O R I G I N A L A R T I C L E

UDC: 355/359:61]::616.248-07
DOI: 10.2298/VSP150612162K

The importance of impulse oscillometry in bronchial provocation testing in confirming the diagnosis of asthma in male army recruits

Značaj impulsne oscilometrije kod bronhoprovokativnog testiranja za potvrdu dijagnoze astme kod muških vojnih regruta

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Abstract

Background/Aim. Impulse oscillometry (IOS) is a technique valid for measuring the lung function in obstructive lung diseases and bronchial provocation tests. However, no consensus exists for its use. The aim of the study was to assess impulse oscillometry sensitivity for detection of early airways changes during bronchial provocation testing and to compare with changes obtained with spirometry and bodyplethysmography in male army recruits. **Methods.** Male military recruits were submitted to bronchial provocation test with histamine by the aerosol provocation system. Out of 52 male military recruits subjected to attempts to make the diagnosis of asthma the study included 31 subjects with fall of forced expiratory volume in one second (FEV1) above 20%. The changes of impulse oscillometry were measured one step before and after provocation dose (PD) of histamine and compared with the changes of bodyplethysmography and spirometry. **Results.** The average age of male army recruits was 23.3 year. After bronchoprovocation there was an average increase of the total resistance at 5 Hz (R5) by 66.6%, resonant frequency (Fres) by 102.2%, Goldman index (AX) by 912.1%, the arway resistance (Raw) by 121.5%, and a decrease in reactance at 5 Hz (X5) by 132.1% and FEV1 by 25.6%. One step before the last inhaled of PD20 there was an average increase of 26.7% in R5, 24.1% in Fres, 85.3% in AX, 11.9% in Raw and a decrease in X5 by 26.9% and FEV1 by 4.3%. A correlation between impulse oscillometry and bodyplethysmography parameters was obtained. **Conclusion.** This paper demonstrates a sufficient sensitivity of impulse oscillometry to detect changes in airways, so it may play a complementary role in the diagnosis of asthma in male military recruits.

Key words:
asthma; diagnosis; bronchial provocation tests; histamine; respiratory function tests; sensitivity and specificity; military personnel; men; personnel selection.

Apstrakt

Uvod/Cilj. Impulsna oscilometrija (IOS) je važeća tehnika za merenje respiratorne impedancije kod opstruktivnih bolesti i bronhoprovokativnih testova, ali ne postoji konsenzus za njeno korišćenje. Cilj studije bio je da se proceni osetljivost impulsne oscilometrije u detekciji ranih promena u disajnim putevima za vreme bronhoprovokativnog testiranja i da se uporedi sa promenama spirometrije i pletizmografije kod muških vojnih regurta. **Metode.** Muškim vojnim regurtima je urađen bronhoprovokativni test sa histmainom preko aerosolnog provokacionog sistema. Od 52 muška vojna regruta kod kojih je pokušano potvrđivanje dijagnoze astme u studiju je bio uključen 31 ispitanik sa padom *forced expiratory volume in one second* (FEV1) iznad 20%. Merene su promene impulsne oscilometrije pre i posle pada FEV1 za 20% nakon provokacione doze (PD) histamina i upoređivane sa promenama spirometrije i telesne pletizmografije. **Rezultati.** Prosečna starost muških vojnih regruta bila je 23,3 godine. Posle bronhoprovokacije prosečno je povećan realni otpor (resistanca) na 5 herca (R5) za 66,6%, rezonantna frekvenca (Fres) za 102,2%, Goldman-ov indeks (AX) za 912,1%, endobronhijalna rezistanca (Raw) za 121,5% i smanjena reaktansa na 5 Hz (X5) za 132,1% i FEV1 za 25,6%. Korak pre inhalirane PD20 doveo je prosečno do povećanja R5 za 26,7%, Fres za 24,1%, AX za 85,3%, Raw za 11,9% i X5 za 26,9% i FEV1 od 4,3. Visok stepen korelacije dobijen je između telesne pletizmografije i IOS. **Zaključak.** U radu je dokazana dovoljna osetljivost impulsne osecilometrije za detekciju ranih promena u disajnim putevima, te ona može igrati komplementarnu ulogu u dijagnozi astme kod muških vojnih regruta.

