

# Close correlation of cortisol with pain intensity and Aldrete score in immediate post anesthesia period.

George Ntonas<sup>1</sup>, Theofania Vogiatzaki<sup>2</sup>, Charalampos Chatziioakeimidis<sup>1</sup>,  
Pelagia Chloropoulou<sup>2</sup>, Christos Iatrou<sup>2</sup>

<sup>1</sup>General Hospital of Thessaloniki «O Agios Dimitrios», Department of Anesthesiology, Thessaloniki, Greece

<sup>2</sup>Democritus University of Thrace, Department of Anesthesiology, Alexandroupoli, Greece

**ABSTRACT:** *Background:* Few studies have been made on postoperative pain, the patient's stress and Aldrete scale score at the awakening period. In this study we investigated the correlation of the serum cortisol concentration between both pain scale score and Aldrete scale score at the early postoperative period. It is obvious that an Aldrete scale score less than 9, at the awakening, is possible to prolong the surgical patient's staying in Post anesthesia care unit (PACU). Determining of this relation is important in clinical setting.

*Methods:* Twenty five (25) - ASA physical status I, II - patients scheduled, to undergo a medium severity surgery, with general anesthesia were enrolled in this study. The patients received as pre-medication 100mg hydroxyzine (P.O) and 150 mg ranitidine (P.O). Anesthesia was induced with: ondasetron 4mg IV, fentanyl 0.2mg IV, propofol 2mg.kg<sup>-1</sup> IV, cis-atracurium 1mg.kg<sup>-1</sup>IV, midazolam 3mg IV. Anesthesia was maintained with sevoflurane, air, oxygen and remifentanyl -as analgesic factor-. As postoperative analgesia morphine 0.1mg.kg<sup>-1</sup>IV, 30 min before the end of surgery was used. Blood samples were collected at the end of the surgery as well as after the awakening of the patients, and the concentration of serum cortisol was determined.

*Results:* In the samples of the 25 patients, the mean ( $\pm$  SD) concentration of cortisol was 22.13  $\mu$ g/dl ( $\pm$  12.44). The patients Aldrete Scale mean score was 8.52 ( $\pm$  1.15). The range of Aldrete score was 4 (6-10). Also, the mean pain score of patients was 2.88 ( $\pm$  1.64), with range of pain score: 6 (0-6). Nine of the enrolled patients reached a score of 9 at the Aldrete scale and five reached a score of 10 at the Aldrete scale, at the awakening. Patients with Aldrete scale score less than 9, at the awakening, prolonged their staying in PACU from 60 to 165 minutes.

*Conclusion:* There is clearly a positive correlation between the concentration of serum cortisol and Aldrete scale score, at the awakening stage of the surgical patient, but without any statistical significance.

There is a statistically significant positive correlation between the concentration of serum cortisol and the pain scale score.

*Key Words:* Serum cortisol, Anesthesia, Postoperative period, Pain, Aldrete scale score.

## INTRODUCTION

The aftermath of any surgery is that the patient's body is pushed to the edge of its ability to rebound naturally. Stress response to surgery is affected by several factors, including the type of surgery and anesthesia, duration of operation, magnitude of surgical injury and the degree of postoperative pain<sup>1</sup>. Anesthesia may cause the extent of this response to vary. Anxiety, tissue injury and surgical pain are generally considered to be a patented stimulus to adrenocorticotrophic hor-

mone (ACTH) and cortisol secretion<sup>2,3,4</sup>. There are studies that point to an increased cortisol concentration in serum during early postoperative period<sup>5</sup>. Also, neurohumoral, immunologic, and metabolic alterations, differentiate the stress response to surgery and trauma. These metabolic and endocrine derangements lead to adverse effects, including increased oxygen consumption, catabolism and impaired immune function and have been associated with poor postoperative course and clinical outcome<sup>6,7,8</sup>. There are a few gen-

