CLINICAL STUDY

Acute hemodynamic effects of non-invasive ventilation in patients with obesity hypoventilation syndrome

Pobeha P, Paranicova I, Trojova I, Tkacova R, Joppa P

Department of Respiratory Medicine and Tuberculosis, Faculty of Medicine, P. J. Safarik University and L. Pasteur University Hospital, Kosice, Slovakia. **pavol.joppa@upjs.sk**

ABSTRACT

OBJECTIVE: To evaluate the acute effects of volume-targeted non-invasive ventilation (NIV) on hemodynamic parameters assessed by impedance cardiography in patients with obesity hypoventilation syndrome (OHS).

BACKGROUND: Despite the well-described beneficial effects of NIV using volume-targeted pressure support ventilation modes on respiration in OHS patients, questions were raised about the impact of this treatment on the cardiovascular system.

METHODS: In 15 patients (10 men; mean age, 55.8 ± 9.3 years) impedance cardiography recordings were taken at baseline, after 120 minutes while on NIV and 20 minutes after NIV termination. A repeated-measures analysis of variance was used for comparisons.

RESULTS: Compared to baseline, a reduction in heart rate (from 80 ± 11 to 73 ± 10 beats per min, $p<0.05$) was observed on NIV whereas the stroke volume and cardiac index remained stable throughout all three assessed intervals ($p=0.347$, $p=0.344$; respectively). The pre-ejection period increased on NIV (from 113 ± 16 to 127 ± 20 ms, $p<0.05$), and the left ventricular ejection time increased after NIV termination compared to baseline (from 259 ± 25 to 269 ± 25 ms, $p<0.05$).

CONCLUSION: Volume-targeted NIV may acutely improve systolic time intervals without any negative impact on the left ventricular function in OHS patients *(Tab. 2, Ref. 17)*. Text in PDF *www.elis.sk*

KEY WORDS: obesity hypoventilation syndrome, obstructive sleep apnoea, hypercapnia, non-invasive ventilation, impedance cardiography, cardiac output.

Introduction

Non-invasive ventilation (NIV) is a standard treatment for chronic respiratory failure in patients with obesity hypoventilation syndrome (OHS) and comorbid obstructive sleep apnoea (OSA) (1). However, despite the well-described beneficial effects of NIV using volume-targeted pressure support ventilation modes on respiration in OHS patients (2, 3), questions were raised about the impact of this treatment on the cardiovascular system (4). In particular, NIV was shown to acutely reduce cardiac output and stroke volume in disorders other than OHS (5, 6). Nevertheless, studies on hemodynamic effects of NIV in patients with OHS (7, 8) are scarce, although there is evidence suggesting that long-term NIV use may improve left ventricular diastolic dysfunction

in such patients (8). Therefore, our study aimed to evaluate the acute effects of volume-targeted NIV on hemodynamic parameters in patients with OHS using a non-invasive method of impedance cardiography.

Material and methods

Clinically stable patients with OHS referred for the initiation of long-term NIV were consecutively recruited between 2017 and 2018. Arterial blood gas analysis and diagnostic sleep study were performed before the initiation. The diagnosis of OHS was defined by the combination of obesity [body mass index (BMI) > 30 kg/m²], sleep-disordered breathing, and awake daytime hypercapnia [resting arterial partial pressure of CO_2 ($paCO_2$) greater than 6.0 kPa], in the absence of an alternate explanation for hypoventilation (9). All the patients underwent a transthoracic echocardiography with the assessment of left ventricular systolic function; those with an ejection fraction lower than 45 % were excluded. The study was approved by the L. Pasteur University Hospital Ethics Committee and all the patients signed a written informed consent.

Patients underwent a night with automated positive airway pressure (PAP) device (Prisma 20A, Löwenstein medical, Germany) to titrate the expiratory PAP. On the morning following the titration, NIV was initiated using the bi-level PAP device (Prisma 30ST, Löwenstein medical, Germany) with a volume-targeted

spontaneous/timed ventilation mode using oro-nasal masks. Tidal volume was set to 8 ml/kg of ideal body weight (3). Hemodynamic changes were measured during two hours of initial NIV. Measurements were performed using beat-to-beat non-invasive monitoring with impedance cardiography (Niccomo, Medis, Germany) as previously described (10). In brief, impedance cardiography recordings were taken after 15 minutes at rest in a supine position suitable for NIV, and three 60-second intervals were marked during the recording – baseline (pre-NIV), during the stable phase of NIV after 120 minutes on NIV, and 20 minutes after NIV termination (post-NIV). Within the marked intervals, the following parameters were analysed: oxygen haemoglobin saturation with a pulse oximeter (SpO_2), heart rate, left ventricle cardiac output to body surface area – cardiac index (CI), stroke volume, pre-ejection period (PEP), left ventricular ejection time (LVET), systolic time ratio (STR), ejection time index (ETI) and ratio (ETR).

Statistical analyses

To compare the hemodynamic parameters recorded pre-NIV, on NIV, and post-NIV, a repeated measures analysis of variance (RM-ANOVA) was used. Holm-Sidak test was applied for post-hoc pair-wise comparisons. The results are presented as the mean ± standard deviation. A two-tailed *P*-value of <0.05 was considered statistically significant. Analyses were conducted using SPSS for Windows software (version 14.0).