Ključne reči:
astma; dijagnoza; inhalacioni testovi; histamin; respiratorna funkcija, testovi; senzitivnost i specifičnost; kadar, vojni; muškarci; kadar, selekcija.

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Introduction

Asthma is a chronic inflammation, associated with airway hyperresponsiveness that leads to recurrent episodes of wheezing, shortness of breath, chest tightness and coughing particularly at night or early in the morning [1]. It is characterized by reversible airflow obstruction, inflammation and hyperactivity of the airways [2].

Bronchial hyperresponsiveness (BHR) or increased sensitivity of the airways can be defined as a greater tendency to narrowing of the airways in response to inhalation of chemicals (metilcholin, histamine, carbachol) and physical agents (cold air, hyper- and hypo-osmolarity solutions), allergens, or exertional [3]. It is caused by genetic or environmental factors. Bronchial hyperresponsiveness presents the physiological trademark of asthma, and it does not involve setting diagnosis of asthma. The presence and degree of BHR is measured by standardized bronchial provocation tests (BPT). They are performed by inhalation of substances that cause narrowing of the airways and increased work of breathing. Asthma patients respond to non-specific agents quickly and more strongly, up to 100 times higher than healthy ones. Bronchial provocation testing is usually performed with histamine as provocative substances [4, 5].

The diagnosis of asthma is a set of characteristic symptoms, skin allergy tests to inhalation allergens, total and specific immunoglobulin E (IgE), sputum eosinophilia, and demonstrate BHR with spirometry, bodyplethysmography and impulse oscillometry as a new method of measuring pulmonary function [6].

The impulse oscillometry system (IOS) is used for determining the mechanical properties of the lungs and respiratory system through the relationship of pressure (P) and flow (V) measurement of respiratory impedance (Z) over the input pulses. Z representing the interaction between the impulse of pressure, resistance and the reactivity of the respiratory system, which includes the resistance (R) and reactance (X). Resistance is the result of a mechanical breathing and airway resistance. Reactance represents a reactive resistance which is contained in that part of the lung where it is not possible to measure the real resistance, and it is on the periphery. Reactance contains two components: capacitance (C) and inertance (I). Respiratory impedance is measured by impulse oscillometry [7]. Impulse oscillometry testing does not depend on cooperation of patients, because it is perfect in pulmonology [8], pediatrics [9], geriatrics [10], occupational medicine [11], anesthesiology [12], otorinolaryngolgy [13], sports medicine [14], and experimental medicine [15]. Impulse oscillometry has demonstrated high sensitivity in the assessment of BHR at BPT in the early diagnosis of asthma [16–19].

The aim of the research was to determine the sensitivity of impulse oscillometry in the early detection of bronchial hyperreactivity during BPT and compare the parameters of IOS with the results of spirometry and bodyplethysmography in male army recruits.

Methods

Out of 52 male military recruits, subjected to establishing the diagnosis of asthma, the study included 31 subjects, aged 23.3 years in average.

Bronchial provocation test with histamine was analyzed by measuring impulse oscillometry, spirometry, and bodyplethysmography. The changes of impulse oscillometry before and after the fall in forced expiratory volume in one second (FEV1) by 20% after provocation dose (PD20), and comparisons were performed with changes in spirometry (FEV1) and bodyplethysmography endobronchial resistance (Raw), specific resistance (Sraw), and specific conductance (SGaw) [20].

Criteria for inclusion of subjects in the study were: male military recruits aged from 17 to 27 years; asthma according to medical records; indications on guidelines for BPT. Criteria for exclusion from the study were the absolute and relative contraindications to the guidelines [21].

