernatant is decanted, it is sufficient to end the competition and to isolate the antibody bound fraction of the labeled cortisol. The tube is counted in a gamma counter and provides a number which, by a calibration curve, becomes a measure of the cortisol present in the patient's sample.

Evaluation procedure

The subjects agreed to participate in the study voluntarily, signing the informed consent. A sample of saliva was obtained the day before the operation at 8 a.m. The patient was asked to rinse his/her mouth and to deposit the saliva in a polypropylene tube having a 5 ml round bottom. It was verified that the patient had not taken any medication that could alter the cortisol levels in saliva. Several studies indicate that cortisol levels fluctuate during the day, and that they are greater during the morning[12,13]. The saliva was conserved at a temperature of –32 °C. Following that, it was centrifuged and analyzed with the immunoassay technique. Then, the patient was administered the State-Trait Anxiety Inventory (STAI). After the surgery, the patient's course was recorded daily using a protocol designed for this study. This protocol included specific features on the recovery of the patients and was based on the follow-up that the nursing staff made and on the Moix described recovery criteria[14]. It was recorded if the patient was correctly nourished, if he/she had pain, rested adequately, had fever or other complications. The «good recovery» group (59.52% of the patients) included those patients who, according to the opinion of the medical team, had no complication after the surgery. The «bad recovery» group (40.48 of the patients) included those subjects who, after the operation, had some type of complication (fever, infection, lack of appetite, sleep difficulty, excessive pain, difference between time estimated for hospital stay and real time of stay). Finally, the State-Trait Anxiety Inventory (STAI) was re-administered on the day on which the patient was discharged.

Data analysis

The data obtained were analyzed using the SPSS program, version 14.0. The statistical techniques used included descriptive ones (arithmetic mean and standard deviation), analysis of the variance (ANOVA) and comparison of groups (Student's t test). The referenced p values in this manuscript correspond to the statistical significance of the Coat-A-Count Cortisol Kit two-tailed tests, considering those values equal to or inferior to a p of 0.05 as significant.

RESULTS

Anxiety

The results indicated that the grade of anxiety decreased after the intervention. The patients had greater scores on the Anxiety-State Questionnaire before the operation (t= 7.83; gl=41; p<0.001) (Anxiety-State before the operation, Mean: 25.80, SD.: 12.74; Anxiety-State after the intervention: Mean: 14.78, SD: 8.54). The Anxiety-Trait was also significantly greater before the operation (t=2.19; gl=41; p= 0.034) (Mean: 20.02; SD: 9.85; Anxiety-Trait after the intervention: Mean: 18.04; SD: 7.92)

Anxiety–cortisol ratio

When we analyzed the cortisol variable, we found that all the values were within normality. Furthermore, we did not find any differences based on gender (t=0.91; gl=41; p =0.369) nor age (young or mature) in the scores of this variable (t=1.47; p=0.148).

After, we checked to see if there was a relationship between cortisol values on the grade of anxiety of the patient. To do so, we divided the scores obtained in the STAI into two groups. The first group, called «elevated anxiety», included patients whose scores on the STAI exceeded the mean of our sample. The second group, called «low anxiety», included patients whose scores on the STAI that were below the mean.

We performed an Analysis of the Variance in which we related the level of cortisol collected in saliva with low anxiety and elevated anxiety groups. We verified that the score obtained on the STAI was related with the cortisol level (State before the operation, F=5.29; gl=41; p=0.040; Trait before the operation, F=8.65, gl=41; p<0.001). The patients of the elevated anxiety group had higher levels of cortisol in saliva than the low anxiety group (table 1).

Anxiety–cortisol–recovery relationship

After, we checked to see if there was any relationship between the levels of anxiety, cortisol values and subse-

Table 1	Data obtained in the Anxiety State–Trait Inventory before and after the operation. Difference of risk and values of p for the Student's t test for related samples

| STAI | Mean (SD) n = 42 | | Risk diference | |
	Before surgery	After surgery	Mean of the difference (95% CI)	p
State	25.80 (12.74)	14.78 (8.54)	11.02 (8.01, 14.24)	0.001
Trait	20.02 (9.85)	18.08 (7.92)	1.94 (0.05, 4.04)	0.034

quent recovery of the patient. The variable «recovery» was listed as good or bad based on the criteria established in previous studies by other authors in which it was recorded if the patient suffered excessive pain, if infection, fever appeared, if the patient rested adequately and was correctly nourished[14].

In order to analyze the data, we performed an Analysis of Variance with three variables. The first variable was called Anxiety and had two levels: «low anxiety» and «high anxiety». The next variable was called recovery and also had two levels: «good recovery» and «bad recovery». The third variable contained the cortisol values obtained by the patients.

We found significant differences in the cortisol level related with anxiety and recovery of the patients (F=5.13; gl =41; p=0.047). The subjects who scored high on the Anxiety-Trait Test had a greater level of cortisol in saliva and their recovery was worse in comparison with those patients who had low anxiety.

