Study of the brain natriuretic peptide in blood plasma after pneumonectomy and its role as a predictor of post-operative complications

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ABSTRACT

The brain natriuretic peptide (BNP) is a peptide responsible for the homeostasis of the cardiovascular system. In this study, the kinetics of BNP blood plasma levels after pneumonectomy, where certain hemodynamic alterations do occur were analyzed and a possible predictive value of postoperative complications is examined. Thirty-five patients enrolled, underwent a scheduled pneumonectomy for non-small cell cancer of the lung. The BNP plasma levels were recorded pre-operatively, immediately after the ligation of pulmonary artery, at 3, and at 24 hours post-operatively. The collected data were analyzed with descriptive statistical analysis, using students t-test, Chi-square, ANOVA, and Pearson’s correlation coefficient. The differences considered significant at p<0.05. BNP showed a statistically significant increase after the ligation of the pulmonary artery in all of the patients. The patients were divided into 2 groups according to the presence or not of the complications. In the complications group the BNP increase was significantly greater than in the non-complication group. There was direct correlation of BNP value at 24 hours post-operatively and the occurrence of complications. The cut-off value was set at 100 pgr/ml (sensitivity 91.6% and specificity 93.75%). Pre-operatively BNP values above 15 pgr/ml have 17.41% probability for a complication to occur (60% sensitivity and 70.83% specificity). The results of the study of the BNP after pneumonectomy are interesting and are in the path of a safety and economical routine clinical use for the prediction and prevention of post-operative complications.

INTRODUCTION

The brain natriuretic peptide (BNP) is one of the regulator hormones for the homeostasis of the circulatory system, secreted from the cardiac chambers, in response to increased mechanical stretch and ischemia, affecting the intravascular volume, the osmosis, and the arterial pressure.1-3 After pneumonectomy, there is an increase of the BNP due to the consequent hemodynamic changes and no to myocardial damage. It is examined if the kinetics of plasma BMP may have a clinical value in predicting the postoperative complications.

MATERIALS AND METHODS

Thirty-five (N=35) patients enrolled in this study, all with bronchogenic carcinoma that underwent scheduled pneumonectomy. The operations performed by the same operating team at the time period from September 2008 to July 2014 in METAXA Cancer Hospital of Piraeus in Greece. The scientific committee of the hospital approved the ethical and scientific entity of this study and all of the patients had signed a consent form.

The inclusion criteria for the patients to this study were pre-operative FEV(1) ≥80%, predicted postoperative FEV1 ≥1000ml, normal thyroid and renal function, pulmonary artery pressure <30 mmHg, and left ventricle ejection fraction ≥50%. Patients who were not met the above criteria or with chronic obstructive pulmonary disease, restrictive pulmonary disease, chronic inflammatory lung disease, abnormal thyroid hormones, congestive heart failure and / or with a known history of coronary artery disease were excluded from the study.

The BNP measured in the plasma preoperatively, immediately after the ligation of the pulmonary artery, at 3rd and at 24th post-operative hours. The collected data were analyzed with descriptive statistical analysis, using students t-test, Chi-square, ANOVA, and Pearson’s correlation coefficient. The differences considered significant at p <0.05.

Twenty-eight patients were men and seven women of age 64.51 (SD 8.4, min=46, max=85, median=66) years and of average BSA 1.99 (min=1.75, max=2.31). Twenty (57%) left and 15 (43%) right pneumonectomies performed. The mean operation time was 140 (SD 30) min, the amount of fluid given during operation were 1.5 (SD 0.5) liters. Postoperatively all
the patients had intravenous crystalloid fluids for 24 hours at a maximum of 15 ml/kg/h. The analgesia of the patients was kept at a similar subjective level with morphine.

RESULTS
The average preoperative BNP value was 17.51 pgr/ml. The average preoperative pulmonary artery pressure (PaP) was 18.77 (SD 5.7, min=10, max=28), and the preoperative heart’s left ventricle average ejection fraction (EF) was 59% (SD 5.2%, min=45%, max=65%). There was no correlation between the pre-operative BNP and the body surface area (r=0.009).

The BNP was significantly increased in all of the patients by 105.33 pgr/ml, (p=4.9E-11) thus, the average postoperative BNP value at 24 hours was 119.7 pgr/ml. The pulmonary artery pressure value significantly increased at 24 hours postoperatively by 3.74 mmHg, average PaP value was 23.22 mmHg (p=4-E11).

The patients were divided into two groups according to the presence or not of postoperative complications. Twenty-three patients (66%) had not postoperative complications (Group A) while, twelve patients (34%) had (Group B). In both groups, the BNP value was significantly increased from the pre-operative value through the postoperative value at 24 hours, Group A (p<0.00001), Group B (p<0.000033).

Three post-operative complications were recorded, after postoperative day 2 and during hospitalization; these were atrial fibrillation (AF, n=12), post-pneumonectomy pulmonary edema (PPE, n=1), and bronchopulmonary fistula (BF, n=3). The incidences of these complications were AF 34%, BF 9%, and PPE 3%. The patient with PPE died. The overall mortality was 3%.

