

Evaluation of breathing exercise in hormonal and immunological responses in patients undergoing abdominal surgery¹

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ABSTRACT

PURPOSE: To evaluate the effects of sustained deep inspiration in the prevention of postoperative pulmonary complications, the hormonal and immunological responses in patients submitted to abdominal surgery.

METHODS: This randomized clinical trial study included 75 patients submitted to abdominal surgery, of which 36 were randomly allocated in the experimental group and underwent sustained deep inspiration during five seconds, in three sets of ten repetitions per day. The others 39 patients were allocated in the control group and were not submitted to any breathing exercise. The following parameters were measured preoperatively, 24h and 48h postoperatively: chest x-ray, serum ACTH, cortisol, IL-4, IL-10, TNF- α , forced expiratory volume in first second (FEV1), forced expiratory flow 25-75% (FEF 25-75), forced vital capacity (FVC), paO_2 and $paCO_2$.

RESULTS: Mean serum cortisol in patients of the experimental and control groups before surgery were 12.8 mcg/dl (4.6-50) and 10.48 mcg/dl (1-29.1), respectively ($p=0.414$). The experimental group had significantly increase in serum cortisol levels, 23.6 mcg/dl (9.3-45.8), especially 24h postoperatively ($p=0.049$).

CONCLUSION: Sustained deep inspiration in patients submitted to abdominal surgery determined important changes in serum cortisol, however, without significantly influence the postoperative pulmonary complications and the endocrine and immune responses.

Key words: Physical Therapy Modalities. Surgery. Hormones. Cytokines.

Introduction

Patients submitted to surgery of the upper abdomen usually develop reductions in lungs' volume and capacity of about 40% to 60%¹. These changes may provide a series of postoperative pulmonary complications, which are the main cause of morbidity and mortality, and may be aggravated by metabolic and immunological changes in response to surgical and anesthetic trauma^{2,3}.

In an attempt to reduce postoperative complications such as atelectasis and pneumonia, some authors have sought to provide staging lung physiotherapy techniques such as sustained deep inspiration. These breathing exercises can improve alveolar ventilation, oxygenation, favouring the removal of secretions, and also maximize exercise tolerance and decrease oxygen consumption^{4,6}. Silva *et al.*⁷ reported the use sustained deep inspiration respiratory pattern is described as the best method of prevention and treatment of postoperative pulmonary complications, as it generates an adequate trans-pulmonary pressure gradient. Olsen *et al.*⁸ found that prophylactic respiratory physiotherapy reduces pulmonary complications and improves the mobilization and oxygen saturation after surgery.

The technique of sustained deep breathing can clinically prevent postoperative pulmonary complications due to laparotomy or laparoscopic surgical procedures, which may also alter hormonal and immune responses. Thus, this study sought to evaluate the effectiveness of sustained deep inspiration in the prevention of postoperative pulmonary complications, as well as the hormonal and immune responses induced in patients undergoing surgery of the upper abdomen.

Methods

A randomized clinical trial was conducted by the team of Digestive Surgery of the Federal University of Triangulo Mineiro Hospital, Uberaba-MG. The study was reviewed and approved by the Ethics Committee of the Federal University of Triangulo Mineiro (Protocol No. 571). In addition, each patient provided signed informed consent after being informed, pursuant to resolution 196/96 of the National Health.

The inclusion criteria for this study were patients undergoing elective surgery of the upper abdomen, aged over 18 year and lucid. Exclusion criteria were patients with endocrine diseases, acute or chronic pulmonary disease, altered level of consciousness and refusal to the proposed therapeutics.

The study group consisted of 75 adult patients, which

were randomized in two groups: the experimental group, which was submitted to sustained deep inspiration exercises, and consisted of 36 patients, 17 (47%) male and 19 (53%) female; and the control group, which was not submitted to any kind of respiratory exercise, composed of 39 patients, 15 (38.5%) male and 24 (61.5%) female.

