Evaluation of the Effects of Noninvasive Ventilation on Blood Gas and Depression Levels of Patients with Obesity Hypoventilation Syndrome

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Abstract

Background: Obesity hypoventilation syndrome (OHS) is associated with increased mechanical load on respiratory system. Here, we aimed to investigate and evaluate the effects of noninvasive ventilation (NIV) on physical and mental status of patients with OHS.

Materials and Methods: The current study is an observational study that was performed in 2020 on 50 patients with OHS in Isfahan, Iran. Beck’s Depression Inventory (BDI-II) and Hospital Anxiety and Depression Scale (HADS) questionnaires were also filled for all patients assessing their depression levels that were confirmed by psychiatrists. PO2 and PCO2 of patients were evaluated using venous blood gas (VBG) before interventions. Patients with a definite diagnosis of OHS and depression entered the study and underwent treatments with NIV. One month after the interventions with NIV, the blood gases of patients were evaluated using VBG and BDI-II, and HADS questionnaires were also filled for all patients, evaluating their depression.

Results: The mean age of the subjects was 63.5 ± 13.5. The mean blood oxygen after the use of NIV in patients with OHS increased significantly (P = 0.001). The mean of carbon dioxide after using NIV in patients with OHS decreased significantly (P = 0.001). Based on the BDI-II and HADS scales, the mean score of depression after using NIV decreased significantly (P = 0.001 for both).

Conclusion: NIV therapies are associated with improvements in blood oxygen and CO2 of patients with OHS. The levels of depression also decreased after treatments that were confirmed by psychiatrists.

Keywords: Depression, noninvasive ventilation, obesity hypoventilation syndrome

INTRODUCTION

Hypventilation is a condition in which the patient inhales and exhales more slowly. Healthy breathing is characterized by the right balance between inhaling and exhaling.[1] At the time of hypoventilation, this balance is disturbed by the release of carbon dioxide to a lesser extent than the absorption of oxygen. Lack of oxygen leads to brain hypoperfusion by vascular mechanisms.[2] This decrease in blood flow to the brain could result in symptoms such as lightheadedness and tingling in the fingers. Severe hypoventilation can also lead to loss of consciousness.[3] Hypoventilation syndrome is a term for frequent hypoventilations. Based on various studies, hypoventilation could alter brain function in long term due to its effects on brain blood flow and could also cause depression symptoms in patients.[4]
Obesity hypoventilation syndrome (OHS) is defined as the presence of obesity (body mass index ≥30 kg/m²) with high levels of blood carbon dioxide (PaCO₂ >45 mmHg) in patients without neuromuscular, metabolic, or chest wall deformities.[5] The diagnosis of OHS is important because of the potential for clinical exacerbation leading to respiratory failure and high mortality chances in untreated patients.[6] The pathophysiology of OHS includes increased mechanic load on respiratory system, blunting of ventilatory drive, and inadequate chemoreceptor response to hypercarbia and hypoxemia.[7] OHS is associated with obstructive sleep apnea (OSA) in more than 90% of cases.[8] Some studies have classified hypoxia, polycythemia, daytime drowsiness, and nighttime ventilation as symptoms that may be associated with OSA. Physicians believe that both OHS and OSA can negatively affect patients’ cognitive and mental functions.[9,10]

Neurocognitive dysfunction and psychiatric disorders such as depression and anxiety are some of probable comorbid diseases.[11] Neurocognitive impairment is associated with limited creativity, work performance, quality of life, self-esteem, and psychosocial functioning. Cognitive dysfunctions, depression, and anxiety are also frequent in OSA syndrome (OSAS) patients.[12] Former studies have also explained that obesity as a major OHS component is associated with increased chances of depression, anxiety, and also stress with impairments in quality of life.[13‑15]

Diagnosis of OHS is by nocturnal pulse oximetry, capnography, and nocturnal polysomnography.[16] The main treatment strategies of OHS are with weight loss and positive pressure ventilation using noninvasive ventilation (NIV). NIV is widely used for the chronic treatment of these patients. NIV is the use of respiratory support administered through a face mask or nasal mask. NIV is used in acute respiratory failure caused by a number of medical conditions, the most prominent of them, chronic obstructive pulmonary disease.[17,18]