Medical history, physical examination and measurement of lung function were performed in all the subjects. Bronchial provocation test was evaluated with impulse oscillometry, spirometry and bodyplethysmography. The basic measurements with three tests were performed before the start of BPT. Bronchial provocation testing started so that the subjects inhaled 1 mL of physiological saline (0.9% NaCl), and after 2 min continued with measurements of lung function then the results were compared with the results of the basic measurement, and then the test using the same model of histamine inhalation in the dose of 0.03; 0,06; 0.12; 0.25; 0.5; 1.0; 2.0; 4.0; 8.0, and 16 mg/mL) [21, 22]. Histamine was inhaled in the form of solution of 32 mg/mL and 4 mg/mL (the Institute of Virology and Immunology, Torlak, Beograd) *via* the aerosol provocation system (APS) [23], which automatically designates the given dose.

Survey instruments for measuring lung function were pulsed oscillometer, Series Master Screen IOS (Care Fusion, Jaeger, Würtzburg, Germany) for the measurement of respiratory impedance, spirometer for measuring static and dynamic airway volume, and bodyplethysmography to determine the airway resistances and intrathoracic gas volumes were examined with Master Screen Body (Care Fusion, Jaeger, Würtzburg, Germany). Measurements of impulse oscillometry were performed as recommended by the constructor (Smith HJ), spirometry and bodyplethysmography according to the standards of the American Thoracic Society (ATS) and the European Respiratory Society (ERS) were performed [24–26].

Impulse oscillometry was accompanied by the following parameters: total resistance at 5 Hz (R5) (kP/L/s), resistance at 20 Hz (R20) (kP/ L/s), reactance at 5 Hz (X5) (kP/l/s), resonant frequency (Fres) (L/s); Goldman index (AX); spirometry: forced vital capacity (FVC) (L), forced expiratory volume in first second (FEV1) (L), the ratio of FEV1 / FVC (%), forced expiratory flow 50% (-FEF 50) (L); body plethysmography: total endobronchial resistance-Raw (kPa.Ls-1) specific resistance-(Sraw) (kPa.s-1) and specific conductance (Sgaw) (1 / kPa.s-1). The absolute values and their changes (%) of spirometry (FVC, FEV1, FEF50) and bodyplethysmography (Raw, SRaw, SGaw) and impulse oscillometry (R5, X5, Fers) are shown.

To calculate relative values of the parameters of impulse oscillometry (R5, X5), reference values of constructor appliances (Vogel H and Smith HJ) were used, while for spirometry (FVC, FEV 1, FEF 50) and body plethysmography (Raw, SRaw, SGaw), predicted value of the European Respiratory Society was used. Parameters Raw, SRaw and Fres are presented in absolute values. Reactance at 5 Hz was calculated as the difference between the active and planned values, the original formula produced in the software, in the literature referred to as delta X5 [27].

After collecting and controlling data, the standard statistical methods were used: absolute number, percentage, arithmetic mean, standard deviation. The frequency changes of R5, Fres and AX are shown. The degree of correlation was determined by the coefficient of linear correlation. Statistical analysis was performed on a personal computer by means of statistical software package "Statistica".

Results

Data analysis was performed in 31 male military recruits, the average age of 23.2 ± 5.3. A total of 56% were smokers and 44% non-smokers.

Spirometry was performed in all the patients. The mean basic values of FVC were 5.6 L, for FEV1, and 4.56 L, for FEF50 4.73 L. The average values of changes of FEV1 for 4.3% and FEF50 for 6.8% was decreased before PD20. The mean values of changes of FEV1 to 25.6% and 46.7% for FEF50 were obtained after PD20 (Table 1).

