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Determination of the Effects of Digoxin on the Right Ventricular Function in Patients Undergoing Pneumonectomy

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ABSTRACT

Introduction: Pneumonectomy is the standard treatment of lung cancer, even though patients should undergo several evaluations before surgery; deterioration of cardiopulmonary function after pulmonary resection is inevitable. We have evaluated the effects of digoxin on the improvement of right ventricular function and prevention of probable complications after lung resection surgery.

Materials and Methods: All patients who were candidate for pneumonectomy or extensive lobectomy in Ghaem hospital from 2010 to 2012 were enrolled into this study and were divided into two groups randomly. The first group (group D) received digoxin during surgery and in the second group (group C) normal saline was administered as placebo. Echocardiographic evaluation of the patients was accomplished the day before and the day after surgery.

Results: Among 20 patients in each group, male to female ratio was almost 2:1 and mean age was 63.8 (ranged 46-83 years). The most common cause of pneumonectomy was lung cancer. Comparison of the preoperative demographic variables, blood biochemistry, pulmonary function tests, echocardiographic and blood gas indexes showed no statistically significant differences between two groups. But postoperative evaluations showed a significant improvement in left ventricular ejection fraction in group D. Right ventricular systolic and diastolic diameters and pulmonary artery pressure were decreased significantly as well.

Conclusion: According to our results, we suggest a single dose of digoxin during lung resection surgery to improve cardiac performance after pneumonectomy.

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Introduction

Pneumonectomy and partial resection of lung (Lobectomy) are the standard treatment of lung cancer. Patients should undergo several evaluations before surgery; however; deteriora-

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tion of cardiopulmonary function after pulmonary resection is inevitable (1, 2).

Pneumonectomy reduces pulmonary vascular bed that may lead to sudden and severe increase in pulmonary vascular resistance and pulmonary hypertension which subsequently increase right heart afterload. Right ventricle is more sensitive to alteration of afterload (compare to left ventricle) due to its weaker muscular-ture. Therefore right ventricle will be distended and ventricular dysfunction and arrhythmia may happen. The incidence of arrhythmia increases with the extent of the surgical procedure from 5% after lobectomy to about 30% after pneumonectomy (1). The suggested risk factors are age, extent of operation, co existing heart disease, reduction of pulmonary vascular bed, hypoxia, emphysema, mediastinal shift, irritation of vagus and tumor implantation in the pericardium, and the influence of anesthetic drugs. Arrhythmias may also occur a few days after operation and are transient. Supraventricular arrhythmias (SVA) such as atrial fibrillation (AF) are observed in about one quarter of cases after pneumonectomy. The perioperative use of metoprolol, diltiazem or verapamil has been shown to reduce the frequency of AF after lung resection. Poor data exist about the nature and the duration of the analgesia regimen used. To date, the influence of different types of analgesia on arrhythmias has not been studied.

In this article we have assessed cardiac function and incidence of arrhythmia among patients who underwent pneumonectomy and we evaluated the effects of digoxin on improvement of the right ventricular function and prevention of probable complications. This article is focused on the administration of the digoxin to enforce the right heart muscles to prevent volume disturbance and stabilize right heart hemodynamic.

Materials and Methods

This study was approved by Ethic Committee of Mashhad University of Medical Sciences approved this study. Written informed consent was obtained from all patients.

40 patients who were candidate for pneumonectomy or extensive lobectomy in Ghaem Hospital from 2010 to 2012 were enrolled into our study.

Those patients with history of previous ischemic heart disease (IHD), heart failure, cardiac arrhythmia, advanced COPD, previous treatment with anti arrhythmic drugs or digoxin were excluded.

Patients were divided into two groups randomly. In one group digoxin was injected (group D) and in the other group, normal saline was injected as placebo (group C). 0.25 mg of digoxin was administered before pulmonary artery cross-clamping and 0.25 mg was injected after cross clamping to the patients in group D. Echocardiographic examination was accomplished the day before surgery by an expert cardiologist. Cardiac function and all the indices including right ventricular diastolic diameter (RVDd), right ventricular systolic diameter (RVDs), RV diameter, RV sys velocity, LVEF, TAPSE, PAP were measured.

Intensive monitoring was applied to all patients during and after operation. Direct measurement of blood pressure (arterial line), central venous pressure (CVP)and arterial blood gases were recorded. Echocardiographic examination of the patients was repeated the day after surgery. All data including demographic, echocardiographic, hemodynamic findings were recorded in a questionnaire.

Statistical analysis

Data was analyzed by SPSS software (ver 11.5) and non parametric tests such as Mann-Whitney test and Fisher's exact test were used to compare data between the two groups. *P*-value <0.05 was considered significant.

Results

70% of patients in group D (n=20) and 60% of group C (n=20) were male and male to female ratio in group D was 14/6 and in group C was 12/8.

Mean age in group D and C were 64.7±7.28 and 62.9±11.04 years, respectively. So both groups were almost identical with respect to sex and age distribution (*P*=0.762 and *P*=0.914 respectively).

Demographic data, blood biochemistry; and pulmonary function tests were also assessed and compared between the two groups and the results are shown in Table 1. No significant difference was determined between them.

Table 1. Comparison of demographic, blood biochemistry and pulmonary function tests in group D and C.

