Koroner Anjiyografi Yapılan Hastalarda İohexolün Solunum Fonksiyon Testi Parametrelerine Etkisi

EFFECTS OF IOHEXOL ON PULMONARY FUNCTIONS IN PATIENTS UNDERGOING DIAGNOSTIC CORONARY ANGIOGRAPHY

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Özet

Amaç: Damar içine uygulanan anjiyografik kontrast ajanlara bağlı olumsuz yan ekilerin varlığı daha önceki çalışmalarda bildirilmiştir. Bu çalışmanın amacı günlük uygulamada "iohexolün"ün koroner anjiyografi sırasında kullanımına bağlı solunumsal etkilerini incelemektir.
Materyal ve Metod: Koroner arter hastalığı ön tanısıyla koroner anjiyografi yapılan 30 hasta çalışmaya alındı. Kronik obstruktif akciğer, bronşiyal astım, miyokard infarktüsü ve ekokardiyografik olarak saptanmış sol ventrikül sistolik disfonksiyonu olan hastalar çalışmaya alınmadı. Koroner anjiyografiden hemen önce ve sonra solunum fonksiyon testi yapıldı ve kan gazı bakıldı. Hastalar anjiyografide koroner arter hastalığı olanlar (Grup1) ve olmayanlar (Grup2) şeklinde ikiye ayrıldı. Koroner anjiyografi işlemi tek deneyimli bir operatör tarafından yapıldı. Protokol gereği hastaların hiç birine sol ventrikülografi yapılmadı.
Bulgular: Koroner anjiyografi öncesi ve sonrası sonuçlar karşılaştırıldı. İşlem sonrası bakılan birinci saniye sonu forse orta ekspiryum volüm (FEV_1), maksimum mid-ekspiryum akım hızı (MMFR) 25-75, arteriyel oksijen basıncı (PaO_2),bikarbonat (HCO_3) değerleri tüm hastalarda anlamlı derecede düşük bulundu ($p < 0.01$). İşlem sonrası bakılan FEV1 ve PaO2 Grup1'de diğer gruplara göre anlamlı derecede daha düşük bulundu ($p < 0.01$)
Sonuç: Bilinen bir akciğer hastalığı olmayan hastalarda iohexol kullanılarak yapılan tanısal koroner anjiyografi, solunum fonksiyon testi parametrelerinde küçük, ama önemli bir bozulmaya yol açmaktadır. Bundan dolayı bilinen akciğer hastalığı olanlarda opak madde kullanımında dikkatli olunması gerekli olduğu sonucuna varıldı.

Anahtar kelimeler: İohexol, koroner anjiyografi, spirometri

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Summary

Background: Adverse respiratory reactions have been reported with intravascular radiographic contrast media. The aim of the present study was to assess the effects of iohexol on pulmonary functions in patients undergoing diagnostic coronary angiography.
Methods: Thirty patients diagnosed as coronary artery disease undergoing diagnostic coronary angiography were enrolled in the study. Subjects with chronic obstructive pulmonary disease, asthma, allergic bronchitis, myocardial infarction and documented systolic dysfunction by transthoracic echocardiography were excluded. The respiratory functions of the patients before and immediately after the coronary angiography were measured and arterial blood gas analyses were performed. The subjects were divided into two groups according to results of angiography as having coronary artery disease (Group 1) and without significant coronary artery disease (Group 2). The angiography procedures were performed by a single, experienced angiographer. Left Ventriculography was not performed on any patient
Results: The results gathered before and after angiography procedure were compared. Forced expiratory volume in the first second (FEV_1), maximum mid-expiratory flow rate, (MMFR) 25-75, arterial oxygen pressure (PaO_2) and bicarbonate (HCO_3) were significantly reduced ($p < 0.01$), where as forced vital capacity (FVC), pH, oxygen saturation and arterial carbondioxide pressure were not changed. The comparison between two groups resulted that FEV_1 and PaO_2 were significantly decreased after angiography in Group 1.
Conclusions: Diagnostic coronary angiography using iohexol decreases ventilatory functions in a small but significant extent in patients without any overt pulmonary disease. Therefore they should be used cautiously in patients with chronic lung disease.

Keywords: Iohexol, coronary angiography, ventilatory function

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Introduction

The search for a better contrast agent continues. Although they are not totally inert, non-ionic dimeric agents are used extensively in cardiologic imaging procedures and percutaneous coronary interventions today [1]. Iohexol is one of these and used widely in cardiology. However, the ventilatory effects of iohexol after diagnostic coronary angiography have not been studied yet. It is well documented that, administration of high, low or iso-osmolar radiographic contrast media, into the circulation is accompanied by respiratory adverse reactions. This has been considered to be contributory to the morbidity and mortality associated with coronary angiography. Although cardiovascular, haematological and hemodynamic effects of iohexol were studied extensively in human subjects [2], there is a lack of evidence about the ventilatory effects after its use in human subjects. The objective of the present study is to determine effects of iohexol on pulmonary functions during diagnostic coronary angiography.