**Table 1.** The Aldrete scale score.

ALDRETE SCALE SCORE		
Activity	Able to move 4 extremities	2
	Able to move 2 extremities	1
	Not moving extremities	0
Circulation/BP	+/- 20% of pre-anesthetic level	2
	+/- 20 - 50 % of pre-anesthetic level	1
	+/- 50% of pre-anesthetic level	0
O <sub>2</sub> Sat	O <sub>2</sub> sat >92%	2
	Needs supplemental O <sub>2</sub> for O <sub>2</sub> sat >92%	1
	O <sub>2</sub> sat <90% with supplemental O <sub>2</sub>	0
Consciousness	Alert, oriented	2
	Arousable by voice	1
	Not responsive	0
Respiration	Able to deep breath & cough	2
	Regular, quiet, adequate	1
	Obstructed, noisy, inadequate	0

eral features that identify patients who will need close attention; these include (Freeley & Macario, 2005; Tarrac, 2006):

Poor ASA status

General (vs Regional ) anesthesia

Prolonged duration of anesthesia (>2 hours)

Abdominal, renal, urologic, orthopaedic, or emergency surgery

The Aldrete Scoring System, or a modified version of it, (Table 1) is a numerical summary technique that is widely used for evaluating the level of recovery of patients after general anesthesia (Ead, 2006). This system, is formulated so that a score of 9/10 or 10/10 suggests the patient is ready for discharge from the Post anaesthesia care unit (PACU).

This study evaluates the correlation between the concentration of serum cortisol, Aldrete score and pain, at the end of surgery after the awakening of the patient.

## PATIENTS AND METHOD

After obtaining approval from the local ethical committee and preparing consent forms to be signed, twenty five (25) - ASA physical status I, II - patients who were scheduled to undergo a medium severity surgery with general anesthesia, were enrolled in this study. The patients received as pre-medication 100 mg hydroxyzine (P.O) and 150 mg ranitidine (P.O). Anesthesia was induced with: ondasetron 4 mg IV, fentanil

0,2 mg IV, propofol 2 mg.kg<sup>-1</sup> IV, cis-atracurium 1mg.kg<sup>-1</sup>IV, midazolam 3 mg IV. Sevoflurane, air, oxygen and remifentanil -as analgesic factor- were used as intraoperative anesthesia. As postoperative analgesia morphine 0.1mg.kg<sup>-1</sup>IV, 30 min before the end of surgery was used.

Blood samples were collected at the end of surgery and after the awakening of the patient and the concentration of cortisol was measured. (The collected samples are stable for five days at 2-8° C, 3 months at -20° C and freeze only once<sup>9</sup>).

The quantitative determination of cortisol was possible with the electro- chemiluminescence immunoassay method «ECLIA». The method makes use of a competition test principle using a polyclonal antibody which is specifically directed against cortisol. Endogenous cortisol in the sample which has been liberated from binding protein with danazol competes with exogenous cortisol derivative in the test which has been labelled with ruthenium complex for the binding sites on the biotinylated antibody<sup>10,11</sup>.

The statistic analysis was based on SPSS. Data were presented as mean ± SD. Normal distribution of the values was tested with the Kolmogorov-Smirnof test (p = 0.507).

The sample of the concentration of cortisol is not homogeneous (p = 0.56). Also, the Aldrete scale score is a sample that is not homogeneous (p = 0.56) and similar results were found for the pain score

**Table 2.** The correlation rate between the amount of serum cortisol ( $\mu\text{g}/\text{dl}$ ) and Aldrete scale.

	Aldrete scale
Correlation rate	0.009
p-Value	0.965
N	25

**Table 3.** The correlation rate between the amount of serum cortisol ( $\mu\text{g}/\text{ml}$ ) and Pain scale.

	Pain score	
Correlation rate	0.21	
P-value	0.07*	

( $p = 0.13$ ). The Pearson-correlation analysis was used to estimate the correlations between the concentration of cortisol, the Aldrete scale score and the pain score. The t-test analysis was used to evaluate the statistic significance of the fluctuations of parameters.

**RESULTS**

In the samples of the 25 enrolled patients, the concentration of cortisol was  $22.13 \mu\text{g}.\text{dl}^{-1} (\pm 12.44)$ . The patients' Aldrete Scale score was  $8.52 (\pm 1.15)$ . The range of Aldrete score was: 4 (6-10). Also, the mean pain score of patients was  $2.88 (\pm 1.64)$ , with a range of 0-6.

There is a positive correlation between the concentration of cortisol and the Aldrete scale score (Figure 1), but it is not statistically significant (Table 2).