Body plethysmography was also done in all the subjects. The average values of Raw before BPT were 0.25 kPa-L. The mean values of changes of Raw for 11.4% and 14.9% for SRaw were increased and SGaw for 6.0% was decreased before PD20. In the control group the mean values of changes of Raw for 104.2%, SRaw for 121.5% was increased and SGaw for 47.1% was decreased.

Impulse oscillometry basic values of R5 0.34 kPa/L/s, X5 -0.09 kP/L/s, Fres 10.2 L /s and AX 0.23 were shown. The average values of changes of R5 for 26.7%, X5 for 26.9%, Fres for 24.1% and AX for 85.3% were increased before PD20. The average values of changes of R5 for 66.4%, X5 for 132.1%, Fres for 102.2% and AX for 912.1% were increased after PD20.

The values of the main parameters of impulse oscillometry R5 and Fres were followed by frequency changes before and after PD20 over four class intervals (less than 20%, 21–30%, 31–40% and over 40%), and also AX parameter (below 100 %, of 101–150%, 151–200%, more than 200%) (Table 2).

In the study group the frequency of changes of R5 under 20% of the values were 60% of the cases, in 20% from

Table 1

Descriptive statistics before and after histamine bronchoprovocation dose 20 (PD20)

Variable	Basic values	Before PD20	Δ Before PD20	After PD20	Δ After PD20
	mean ± SD	mean ± SD	mean ± SD	mean ± SD	mean ± SD
Spirometry					
FVC	5.60 ± 0.81	5.00 ± 1.38	-1.39 ± 6.37	4.77 ± 0.88	-12.70 ± 10.08
FEV1	4.56 ± 0.64	4.47 ± 0.64	-4.30 ± 6.99	3.37 ± 0.60	-25.66 ± 11.48
FEF50	4.73 ± 1.05	4.40 ± 0.97	-6.86 ± 14.64	2.60 ± 0.86	-46.74 ± 10.10
Body plethysmography					
Raw	0.25 ± 0.07	0.27 ± 0.06	11.98 ± 32.53	0.48 ± 0.18	104.29 ± 97.32
SRaw	1.05 ± 0.34	2.11 ± 1.05	14.93 ± 31.62	1.23 ± 0.34	121.53 ± 107.32
SGaw	1.03 ± 0.32	0.86 ± 0.22	-6.02 ± 28.55	0.51 ± 0.19	-47.10 ± 20.37
Impulse oscillometry					
R5	0.34 ± 0.09	0.41 ± 0.15	26.74 ± 19.04	0.54 ± 0.17	66.64 ± 62.91
X5	-0.09 ± 0.05	-0.11 ± 0.05	26.90 ± 36.31	-0.17 ± 0.15	132.18 ± 148.13
Fres	10.27 ± 2.60	13.49 ± 4.01	24.13 ± 19.31	19.66 ± 6.96	102.22 ± 95.22
AX	0.23 ± 0.16	0.38 ± 0.29	85.30 ± 73.09	1.41 ± 1.42	912.12 ± 1422.73

FVC – forced vital capacity; FEV1 – forced expiratory volume in one second; FEF50 – forced expiratory flow 50%; Raw – endobronchial resistance; SRaw – specific resistance; SGaw – specific conductance; R5 – total resistance at 5 Hz; X5 – reactance at 5 Hz; Fres – resonant frequency; AX – Goldman index.

Table 2

Frequency of changes of impulse oscillometry (IOS) parameters before and after histamine bronchoprovocation dose 20 (PD20) for resistance at 5 Hz (R5), resonant frequency (Fres) and Goldman index (AX)

Intervals (%)	ΔR5 before PD20 (%)	ΔR5 after PD20 (%)	ΔFres before PD20 (%)	ΔFres after PD20 (%)	Intervals (%)	ΔAX before PD20 (%)	ΔAX after PD20 (%)
< 20	60.0	16.0	64.0	8.0	< 100	72.0	4.0
21–30	20.0	24.0	16.0	4.0	101–150	20.0	16.0
31–40	12.0	16.0	16.0	12.0	151–200	4.0	20.0
> 40	8.0	44.0	4.0	76.0	> 200	4.0	60.0

ΔR5 – interval of total resistance; ΔFres – interval of resonant frequency; ΔAX – interval of Goldman index.