In Group A, the total BNP value was increased by 81.45 pgr/ml, average BNP value at 24 hours was 93.04 pgr/ml. The BNP value was significantly increasing from the pre-operative to peri-operative and to post-operative (at 3 hours) values (p= 0.034, p=0.0063, p=0.0038, respectively). The average PaP was increased by 1.91 mmHg (p=0.04).

In Group B, the total BNP value was increased by 151.1 pgr/ml. The increasing of the BNP value between the pre-operative and the peri-operative was not significant (p=0.129), while there was a significant increase between the peri-operative and post-operative at 3 hours values (p=0.0006). The average post-operative BNP value at 24 hours was 170.8 pgr/ml. The PAP value was also significantly increased more than in Group A, by 7.253 mmHg (p=0.0019).

There was an obvious difference in the increasing of the BNP value between the two Groups, with the greater increase in Group B (p=0.002). Moreover, the patients with right pneumonectomy, had more, though insignificant, complications than the patients with the left (p=0.49). The difference of the pre-operative BNP values between the two groups was insignificant (p=0.12).

At 24 hours and before the clinical appearance of any of the recorded complications, in Group A, 30% of the patients (n=7) had BNP above 100 pgr/ml, (min=106 pgr/ml, max=150.6 pgr/ml, median=90 pgr/ml); while in Group B, 11 (92%) patients had BNP values above 100 pgr/ml (min=113.9 pgr/ml, max=280.9 pgr/ml, median=170 pgr/ml). The question was if BNP value above 100 pgr/ml can be set as a threshold value (p=0.000581). In this relatively small number of patients this value at 24 hours post-operatively, was set at 113 pgr/ml (p=0.000581). The sensitivity of this value was 91.6% and the specificity was 93.75%. At 3 hours post-operatively the sensitivity and the specificity were 33.3% and 68.42%, respectively. While, if at the three hours post-operatively, the cutoff value was set at 60 pgr/ml, then the sensitivity and specificity were 83.3 % and 81.48%, respectively. In the pre-operative BNP plasma level, the value 15 pgr/ml has 17.14% probability with 60% sensitivity and 70.83% specificity, for the occurrence of post-operative complications.

Definitively, in Group B, the BNP values at 24 hours post-operative were significantly higher than those of Group A (p=0.00075). There was a very weak correlation of the higher pre-operative BNP value and the severity of post-operative complications (R=0.145). On the contrary, there was a strong correlation of the post-operative BNP value at 24 hours, and the severity of complications (R=0.817).

DISCUSSION
In summary, the hemodynamic alterations that do occur after pneumonectomy are increase of the right ventricular end diastolic volume index, decrease of the ejection fraction of the right ventricle, and increase in pulmonary vascular resistance. All these result in significant dilatation and dysfunction of the right ventricle, which in turn results in increase of the BNP plasma levels.

The results of this study showed that indeed there was a statistically significant increase of both BNP and pulmonary artery pressure values after pneumonectomy, regardless the presence or not of post-operative complications. The BNP started increasing immediately after the ligation of the pulmonary artery, indicative of the ongoing...
hemodynamic alterations and of the required adjustments. In the patients with post-operative complications, the BNP plasma values at 3 hours and at 24 hours were statistically significant higher than in those patients without complications. The BNP value was higher before the obvious clinical appearance of the complications, which indicates a predictive role of clinical use.

The inclusion criteria to this study were strict in order to gain a more accurate image of the BNP kinetics, since all the exclusion criteria positively affect the pre-operative BNP plasma level. Although, the use of Swan-Ganz catheter is ideal for real time and more detailed measurements of circulatory parameters, was intentionally avoided due to the possibility of pulmonary artery injury.

Tamaya et al. have presented that the changes of the BNP after pneumonectomy more prominent than after lobectomy and were indicative of cardiopulmonary adjustment. Cagini et al. have concluded that the BNP has a strong predictive value of postoperative cardiopulmonary complications. Moreover, the pre-operative BNP plasma levels can be used as predictors of post-operative cardiac arrhythmias; Nojiri et al. have defined that a pre-operative BNP value of >30 pgr/ml had a sensitivity of 77% and a specificity of 93%.

In the case of atrial fibrillation the dilated right ventricle, due to overload/afterload, will consequently cause a right atrial dilatation, a well-known cause of atrial fibrillation. Post-pneumonectomy pulmonary edema is a complication mainly due to volume overload and increased vascular permeability. Although acute bronchopleural fistula is surgical complication the acute septic condition that results in an expected increase of the BNP, which is known to be correlated with high mortality.

The BNP plasma level predictive value for post immediate pneumonectomy complications have to be adjusted to a threshold value; Nojiri et al. have already set this value at 30 pgr/ml pre-operatively. Salvatici et al. have set a post-operative cut-off value of 182.3 pgr/ml for atrial fibrillation, suggesting also the initiation of anti-arrhythmic preventive therapy. In our study, where N was relatively small, these values were different and were both set in lower values.

The BNP does effectively reflects, in real time, the hemodynamic changes that occur after pneumonectomy and it has a strong predictive value for the occurrence of the post-operative complications, thus it is recommended the routine use of plasma BNP test in the immediate (at 24 hours) post-operative period. The next planned work is to examine BNP in concordance with the post-operative troponin levels in same clinical direction and moreover to identify the presence or not of subtle cardiac damage.

REFERENCES