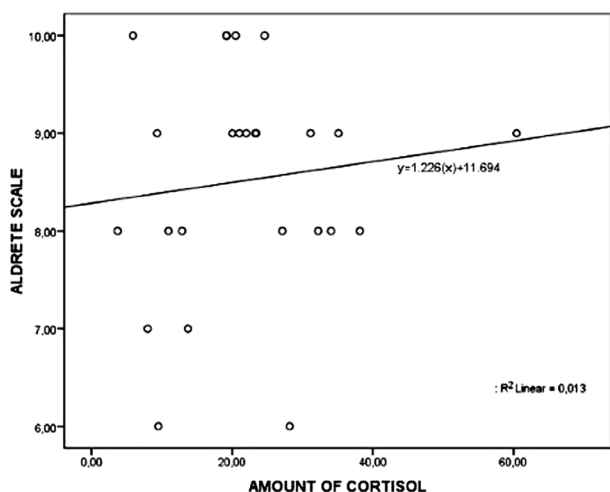
The present study proved that there is a positive correlation between the concentration of cortisol and the Pain scale score (Figure 2), and this result is statistically significant ( $p \leq 0.1$ ) (Table 3).

Nine of the enrolled patients reached a score of 9 (Table 4) and 5 patients reached a score of 10 at the Aldrete scale, at the awakening (Figure 3). Patients with Aldrete scale score less than 9, at the awakening, prolonged their staying in PACU from 60 to 165 minutes (Table 5).

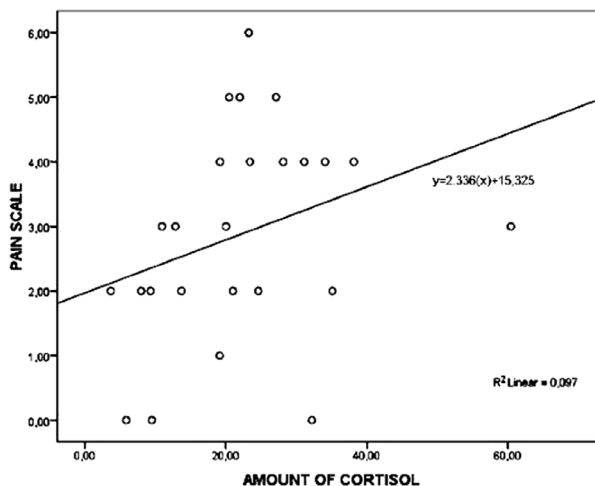
As regards pain score values, the data show that 3 patients succeeded 0 on the 10-point pain scale score, 1 patient had 1 point, 7 patients with 2 points, 4 patients with 3 points, 6 patients with 4 points, 3 patients with 5 points and 1 patient reached 6 points at the awakening (Figure 4) and (Table 6).

**DISCUSSION**

The present study has shown a positive correlation between cortisol and post operative pain, after the awakening of the surgical patient. In fact, cortisol secretion increases rapidly following the start of surgery as a result of the adrenal cortex stimulation by ACTH. A feedback mechanism operates so that increased con-



**Figure 1.** The correlation between the amount of serum cortisol ( $\mu\text{g}/\text{dl}$ ) and Aldrete scale score.



**Figure 2.** The correlation between the amount of serum cortisol ( $\mu\text{g}/\text{dl}$ ) and Pain scale score.

**Table 4.** The frequency and the percent frequency of Aldrete scale score.

**ALDRETE SCALE**

Valid	Frequency	Percent (%)
6	2	8
7	2	8
8	7	28
9	9	36
10	5	20
Total	25	100

**Table 5.** The Aldrete scale score and the time of staying in PACU.

**ALDRETE SCALE SCORE - TIME OF STAYING IN PACU (min)**

Valid	Frequency	Time of staying in PACU (min)	Percent (%)
6	2	150-165	8
7	2	110-120	8
8	7	60-90	28
9	9	40-60	36
10	5	30-45	20
Total	25		100