21–30%, in 12% from 31–40% and 8% of the cases over 40% of the values. In the control group the frequency of changes under 20% ocurred in 16% of the study subjects, in 24% from 21–30%, in 16% from 31–40% and more than 40% of the values in 44% of the cases. In the group before PD20 the changes of Fres were in 64% of the subject below 20% of values, in 16% from 21–30%, in 16% from 31–40% and more than 40% of values in 4% of the cases. In the control group changes below 20% occurred in 8%, from 21–30% in 4%, from 31–40% in 12%, and more than 40% of values in 76% of the cases. In the group before PD20 change AX in 72% of the patients were below 100% of values, in 20% from 101–150%, in 4% from 151–200% and in 4% of the cases over 200% of values, while in the control group changes below 100% of values were in 4% of the subjects, from 101–150% in 16%, from 151–200% and over 200% in 16% of values in 60% of the cases (Table 2).

A correlation before PD20 between IOS and body plethysmography was weak according to spirometry (Table 3). A high degree of significant correlation after PD20 was observed between the values of IOS (Table 4) and body plethysmography, and the most pronounced between Raw and R5 (0.74), Fres (0.82) and AX (0.88).

Disscusion

Asthma is a chronic inflammatory disease of the airways characterized by reversible airflow obstruction, inflammation and hypereactivity of the airways. BHR is proving bronchodilation and bronchial provocation tests [2]. Bronchial provocation testing is performed by inhalation of substances that cause narrowing of the airways and increased work of breathing. Bronchial hyperresponsiveness does not involve setting diagnosis but it certainly is an indicator of the existence of asthma. Bronchial hyperresponsiveness is proved by default, just call spirometry and impulse oscillometry can be used as an additional method that has proven to be sensitive. Mean values of changes in the parameters of IOS before PD20 (R5 26.7%, Fres 24.1%) were 6 times greater than changes in spirometry (FEV1 4.3%) and bodyplethysmography (Raw 11.9%, SRaw 14.9%), and also after PD20 average changes of IOS (R5 66.4%, and 102.2% Fres) were higher from 2.5 to 4 times than changes of spirometry (FEV1 25.66%), which makes this method sensitive. The high variability of these parameters of IOS can create confusion over the interpretation of the findings, especially the Goldman index (AX) cannot be used for BPT

Table 3

Pearson's correlation coefficient between changes before histamine bronchoprovocation dose 20 (PD20) [impulse oscillometry (PD20-IOS) vs. spirometry, plethysmography]

Variable	ΔR5 (%) PD20	ΔX5 (%) PD20	ΔFres (%) PD20	ΔAX (%) PD20
ΔFVC (%) PD20	0.15	-0.17	0.00	-0.07
ΔFEV1 (%) PD20	-0.05	-0.32	-0.09	-0.28
ΔFEF50 (%) PD20	-0.10	-0.25	-0.20	-0.30
ΔRtot (%) PD20	0.34	0.13	0.28	0.35
ΔSRtot (%) PD20	0.34	0.29	0.36	0.44*
ΔSGtot (%) PD20	-0.42*	-0.22	-0.33	-0.43*

Correlations before PD20-histmine. Marked (*) correlations are significant at $p < 0.05$;
N = 31 (Casewise deletion of missing data).
ΔR5 – interval of total resistance; ΔX5 – interval of reactance; ΔFres – interval of resonant frequency; ΔFVC – interval of forced expiratory volume; ΔFEV1 – interval of forced expiratory flow 1; ΔFEF50 – interval of forced expiratory flow 50; ΔRtot – interval of total specific resistance; ΔSRtot – interval of total specific resistance; ΔSGtot – interval of total specific conductance.