Table 2	Levels of cortisol in saliva and anxiety grade. Difference of risk and values of p for the Snedecor's F

| STAI | Mean (SD) n = 42 cortisol (ng/dl) | | Risk difference | |
	High anxiety	Low anxiety	Mean of the difference (95% CI)	p
State	0.33 (0.25) n = 17	0.23 (0.13) n = 250.10	(–0.22. 0.03)	0.001
Trait	0.32 (0.30) n = 12	0.25 (0.14) n = 30	0.07 (–0.21. 0.07)	0.034

| Table 3 | Levels of cortisol based on grade of anxiety recorded in the STAI. Differences between groups of «high anxiety» and «low anxiety» in relationship to cortisol and subsequent recovery of the patient. Difference of risk and values of p for the ANOVA |

STAI	Mean (SD) n = 42 cortisol (ng/dl)		Risk difference
	High anxiety	Low anxiety	Mean of the difference (95% CI)
State (n = 42; p = 0.609)			
Good recovery	0.27 (0.19) n = 11	0.20 (0.12) n = 16	0.07 (–0.20. 0.07)
Bad recovery	0.40 (0.31) n = 7	0.27 (0.15) n = 8	0.13 (–0.22. 0.09)
Trait (n = 42; p = 0.609)			
Good recovery	0.20 (0.18) n = 9	0.24 (0.14) n = 18	–0.04 (–0.10. 0.18)
Bad recovery	0.53 (0.36) n = 4	0.26 (0.14) n = 11	0.27 (–0.54. 0.22)

DISCUSSION

After the administration of the Anxiety State-Trait Inventory (STAI), we found that the patients had greater anxiety before undergoing surgery, thus confirming the data obtained in previous studies[15-18].

The Central Nervous System[19] and of the autonomic[20] and neuroendocrine systems[21] are activated during situations that cause anxiety. These three systems continuously have feedback, that increases, maintains or decreases the activation caused by the anxiety. It has been verified that during a situation of stress, there is an increase of plasma cortisol caused by the activation of the Sympathetic Nervous System and HPA (hypothalamic-pituitary-adrenal)[22]. In turn, an increase of TNF-_ (tumor necrosis factor) has been observed during situations of elevated anxiety.

The possibility of measuring cortisol in saliva has increased the study scope in psychobiological research[23]. Different studies have verified that the cortisol present in saliva is related with free cortisol in blood, representing approximately 10% of that found in the plasma[24]. In our study, the cortisol samples in saliva were collected at 8 a.m., since the secretion of the Hypothalamic-Pituitary-Adrenal axis (HPA) has a circadian rhythm that is related with the sleep-wake periods. This rhythm has its maximum secretion in the early morning just before or at the same time as one gets up. It

slowly decreases during the day and it is at its minimum level before going to sleep.

It has been seen that the cortisol levels in saliva increase in situations of acute stress such as during problem solving or while speaking in public. These changes are relatively short since they may occur in only a few minutes. The magnitude of this increase may be influenced by certain characteristics of the situation such as the difficulty of the task, absence of control or social support received by the subject[25-27]. In additional to the characteristics inherent to the situation, several authors have stressed the influence of psychological variables on the adrenocortical response. The data obtained in our work show a greater level of cortisol in patients with elevated anxiety. These results coincide with previous studies where the coping strategies used by the subject were related with activation of the HPA axis[28-32] Lower activation of the HPA axis has been observed in those subjects who can use effective coping strategies in stress situations. In turn, greater activation of the HPA axis has been found in those persons who are not capable of using coping strategies appropriately[33].

On the other hand, several works have established the objective of studying the harmful effects of a high grade of anxiety on health. Several authors conducted a study to check if the emotional style of the subject has a repercussion on their vulnerability to certain infectious type diseases. The data showed that subjects with a positive emotional study had fewer symptoms related with the disease (common cold) and lower levels of adrenaline, norepinephrine and cortisol[34].

CONCLUSIONS

There are studies which have been able to decrease presurgery anxiety in several ways. In the first group of studies, we found several works that have verified that modifying the infrastructure of the hospital (more park areas, windows, music, etc.) helps to reduce the anxiety grade[35]. Other studies have focused on evaluating how the changes in the hospital routine (greater access of the family, sharing a room with a patient who has already been operated on) help to decrease anxiety and to improve post-surgery recovery[36]. Finally, other strategies that have been used to reduce anxiety are based on adequate psychological support through application of cognitive[37], behavior[38] and informative[39] techniques.

Our results indicate a relationship between psychological factors and vulnerability to disease. The data obtained show worse recovery in those patients who manifest a high grade of Anxiety-Trait before undergoing an operation. Furthermore, we found that the patients who score higher on the Anxiety-Trait scale have higher levels of cortisol in saliva. These data have shown a relationship between anxiety, cortisol and subsequent recover of the patient.

Given the importance of assuring the well-being of the patients when they enter into contact with the health care system, isolating the psychosocial risk factors helps to achieve the general objectives of the current health care system, that is, the approach the patient from an integral point of view in order to improve care quality. New data that repeat these findings are needed to be able to provide all the biological and psychological resources at hand for the patients and to act to positively impact on the surgical procedure.

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