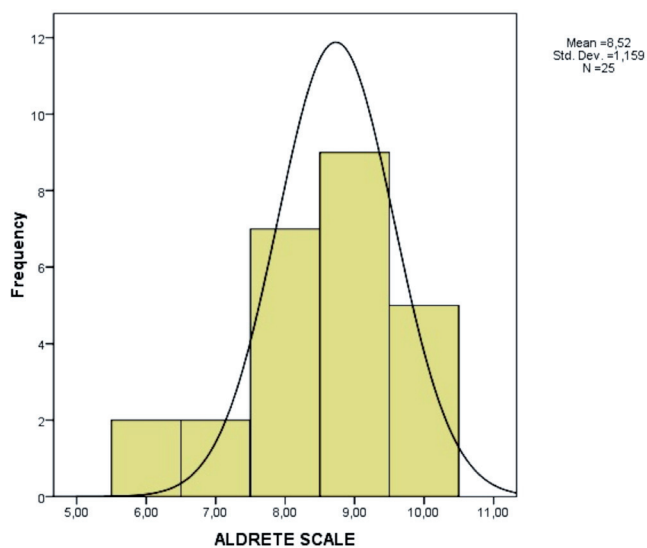
centrations of circulating cortisol inhibit further secretion of ACTH. It appears that surgery renders this control mechanism ineffective so that concentrations of both hormones remain high.

Anesthetic interventions can modify the cortisol response. Marana et al found that, when compared to isoflurane, sevoflurane decreased cortisol release thus increasing stress response to laparoscopic surgery<sup>12</sup>. Several studies concluded that deep anesthesia is related with less postoperative pain and smaller consumption of analgesics. Studies also reveal that the deeper anesthetic level, which is succeeded by higher concentration of sevoflurane, could influence the in-

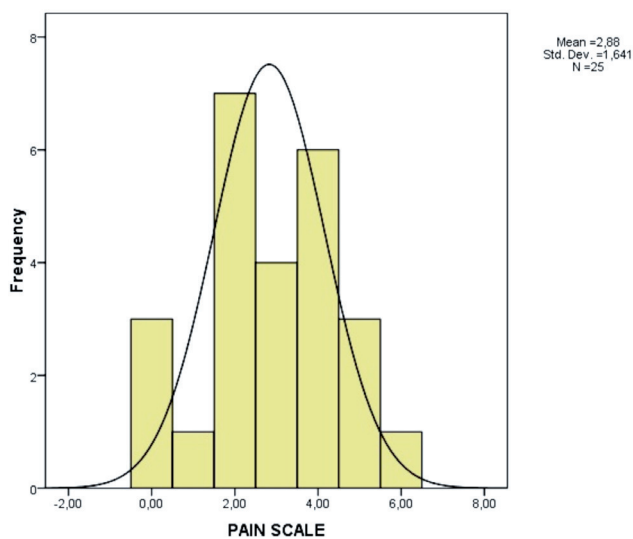
tensity of postoperative pain.

On the other hand, Baldini et al. using desflurane suggested that anesthetic depth has no impact on perioperative cortisol levels during pelvic surgery and, therefore, to the metabolic response to surgery<sup>13,14</sup>. Similar postoperative morphine consumption and VAS scores regardless of light or deep anesthesia was also reported in the same study.

Le Blanc-Louvry I, Coquerel A, Koning E, et al. refer in their study have found out that postoperative pain levels are associated with cortisol concentration, suggesting the importance of hormones in functional recovery postoperatively. In addition the results of an-



**Figure 3.** Histogram that shows the frequency of Aldrete scale values.



**Figure 4.** Histogram that shows the frequency of Pain scale values.

**Table 6.** The frequency and the percent frequency of Pain scale score.

PAIN SCALE		
Valid	Frequency	Percent (%)
0	3	12
1	1	4
2	7	28
3	4	16
4	6	24
5	3	12
6	1	4
Total	25	100

other study indicated that preoperative anxiety may play a critical role in the chain-of-events that controls the postoperative pain response<sup>15,16</sup>.

All the patients were transferred from the PACU, when they reached a score of 9 or higher on the 10-point modified Aldrete scale which, among other parameters, also provides a rough evaluation of mental state. As the present study demonstrated, 9 patients reached a score of 9 at the Aldrete scale (~36% of the patients) and 5 patients reached a score of 10 at the Aldrete scale (~20% of the patients). These scores are achieved at the awakening of the surgical patients. Other patients with an Aldrete scale score less than 9 at the awakening, prolonged their staying in PACU from 60 to 165 minutes (Table 5).

This study demonstrates a positive correlation between the concentration of serum cortisol and Aldrete scale score, at the awakening of surgical patient, without showing any statistical significance.