Preoperatively each patient underwent complete medical evaluation including history, physical examination and chest radiography and was also submitted to spirometry tests, hormones and cytokines dosages.

Sustained deep inspiration

The sustained deep inspiration was performed slowly by the nasal route, until reaching the maximum inspiratory capacity, and then this capacity was maintained for five seconds, this procedure was performed in three sets of ten repetitions, once a day. These exercises were performed preoperatively (24h before surgery), 24h and 48h postoperatively.

Pulmonary evaluation

Spirometry was performed by digital spirometer (MS-11- Medicor, Budapest). This procedure is considered in clinical practice as the basic pulmonary function test. Through this examination were obtained: forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and forced expiratory flow (FEF 25-75). Spirometry characterizes two basic types of respiratory disorders: restrictive (reduced vital capacity and FEV1/FVC ratio) and obstructive (normal or reduced vital capacity by FEV1/FVC).

Laboratory evaluation

Blood collection was performed 24h preoperatively, 24h and 48h postoperatively. The dosages of hormones (ACTH and cortisol) and cytokines (TNF- α , IFN- γ , IL-4, IL-10) were obtained in serum after clot retraction and centrifuging 10ml of venous blood taken from the upper limb of the patients. The serum was kept at -70°C and all measurements made at the same time.

Hormones and cytokines dosages

ACTH and cortisol were measured by chemiluminescence with commercial kits (Immunolite). The dosages of cytokines TNF- α , IFN- γ , IL-4 and IL-10 were performed with commercial

kits (R&D Systems, Billings, USA) by ELISA, with a detection limit of 10pg/mL for each cytokine. The results were determined by the difference between the absorbances obtained at 405nm and measure of automatic ELISA reader (BIORAD 2550 READER EIA).

Statistical analysis

It was performed a descriptive analysis of data, in which the numerical variables were submitted to descriptive measures of centrality (mean and median), dispersion (minimum, maximum and standard deviation) and normality by Kolmogorov-Smirnov test. For categorical variables, we obtained simple absolute and percentage frequencies.

To compare the numerical data obtained were used for parametric Student t test and nonparametric Mann-Whitney test.

In the study of association between categorical variables we used simple frequencies and non-parametric tests of association such as chi-square and Fisher exact test. The significance level for all tests was 5% ($\alpha = 0.05$).

Results

Spirometric results showed that the median values of forced vital capacity (FVC) were 70L/s (37-95) and 69L/s (41-85), respectively in the experimental and control groups, preoperatively. 48h postoperatively, the medians were 33L/s (12-64) and 27L/s (18-49), respectively in the experimental and control groups. There was no significant statistical difference when comparing FVC obtained in both groups at any moment.

The median forced expiratory volume in one second (FEV1) were 67,5L/s (7-106) and 64L/s (12-101) in the experimental and control groups preoperatively. 48h postoperatively, the median was 53L/s (22-86) and 43L/s (19-72), in the experimental and control groups, respectively. At this time, a decrease in FEV1 values, was observed in the experimental group, when compared to the control group, though it was not statistically significant. The median forced expiratory flow (FEF 25-75) of the subjects were 73L/s (14-155) and 78L/s (22-206) in both groups preoperatively and 64,5L/s (20-120) and 53L/s (13-93) after 48h postoperatively respectively. Also, a decrease in FEF 25-75 values, was observed in the experimental group, when compared to the control group, though it was not statistically significant.

Regarding the serum ACTH, the median value of the subjects were 11pg/ml (10 to 58.8) and 10pg/ml (10 to 59.1) in the experimental and control groups preoperatively, respectively. 24h

postoperatively, the medians were 10pg/ml (10 to 41.7) and 10pg/ml (10 to 61.1) and 48h postoperatively was 10pg/ml (10-38.3) and 10pg/ml (10 to 24.5) in the experimental and control groups, respectively. There was no statistically significant difference in the values of serum ACTH levels between the analysed periods.