Numerous studies have shown that proper use of NIV reduces the need for invasive ventilation and its complications. In addition, it may be used for a long time in people who cannot breathe independently as a result of a chronic illness.[19] The use of NIV for OHS and OSA was associated with improvements in patient’s physical conditions and also increasing their quality of life. Changes in both PaO₂ and PACO₂ could also lead to improvements in mental condition of patients and positive effects on neurocognitive functions and psychiatric disorders in OSAS patients.[20] Very few studies have evaluated the effects of NIV on neurocognitive functions in OHS patients, and to the best of our knowledge, no studies have been performed in Iran in this regard. Here, we aimed to investigate and evaluate the effects of NIV on physical and mental status of patients with OHS in Isfahan.

**MATERIALS AND METHODS**

The current study is an observational study that was performed in 2020 on 50 patients with OHS in Isfahan, Iran. The study protocol was approved by Research Committee of Isfahan University of Medical Sciences and the Ethics committee has confirmed it (Ethics code: IR.MUI.MED.REC.1399.232, Iranian Registry of Clinical Trials [IRCT] code: IRCT20200702047987N1).

The inclusion criteria were diagnosis of OHS by expert pulmonologists, confirmation of depression diagnosis by psychiatrists using DSM-5 criteria, signing the written informed consent to use NIV and participate in this study. Exclusion criteria were as follows: using sedative and hypnotic medications, patient’s will to exit the study, and patients’ death during the study. Required sample size was calculated with using the sample size estimation formula to compare the means with considering the 95% confidence level, 80% test power, standard deviation of mean questionnaires scores which was about 1.5 and the effect size was 0.8 in 50 patients. The sampling method of the present study was accessible and easy, so that patients referring to our medical centers for whom the diagnosis of OHS and depression was registered and had acceptable study conditions, the required sampling was done consciously until the ceiling of the volume was completed.

A total number of 50 patients with OHS entered the study based on inclusion and exclusion criteria. Diagnosis of OHS was performed by expert pulmonologists based on clinical data and sleep tests results. Demographic data of all patients including age, gender, past medical history, and past drug history were collected. Beck’s Depression Inventory (BDI-II) and Hospital Anxiety and Depression Scale (HADS) questionnaires were also filled for all patients assessing their depression levels that were confirmed by psychiatrists.

BDI-II consists of 21 groups of statements, each scoring from 0 to 3. The total score of BDI-II is calculated from 0 to 63. Patients with scores of 0–10 are considered as normal, patients having 11–16 scores are considered mild mood disturbance, patients having 17–20 are considered borderline clinical depression, patients with 21–30 are considered moderate depression, patients having 31–40 are considered severe depression, and patients with over 40 scores are considered extreme depression. HADS is also consisted of 7 statements evaluating depression and 7 statements to evaluate depression in patients. Each scoring from 0 to 3. Patients with total depression score between 0 and 7 are considered as normal, 8–10 as borderline abnormal, and 11–21 as abnormal.

Venous blood gas (VBG) was also taken from all patients at 8 am before interventions evaluating the PO₂ and PCO₂. Patients with definite diagnosis of OHS and depression entered the study and underwent treatments with NIV. The method of treatment with NIV was the same for patients and the amount of air flow and adherence to treatment in patients was measured by examining the general condition of patients and also the amount of blood oxygen saturation by pulse oximetry and blood gases by VBG. The titration and NIV settings were conducted according to the study of Piper et al. in 2017.[21]
One month after the interventions with NIV, the blood gases of patients were evaluated using VBG, and BDI-II and HADS questionnaires were also filled for all patients, evaluating their depression.

Data regarding blood gases and depression were collected and compared to before interventions in patients.