Material and Methods

Thirty patients (19 male and 11 female, mean age 55 ± 6 years) referred for diagnostic coronary angiography were enrolled in the study. Exclusion criteria were subjects with chronic obstructive pulmonary disease, asthma, allergic bronchitis, myocardial infarction and documented systolic dysfunction by transthoracic echocardiography, patients with aortic valve disease, coronary bypass grafts, those needing additional right heart catheterization and known allergy for contrast agents. After informed consent was obtained, the respiratory functions of the patients before the coronary angiography were measured by "Vitalograph-alpha" (Ennis, Ireland) spirometer. After the patient was seated (not in supine position), the forced expiratory volume in the first second (FEV_1) and forced vital capacity (FVC), maximum mid-expiratory flow rate (MMFR) were measured. The use of the spirometer was first demonstrated by the operator and the patient was allowed practicing the procedure before formal recordings were made. The best of three attempts, with a difference of no more than 5% was recorded [3]. The maximum volumes obtained were taken into account. Predicted volumes were obtained from standard nomograms for comparison. The percent reached according to the predicted values of the ventilatory variables were taken into account for statistical analysis. The measurements were repeated immediately after the coronary angiography procedures via radial artery route were completed. Also, arterial blood gas analyses were performed before and immediately after coronary angiography. Arterial oxygen (PaO_2) and carbondioxyde ($PaCO_2$), pH, bicarbonate (HCO_3) and oxygen (O_2) saturation were recorded.

The contrast agent studied was iohexol; a non-ionic monomeric media with a molecular weight of 821.14 and iodine content of 46%. The concentration used for the study was commercially available formulation (Omnipaque-350) containing 350 mg/mL of iodine with an osmolality of 844 mOsm/kg of water.

The angiography procedures were performed through the radial artery route by a single, experienced angiographer with 5 F Judkin's diagnostic catheters with catheter exchange over a 0.035-inch guide wire. Totally five multiple angled views of the left and right coronary arteries were recorded in all patients by hand injection. Mean procedural duration was 19.1 ± 4.6 min and mean contrast media used was 86.8 ± 37.94 millilitres. No patients were performed ventriculography.

Statistical Evaluation

Statistical analysis was performed using Statistics Package for Social Sciences (SPSS 10.0 for windows) software. The variables gathered before and after angiography were compared using paired t-test. Also the subjects divided into two groups according to results of angiography as having coronary artery disease (Group 1) and without significant coronary artery disease (Group 2). Quantitative variables between groups were given as mean ± standard deviation. Quantitative values between groups were compared by Student' *t* test and qualitative values were compared by chi-square test. A *p* value of < = 0.05 was considered to be significant.

Table 1. The comparison of pulmonary tests and clinical variables before and after coronary angiography.

	Before angiography	After angiography	*P* value
FEV_1 (%)	103 ± 15	95 ± 17	< 0.01
FVC (%)	99 ± 13	95 ± 18	> 0.05
MMFR (%)	95 ± 33	84 ± 29	< 0.01
pH	7.48 ± 0.5	7.46 ± 0.42	> 0.05
PaO_2 (mmHg)	87 ± 8	82 ± 10	< 0.01
$PaCO_2$ (mmHg)	33 ± 3.5	32.3 ± 3.4	> 0.05
SO_2 (%)	96.6 ± 3.1	96.3 ± 2.1	> 0.05
HCO_3 (mmol/L)	27.5 ± 1.3	24.1 ± 2.4	< 0.01
SABP(mmHg)	132 ± 20	130 ± 19	> 0.05
DABP (mmHg)	76 ± 13	74 ± 10	> 0.05
RR (rpm)	20 ± 3	20 ± 2	> 0.05
PR (bpm)	82 ± 16	83 ± 13	> 0.05

DABP = diastolic arterial blood pressure; FEV_1 = forced expiratory volume in the first second; FVC = forced vital capacity; MMFR = maximum mid-expiratory flow rate; PR = pulse rate per minute; RR = respiration rate per minute; SABP = systolic arterial blood pressure; SO_2 = oxygen saturation

Table 2. The comparison of results of pulmonary tests in different groups.