Results

Fifteen patients with OHS (10 men) naive to NIV were enrolled. They were generally late-middle-aged (mean age, 55.8±9.3 years) with the mean body mass index of 49.7±7.1 kg/m². Sleep study parameters and arterial blood gas values are displayed in Table 1. All the patients suffered from severe OSA and hypercapnic respiratory failure with a moderate-to-severe hypoxemia (Tab. 1). On NIV, the average attained tidal volume was 515.6±68.8 ml, whereas expiratory and inspiratory PAP was 13.3±2.9 and 23±3.7 kPa on average, respectively.

Two hours of NIV therapy resulted in significant increases in SpO_2 from the baseline that were followed by restitution to pre-NIV values 20 minutes after NIV termination (Tab. 2). Assessment of hemodynamic effects (see Table 2) showed that compared to

Tab. 1. Sleep study parameters and awake arterial blood gas values in the study cohort.

Variable	
ESS, points	9.1±3.1
AHI (episodes/hour)	108.1±21.5
Mean SpO_2 (%)	77.3±8.7
CT90% (%)	77.7±29.2
$paCO_2$ (kPa)	7.5±0.7
paO_2 (kPa)	6.6±0.8

Data are presented as the mean ± SD. ESS – Epworth Sleepiness Scale; AHI – apnoea-hypopnea index; SpO_2 – pulse oximetry saturation; CT90% – cumulative sleep time percentage spent with pulse oximetric saturation below 90 %; $paCO_2$ – arterial partial pressure of carbon dioxide, paO_2 – arterial partial pressure of oxygen

Tab. 2. Hemodynamic changes during 2-hour non-invasive ventilation protocol.

Variable	Pre-NIV	On NIV	Post-NIV	p
SpO_2, %	84.5±6.7	89.7±5.8[a]	85.7±6.4	<0.001
HR, beats/min	80±11	73±10[a]	77±12	<0.001
CI (l/min/m²)	2.4±0.3	2.3±0.4	2.5±0.5	0.347
SV, ml	73±15	79±26	80±27	0.344
LVET, ms	259±25	261±21	269±25[a]	0.018
PEP, ms	113±16	127±20[a]	113±22	0.002
STR	0.45±0.10	0.49±0.10[a]	0.42±0.10	0.003
ETI (ms)	372±17	377±19	392±15[a]	<0.001
ETR (%)	30.9±3.3	31.4±3.8	34.0±3.2[a]	<0.001

Data are presented as the mean (SD). p values were calculated using Repeated Measures One-Way ANOVA. [a] p < 0.05 versus Pre-NIV. NIV – non-invasive ventilation; SpO_2 – pulse oximetry saturation; HR – heart rate; CI – cardiac index; SV – stroke volume; LVET – left ventricular ejection time; PEP – pre-ejection period; STR – systolic time (PEP/LVET) ratio; ETI – ejection time index; ETR – ejection time ratio

pre-NIV, NIV application resulted in reductions in heart rate (p < 0.05) with no significant changes in stroke volume and CI. Indeed, both stroke volume and CI remained relatively stable throughout all three assessed intervals (p=0.347, p=0.344, respectively). Furthermore, significant increases in systolic time intervals PEP and STR were observed on NIV compared to baseline, with restoration after NIV termination (p=0.002, p=0.003; respectively). Measurements of LVET, ETI, and ETR revealed that there were no changes during the NIV period, nevertheless, significant increases in all these variables occurred after NIV termination compared to baseline (p < 0.05 for all).

Discussion

This is the first prospective study assessing acute hemodynamic changes during initiation of NIV in a well-defined group of stable OHS patients with severe OSA using impedance cardiography and its results are intriguing: effective NIV was accompanied by temporary reductions of heart rate and improvements in systolic intervals, without any deterioration of left ventricular systolic function. Previous studies on the effects of NIV on left ventricular function in patients with respiratory failure in disorders other than OHS yielded inconsistent results: acute reductions of stroke volume and CI were observed in some (5, 6) but not in all the studies (11). In the present study, the observed decrease of HR did not result in unfavourable reductions in either CI or stroke volume. In a case report of a single OHS patient with severe OSA, cardiac output was preserved despite a decreased heart rate during sleep on NIV suggesting beneficial effects of NIV on stroke volume (12), in agreement with our observations.

Using volume-targeted bi-level pressure support mode as an effective method of ventilation in patients with OHS (2, 3) is the strength of this study, in association with its prospective design and consistent use of a pre-defined protocol in all the patients. In addition, bi-level pressure support has been previously suggested as a treatment of the first choice for OSA with marked nocturnal hyposaturation (13) and the patients in the studied cohort had co-existing severe OSA with up to 77 % of the cumulative sleep time spent with a saturation below 90 % (Tab. 1). The rather small cohort

of studied patients suggests that our results should be considered preliminary and further investigations are needed to confirm these findings. Furthermore, our study protocol was implemented during the daytime and, therefore, studies investigating heart function while on NIV during sleep are required to complement our observations. The use of impedance cardiography for hemodynamic measurements may represent another study limitation; this method was shown to potentially over- or underestimate the results during NIV compared to the thermo-dilution method (14). Nevertheless, impedance cardiography is an established non-invasive method to assess hemodynamic functions in both experimental (15) and clinical (16) studies, which is reliable when assessing trends (17). In conclusion, our pilot study suggests that volume-targeted NIV is a safe method that may acutely improve systolic time intervals while it does not negatively impact left ventricular function in OHS patients with comorbid OSA. Longitudinal observations with longer follow-up periods are needed to clarify the effects of regularly used nocturnal NIV on left ventricular systolic function in such patients.

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