The median serum cortisol of the patients were 12,8mcg/dl (4.6 to 50) and 10.4mcg/dl (1 to 29.1) in the experimental and control groups, preoperatively. 24h postoperatively, the medians were 23.6 mcg/dl (9.3 to 45.8) and 17.5mcg/dl (3.2 to 30) and 48h postoperatively, these medians were 22,5mcg/dl (9.6 to 43.7) and 15.4mcg/dl (7.8 to 33), in the experimental and control groups, respectively. There was statistically significant difference in serum cortisol levels 24h postoperatively, as it increased in the experimental group compared to the control group ($p=0.049$).

The median serum IL-4 levels of the patients were 16pg/ml (1-187) and 13pg/ml (1-427) in the experimental and control groups, preoperatively. 24h postoperatively, the medians were 1pg/ml (1-183) and 4.2pg/ml (0-418) and 48h postoperatively the values were 1pg/ml (1-109) and 13.6pg/ml (1-467) in the experimental group and control respectively. No statistically significant difference in the values of serum IL-4 levels between the analysed periods.

The median serum IL-10 levels of the individuals were 1pg/ml (0-3120) and 8.9pg/ml (0-6420), the experimental and control groups, preoperatively. 24h postoperatively, the medians were 1pg/ml (1-2380) and 48.4pg/ml (1-5630) and 48h postoperatively the values were 1pg/ml (1-1460) and 1pg/ml (0-1110), respectively. No statistically significant difference in the values of serum IL-10 levels between the analysed periods.

The median serum TNF- α of the subjects were 217pg/ml (1-768) and 313pg/ml (1-1200), in the experimental and control groups preoperatively 24h postoperatively the values were 343,5pg/ml (73-1300) and 213pg/ml (61-1470) and 48h postoperatively the medians were 322pg/ml (61-1620) and 196,5pg/ml (0-1390) in the experimental and control groups. No statistically significant difference in the values of serum TNF- α levels between the analysed periods.

Regarding the gasometry evaluation, the median values of paO_2 were 81mmHg (69-26) and 78mmHg (64-206) preoperatively in the experimental and control groups respectively. 48h postoperatively, the medians were 74mmHg (60-85) and 79mmHg (52-108), respectively. The median $PaCO_2$ of the participants were 31.7mmHg (22-38.7) and 35.85mmHg (33-39) in the study group, preoperatively and 48h postoperatively respectively. In the control group median values were 26.1mmHg (10.4-39) and 32.6 mmHg (28.4-39), preoperatively and 48h postoperatively respectively.

There was no statistically significant difference in any time within and between groups.

Of the 36 patients in the experimental group, 2 (5.6%) had radiographic changes, one (2.8%) pneumonia and another atelectasis (2.8%) and among the 39 control patients, six (15.4%) had abnormal chest radiography, four (10.3%) had pneumonia and two (5.1%) had atelectasis. The percentage of pulmonary complications was higher in the control group who did not perform sustained deep inspiration, but there was no statistical significance ($p = 0.362$).

Discussion

The respiratory muscle dysfunction induced by surgery of the upper abdomen and the anesthesia, has implicated the development of postoperative pulmonary complications such as atelectasis, resulting in increased morbidity and hospital stay⁹.

The respiratory physiotherapy contributes to early recovery of pulmonary function and muscle strength in patients submitted to abdominal surgery and may be indicated in the treatment or prevention of postoperative pulmonary complications¹⁰.

Gastaldi *et al.*¹¹ observed that the mean values of VC, FVC and forced expiratory volume in one second (FEV1) in the group submitted to the breathing exercises had a significant decrease only in first day postoperatively ($p < 0.05$), whereas in group control, these reductions remained until the fifth postoperative day ($p < 0.05$). The FEV1/FVC ratio had no statistically significant difference in either group.

Our study agrees with these results, since there were no statistically significant differences in the values of FEV1/FVC in the experimental group and control group. However, a less significant decrease was observed in FEV1 in the experimental group, 48h postoperatively, when compared to the control group, but without statistical significance.