	Group 1	Group 2	*P*
FEV_1 (BA) (%)	110 ± 12	99 ± 15	NS
FEV_1 (AA) (%)	104 ± 10	90 ± 19	< 0.05
FVC (BA) (%)	100 ± 7	99 ± 16	NS
FVC (AA) (%)	101 ± 13	91 ± 20	NS
MMFR (BA) (%)	116 ± 36	84 ± 25	< 0.05
MMFR (AA) (%)	96 ± 30	76 ± 27	NS
PH (BA)	7.47 ± 0.54	7.49 ± 0.49	NS
PH (AA)	7.46 ± 0.32	7.46 ± 0.48	NS
PaO_2 (BA) mmHg	91 ± 8	84 ± 8	NS
PaO_2 (AA) mmHg	89 ± 9	79 ± 10	< 0.05
$PaCO_2$ (BA) mmHg	34 ± 3	32 ± 3	NS
$PaCO_2$ (AA) mmHg	32 ± 3	32 ± 3	NS
O_2 SAT (BA) (%)	96 ± 5	96 ± 1	NS
O_2 SAT (AA) (%)	96 ± 3	96 ± 1	NS
HCO_3 (BA) (mmol/L)	25 ± 3	28 ± 7	NS
HCO_3 (AA) (mmol/L)	23 ± 2	24 ± 2	NS
SABP (BA) mmHg	132 ± 14	132 ± 23	NS
SABP (AA) mmHg	133 ± 14	128 ± 22	NS
DABP (BA) mmHg	77 ± 12	75 ± 14	NS
DABP (AA) mmHg	74 ± 11	74 ± 11	NS
RR (BA) rpm	20 ± 4	20 ± 1	NS
RR (AA) rpm	20 ± 2	20 ± 2	NS
PR (BA) bpm	78 ± 13	83 ± 18	NS
PR (AA) bpm	84 ± 10	82 ±15	NS
AGE (years)	56 ± 7	54 ± 8	NS

AA = after angiography; BA = before angiography; CAD = coronary artery disease; DABP = diastolic arterial blood pressure; FEV_1= forced expiratory volume in 1s.; FVC = forced vital capacity; MMFR = maximum mid-expiratory flow rate; PR = pulse rate per minute; RR = respiration rate per minute; SABP = systolic arterial blood pressure; SO_2 = soxygen aturation

Results

None of the subjects had symptomatic bronchospasm or major adverse events. The results of the ventilatory tests and arterial blood gas analysis conducted before and after angiography procedures were compared and were expressed in (Table 1). FEV_1, MMFR, PaO_2 and HCO_3 were significantly decreased after angiography ($p < 0.01$). Other variables remain statistically unchanged.

When the patients were grouped according to significant coronary artery disease presence; FEV_1 and PaO_2 were significantly lower in the patients with coronary artery disease (Table 2). Absence of coronary artery disease did not alter the adverse effects documented with ventilatory tests.

Discussion

Coronary angiography is the gold-standard of the diagnostic approach in the patients with suspected coronary artery disease. Although it can be safely and easily performed in a modern cardiac catheterization laboratory, it is nevertheless responsible for a certain degree of morbidity and mortality related to the invasive nature of the procedure and to the use of iodinated contrast agents. Non-ionic dimeric agents (iotrolan, iohexol, iopromide) represents ideal, totally inert X-ray contrast agent. They offer a relatively small, but real reduction in organ-specific toxicities. They, therefore became the agents of the choice for complex high dose interventional angiographic procedures [1]

The efficacy and safety of different contrast agents had been investigated in human subjects by coronary and respiratory artery injection. Kumazaki [3] evaluated the first study in man in which the change in pulmonary arterial pressure was recorded immediately after the rapid injections of hypertonic contrast media (diatroziate and ioxaglate) into the pulmonary artery. Tajima and associates [5] compared diatrizoate and iohexol with a study, concluding diatrozoate produced a significant rise and continuous elevation in both systolic and diastolic pulmonary arterial pressure, where as iohexol caused only a transient mild elevation.

The effects of different contrast agents on ventilatory functions were also studied before. Wilson and associates [5] compared ionic contrast agent sodium iothalamate with non-ionic dimmer iopamidol. The patients in both groups showed a significant reduction in FEV_1 and FVC after diagnostic urography performed with the mentioned agents, and there was no superiority between iopamidol and iothalamate when lowering

adverse effects were concerned.

The reductions in FEV_1 are possibly due to the asymptomatic bronchospasm. The underlying mechanism may involve a direct effect on the bronchi, the release of the bronchospastic mediators from mast cells and platelets, cholinesterase inhibition, vagal reflex and complement activation [6]. Laude and associates [7] concluded that the decrease in PaO_2 might reflect the decrease in alveolar perfusion. In their study with Wister rats, all diatrizoate, ioxaglate and iopromide caused significant falls in PaO_2. But, these changes were insufficient to trigger a ventilatory response. The authors speculated an inhibitory action on respiratory centres in the brain and carotid body. Cipolla and associates [8] investigated the effects of contrast media on pulmonary airway resistance and the mechanism underlying potential bronchoconstrictor effects in guinea pigs. They concluded that there was no apparent relationship between the size of the increase in airway resistance and pharmaceutical formulation. At the time being, the mechanism of bronchospasm after contrast media injection in circulation is still unclear.

The present data compare the ventilatory effects in human subjects after coronary angiography. The contrast media used was iohexol, accepted as one of the “standard” contrast agents in cardiologic procedures and had been in use nearly for two decades. Although this agent is superior to former ionic contrast media in case of adverse effects, it is not completely perfect. The relative rarity of major reactions with iohexol should not lead the decision that they are totally safe and negative effects on ventilatory functions due to possible asymptomatic bronchospasm, should not be ignored.

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