Variable	Group D (n=20) (Mean ± Sd)	Group C (n=20) (Mean ± Sd)	*P*-value
Weight(kg)	66.7±4.31	64.1±6.93	0.809
Height(cm)	169.3±7.90	164.7±9.01	0.621
BMI	21.4±3.08	19.35±4.71	0.882
Hb (gr/dl)	11.9±1.37	11.3±1.09	0.981
Hct (%)	35.4±7.31	32.7±9.02	0.844
Bun (mg/dl)	41.5±23.70	37.8±32.91	0.327
Cr (mg/dl)	1.4±0.71	1.3±0.35	0.935
FEV1(lit)	2.73±0.75	3.15±1.23	0.107
FVC(lit)	3.67±1.35	4.0±1.09	0.339
FEV1/FVC (%)	66.5±9.31	67.3±11.50	0.724

Lung cancer was the most common cause of pneumonectomy among both groups (70% in group D and 80% in group C). There were some other etiologies including advanced lung disease, mediastinal tumors and pleural malignancies. Late extubation was done in 75% of patients in group D and 80% of group C. So Comparison of the extubation time between the two groups did not show any statistically significant difference (*P*=0.822).

A comparison of the pre- and post-operative echocardiographic findings in the two groups is shown in Table 2.

Table 2. Comparison of the pre and post operative echocardiographic indices in group D and C.

Echocardiographic index		Group D (Mean ± Sd)	Group C (mean ± Sd)	*P*-value
RV Dd	Pre operative	35.2±17.47	37.7±10.09	0.521
	Post operative	30.4±4.01	36.3±5.21	0.020
RV DS	Pre operative	28.5±7.91	26.5±8.30	0.393
	Post operative	21.9±7.11	26.2±9.09	0.001
RV sys velocity	Pre operative	0.15±0.03	0.16±0.01	0.728
	Post operative	0.10±0.02	0.14±0.07	0.131
LV EF	Pre operative	46.1±8.30	48.0±7.29	0.871
	Post operative	67.3±11.32	55.4±17.78	0.009
TAPSE	Pre operative	22.4±3.71	23.3±5.00	0.877
	Post operative	19.31±7.88	23.2±8.03	0.155
PAP	Pre operative	28.8±7.01	29.1±8.81	0.645
	Post operative	31.3±8.39	36.7±12.71	0.016

RV Dd: diastolic right ventricular diameter
RV Ds: systolic right ventricular diameter
RV diameter: right ventricular diameter
RV sys velocity: right ventricular velocity
LV EF: Left ventricle ejection fraction
PAP : Pulmonary artery pressure

Comparison of the echocardiographic indices distribution between the two groups using Mann Whitney test showed statistically significant difference only in post-operative RV Dd and RV Ds, LV EF and also PAP.

A comparison of the pre- and post- operative arterial blood gas indices in group D and C is shown in Table 3.

Table 3. Comparing pre and post operative arterial blood gas indexes distribution in group D and C.

Arterial blood gas		Group D (Mean ± Sd)	Group C (mean ± Sd)	P value
PH	Pre operative	7.41±0.09	7.38±0.11	0.831
	Post operative	7.31±0.09	7.26±0.17	0.171
Pco2	Pre operative	47.6±4.09	45.3±3.91	0.607
	Post operative	46.3±7.40	48.5±3.71	0.730
Po2	Pre operative	79.6±10.31	84.7±17.6	0.794
	Post operative	77.3±11.24	70.7±15.31	0.209
Hco3	Pre operative	29.4±7.31	26.7±5.02	0.474
	Post operative	25.2±6.79	28.4±5.31	0.872
BE	Pre operative	2.3±1.71	1.9±1.12	0.882
	Post operative	2.3±0.79	1.4±0.79	0.205

A comparison of the pre- and post- operative arterial blood gas distribution between the two groups by Mann Whitney test did not show any statistically significant difference between them.

Discussion

Pneumonectomy is a standard treatment for several malignant and even non malignant pulmonary diseases. Although patients should undergo several evaluations before surgery; deterioration of cardiopulmonary function after pulmonary resection is inevitable (1, 2).

Pneumonectomy reduces pulmonary vascular bed and this may lead to sudden and severe increase in pulmonary vascular resistance and pulmonary hypertension which subsequently increase the afterload of right heart.

Right ventricle is more sensitive to alteration of afterload due to its weaker musculature. So right ventricle will be distended and ventricular dysfunction and arrhythmia may happen (3).

According to physiologic changes in cardiopulmonary system after pneumonectomy, prophylactic cardiac support may inhibit many of these adverse cardiopulmonary effects. Prophylactic digitalization is still recommended after open lung surgery in order to prevent cardiac arrhythmias in the postoperative period. Since the beneficial effect of this medication is only poorly documented, we have conducted a prospective randomized trial. Patients undergoing elective open lung surgery (pneumonectomy) were divided into two groups one of which received digoxin intraoperatively, the other not. Randomization was performed independently.

Amar *et al* (4) studied the effects of diltiazem versus digoxin on dysrhythmias and cardiac function after pneumonectomy and they reported that Digoxin therapy had no effect on the incidence of postoperative arrhythmia after pneumonectomy. On the other hand, Kaiser *et al* (5) suggested preventive digitalis therapy in open thoracotomy. They reported that prophylactic digitalization is still recommended after open lung surgery in order to prevent cardiac arrhythmias in the postoperative period.

Tanaka and his colleagues (6) also found digoxin to be effective in decreasing the incidence of postoperative atrial fibrillation.

Ritchie *et al* (7) suggested prophylactic digitalization in thoracotomy but they reported minimal effects of digoxin in prevention of cardiovascular complications. Järvinen *et al* (8) reported that prophylactic digitalization significantly reduced postoperative cardiac disorders after pneumonectomy.

Conclusion

In our study, we revealed beneficial effects of digoxin on improving the LV function as shown by improved LVEF.

RV diameter and PAP also significantly reduced which demonstrate the beneficial effects of digoxin.

According to our results and other reports we presumed that administration of 0.5 mg digoxin during lung resection surgery can improve cardiac performance after pneumonectomy.

Conflict of Interest

Authors declare there was not any conflicting interest.

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