Maciel *et al.*¹² reported a significant difference in the values of the FEF 25-75 in the group submitted to sustained deep inspiration exercises in relation to the control group. In our study, no significant difference in the values of the FEF 25-75 were found, although FEF 25-75 in the 48h postoperatively decreased less in the patients submitted to sustained deep inspiration exercises, when compared to the control group.

Cytokines and stress hormones are major mediators of inflammation and trauma response. Measurement of surgical stress, through its dosages is a valid predictor and has been used for comparative analysis in various surgical procedures^{13,14}.

There were no variations in serum ACTH levels between the patients of the experimental and control groups in the preoperative and postoperative periods. Crema *et al.*¹⁵ analyzed plasma levels of ACTH in the immediate postoperative period in patients who were submitted to cholecystectomy. The authors reported a significant increase in the periods 2-6h after surgery in patients undergoing open cholecystectomy compared to the group submitted to laparoscopic surgery, no significant difference was observed 12 and 24h postoperatively. Bisinoto *et al.*¹⁶ analysed the endocrine response in 30 patients undergoing cholecystectomy, comparing conventional and laparoscopic techniques. Plasmatic concentrations of ACTH showed a significant difference after extubation and 12h postoperatively, in the conventional group, and only 12h postoperatively in the group submitted to laparoscopy.

In this study, we detected a significant increase in plasma cortisol levels 24 postoperatively in the experimental group. This change may be related to a lower incidence of postoperative pulmonary complications in patients undergoing sustained deep inspiration, especially due to cortisol anti-inflammatory role¹⁷. Though, other studies reported a significant increase in cortisol postoperatively in both groups independently of the procedure performed¹⁵.

Cytokines differ from endocrine hormones because are produced by different cell types and exert most of their effects locally or through "cell to cell" communication. Cytokines may also trigger beneficial biological responses, such as stimulation function antimicrobial, wound healing and mobilization of substrates. However, the abundant secretion of cytokines is associated with detrimental effects such as hypotension, organ failure and death^{18,19}.

Regarding the cytokines expression, this study observed a reduction in the amounts of IL-4 and IL-10 after 24h and 48h postoperatively in the experimental group, but none statistical significant difference in serum levels of IL-4, IL-10 and TNF- α was found between groups, when comparing the preoperative, the 24h and 48h postoperative periods.

Other studies compared the levels of IL-10 and TNF- α in patients undergoing laparoscopic and open cholecystectomy, but none significant difference between groups was found, although they reported that the expression of proinflammatory cytokines is lower in the group patients undergoing laparotomy.

Brume *et al.*²⁰ analysed the expression of several cytokines and reported that the production of IFN- γ , TNF- α , and IL-2 by T cells was significantly decreased 48.3%, 36.6% and 36.8%, respectively, on the first day postoperatively of conventional cholecystectomy, but not after laparoscopic technique. These

results indicate severe suppression of T_h1-type cytokines after open surgery. In contrast, IL-4 and IL-10 showed no significant changes in both groups, suggesting that the response of T_h2 cells and anti-inflammatory activity remained normal.

Schwenk *et al.*²¹ analysing IL-10 serum levels, found no significant differences in the expression of this cytokine in patients undergoing open and laparoscopic surgery. However, Torres *et al.*²² observed increased expression of IL-10 in the postoperative of patients undergoing laparotomy.

Few trustable data about the dosages of hormones and cytokines, comparing the techniques of surgical laparotomy or laparoscopy in patients undergoing sustained deep inspiration is available in the current literature. Based on the results of this study conclude that the experimental group showed increased levels of serum cortisol postoperatively in patients submitted to surgery in the upper abdomen. The increase in these levels may have occurred because this group has presented a larger number of patients undergoing laparotomy; however these results did not influence significantly the incidence of postoperative pulmonary complications and/or other hormonal and immunological responses.

Conclusions

The sustained deep inspiration exercises may have contributed to control a further increase in cortisol levels, because the exercise avoided a deficit in pulmonary function and consequently a more intense response to the stress caused by surgical trauma.

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