Table 4

Pearson's correlation coefficient between changes after histamine bronchoprovocation dose 20 (PD20) [impulse oscillometry (PD20-IOS) vs. spirometry, plethysmography]

Variable	ΔR5 (%) PD20	ΔX5 (%) PD20	ΔFres (%) PD20	ΔAX (%) PD20
ΔFVC (%) PD20	-0.02	-0.27	-0.05	-0.18
ΔFEV1 (%) PD20	-0.05	-0.21	0.10	-0.06
ΔFEF50 (%) PD20	-0.33	-0.27	-0.23	-0.30
ΔRaw (%) PD20	0.74*	0.60*	0.82*	0.88*
ΔSRaw (%) PD20	0.67*	0.53*	0.77*	0.83*
ΔSGaw (%) PD20	-0.40*	-0.45*	-0.40*	-0.47*

Correlations before PD20-histmin. Marked (*) correlations are significant at $p < 0.05$;
N = 31 (Casewise deletion of missing data).
ΔFVC – interval of forced expiratory volume; ΔFEV1 – interval of forced expiratory flow;
ΔFEF50 – interval of forced expiratory flow 50%; ΔRaw – interval of endobronchial resistance;
ΔSraw – interval of specific resistance; ΔSgaw – interval of specific conductance;
ΔR5 – interval of total resistance; ΔX5 – interval of reactance; ΔFres – interval of resonant frequency; ΔAX – interval of Goldman index.

because it has a high variability. Resistance at 5 Hz and Fres are carriers of the interpretation of findings in BPT. Kohlhaufl et al. [28] conducted a trial with methacholine test among healthy nonsmokers and asymptomatic smokers and proved a 3 times higher value of reactance as compared with FEV1 of asymptomatic smokers, which was probably the consequence of the existence of subclinical bronchiolitis [29]. Short et al. [29] compared IOS and spirometry at challange test and bronchodilatory test in the patients who had used beta blocker proparnolol before and two hours after inhalation of histamine and salbutamol. The values of changes of IOS parameters, R5, R5-20, AX, and Fres were higher than spirometry changes, especially R5 and Fres with the mean values of 30.8% and 39.4%, respectively [29].

Frequency changes R5 and Fres before PD20 in the class intervals over 30% of values were present in 20% of the subjects, which means that every fifth BPT can be estimated as positive step before PD20. Frequency changes after PD20 for R5 in 60% of subjects, and for Fres in 80% of respondents in class intervals over 30% of values were most pronounced, making this method sensitive but not completely specific in assessing BPT.

A correlation between IOS and standard methods before PD20 is not significant; this method gives the possibility of different interpretation. Good correlation of impulse oscillometry with bodyplethysmography complements these two methods in the assessment of BPT. Poor connections to spirometry as the gold standard for estimating pulmonary function shows that impulse oscillometry may provide new information in the assessment of BHR. Mansura et al. [30] analyzed the relationship IOS in 20 patients with stable asthma after BPT with methacholine with asthma symptom score, IOS and spirometry. They proved a significant correlation between the score and IOS, but not with spirometry. Hnatiuk et al. [31] compared parameters of IOS (Z-impedance, R5, Fres, PR-periphery resistance) in 48 subjects and spirometry (FEV1) according to increasing doses of methacholine (0.025, 0.25, 2.5, 10, 25 mg/mL). The changes in impedance correlated significantly with changes of FEV1 for all methacholine doses.

Conclusion

This paper demonstrates a sufficient sensitivity of impulse oscillometry to detect the changes in the airways, so it may play a complementary role in the diagnosis of asthma in male military recruits. The value of step parameter changes before PD20 suggests that IOS is sensitive in the detection of BHR.

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Received on June 12, 2015.
Revised on September 6, 2015.
Accepted on October 5, 2015.
Online First July, 2016.