J-Y Hong, Y. S. Kang, and H. K. Kil in their study in 2008, revealed that total intravenous anesthesia (TIVA) with propofol-remifentanyl brought a quicker emergence with less nausea and vomiting, in day case surgical patients, than anesthesia with sevoflurane – N<sub>2</sub>O. Although, there was less postoperative pain in the sevoflurane-N<sub>2</sub>O group and there were no differences in the perioperative cortisol responses in the two anaesthetic techniques<sup>17</sup>.

Jensen Kenneth, Kehlet Henrik, Lund Claus M, on 2009, concluded that postoperative pain and oxygen requirements (to sustain a SpO<sub>2</sub> > 92%) are the major

determinants for the length of the stay in the post anaesthesia care unit<sup>18</sup>.

The estimation of Aldrete scale score includes at first the determination of SpO<sub>2</sub>, blood pressure, consciousness, heart rate and leg movements.

In the present study it is clearly demonstrated that there is a non statistically significant, positive correlation between the concentration of serum cortisol and the Aldrete scale score, at the awakening of surgical patient. The correlation between serum cortisol and each of the above parameters included in the Aldrete scale score, remain to be estimated in the future.

Further long-term studies related to the influence of the Aldrete scale score, its parameters and pain on cortisol secretion, are required to detect whether, as we believe, this relation is important in clinical setting.

## CONCLUSIONS

The results show that there is a positive correlation between the concentration of serum cortisol and Aldrete scale score, at the awakening of surgical patient, without any statistical significance.

In addition, there is a statistically significant positive correlation between the concentration of serum cortisol and the pain scale score.

## Συσχέτιση της κορτιζόλης με την ένταση του πόνου και την κλίμακα Aldrete στην άμεση μεταναισθητική περίοδο.

Γεώργιος Ντόνας<sup>1</sup>, Θεοφανία Βογιατζάκη<sup>2</sup>, Χαράλαμπος Χατηιωακειμίδης<sup>1</sup>, Χρήστος Ιατρού<sup>2</sup>

<sup>1</sup>Γενικό Νοσοκομείο Θεσσαλονίκης «Ο Άγιος Δημήτριος», Αναισθησιολογικό Τμήμα, Θεσσαλονίκη, Ελλάδα

<sup>2</sup>Δημοκρίτειο Πανεπιστήμιο Θράκης, Αναισθησιολογικό Τμήμα, Αλεξανδρούπολη, Ελλάδα

**ΠΕΡΙΛΗΨΗ:** Στην παρούσα εργασία μελετάται η διακύμανση της συγκέντρωσης της κορτιζόλης του ορού σε σχέση με τον πόνο και τη κλίμακα Aldrete, στην άμεση μετεγχειρητική περίοδο, σε ασθενείς που υποβλήθηκαν σε γενική αναισθησία. Παρατηρήθηκε ότι ασθενείς με Aldrete scale score μικρότερο του 9, κατά την άμεση μετεγχειρητική περίοδο, έχουν ανάγκη από επιμήκυνση της παραμονής τους στη Μονάδα Μεταναισθητικής Φροντίδας. Στη μελέτη μας περιελήφθησαν 25 ασθενείς που υποβλήθηκαν σε μέσης βαρύτητας επεμβάσεις, με γενική αναισθησία. Για τη μετεγχειρητική αναλγησία χορηγήθηκε μορφίνη 0,1 mg/kg iv. Μετρήσεις της συγκέντρωσης κορτιζόλης πραγματοποιήθηκαν αμέσως μετά την αφύπνιση των ασθενών. Η μέση συγκέντρωση της κορτιζόλης είναι 22,13μg/dl ( $\pm$  12,44), η μέση τιμή της κλίμακας Aldrete είναι 8,52 ( $\pm$  1,15) καθώς και η μέση τιμή που καταγράφηκε στη δεκάβαθμη κλίμακα του πόνου είναι 2,88 ( $\pm$  1,64). Παρατηρήθηκε ότι υπάρχει θετική συσχέτιση μεταξύ της συγκέντρωσης της κορτιζόλης και της κλίμακας Aldrete, καθώς επίσης διαπιστώθηκε στατιστικά σημαντική θετική συσχέτιση μεταξύ του πόνου και της συγκέντρωσης κορτιζόλης.

*Λέξεις Κλειδιά:* Κορτιζόλη ορού, αναισθησία, Μετεγχειρητική περίοδος, Πόνος, Κλίμακα Aldrete.

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