**Results**

Overall, 50 patients with OHS participated in the present study. Table 1 deals with the demographic characteristics of the subjects. According to the results of Table 1, the mean age of the subjects was 63.5 ± 13.5. Furthermore, 58% of the participants were men and 42% were women.

Table 2 examines and compares the mean arterial blood carbon dioxide and blood oxygen levels before and 1 month after the use of NIV in patients with OHS.

According to the results of Table 2, the mean blood oxygen after the use of NIV in patients with OHS increased significantly ($P = 0.001$). Furthermore, the mean of carbon dioxide after using NIV in patients with OHS decreased significantly ($P = 0.001$).

Table 3 also examines and compares the mean score of depression before and after NIV use in patients with OHS based on BDI-II and HADS questionnaires. As the results in Table 3, based on the BDI-II scale, the mean score of depression after using NIV in patients with OHS decreased significantly ($P = 0.001$). Furthermore, the mean score of depression based on the HADS after using NIV in patients with OHS decreased significantly ($P = 0.001$).

Furthermore, the frequency distribution of depression severity based on BDI-II and HADS questionnaires before and after NIV use in patients with OHS is shown in Table 4.

We also analyzed the questions of HADS one by one before and after interventions with NIV. These data are indicated in Tables 5 and 6.

Mean and standard deviation of each question in the BDI-II questionnaire before and after interventions with NIV were also calculated and are summarized in Table 7.

**Discussion**

Here, we showed that the use of NIV in patients with OHS was associated with significant increase in blood oxygen levels and significant decrease in the mean blood carbon dioxide levels. Using BDI-II and HADS questionnaires, we also showed that the usage of NIV was associated with decreased depression scores showing their effectiveness in decreasing the levels of depression in these patients. There have been several previous studies in this regard.

In a recent study by Soghier et al. in 2019, they investigated the studies related to the use of NIV and continuous positive airway pressure (CPAP) in patients with OHS. They concluded that both NIV and CPAP could be used in patients suffering from OHS. This report also indicated that treatments with NIV are associated with decreased CO2 levels and increase in blood oxygen levels.\[22\] Baiamonte et al. also evaluated clinical and compliance data provided by a single home care provider in 602 patients with OHS. They showed that depression was one of the most important issues in these patients which indeed reduced the patient’s complacence to ventilatory treatments.\[23\] Our results were in line with these findings emphasizing the

| Table 1: Demographic data of participants |
|-----------------|-----------------|
| **Variable**    | **Mean±SD/n (%)** |
| Age             | 63.5±13.5       |
| Gender          |                  |
| Male            | 29 (58)         |
| Female          | 21 (42)         |

SD: Standard deviation

| Table 2: Determining and comparing the mean levels of blood oxygen and carbon dioxide in individuals before and after noninvasive ventilation use |
|-----------------|-----------------|
| **Variable**    | **Before NIV**  | **After NIV**  | **P**   |
| Blood O$_2$ levels | 77.98±1.3       | 88.02±1.34     | 0.001   |
| Blood CO$_2$ levels | 69.36±12.04     | 48.11±7.3      | 0.001   |

NIV: Noninvasive ventilation

| Table 3: Comparison of depression levels based on Beck’s depression inventory-II and Hospital Anxiety and Depression Scale questionnaires |
|-----------------|-----------------|
| **Variable**    | **Before NIV**  | **After NIV**  | **P**   |
| Depression levels based on BDI-II | 3.4±0.67       | 1.86±0.85     | 0.001   |
| Depression levels based on HADS  | 2.82±0.43      | 2.2±0.83      | 0.001   |

BDI-II: Beck’s depression inventory, HADS: Hospital Anxiety and Depression Scale, NIV: Noninvasive ventilation

| Table 4: Frequency distribution of depression based on Beck and Hospital Anxiety and Depression Scale questionnaires before and after using noninvasive ventilation |
|-----------------|-----------------|
| **Questionnaire** | **Before NIV, n (%)** | **After NIV, n (%)** |
| HADS            |                  |                  |
| Normal          | 1 (2)            | 13 (26)          |
| Borderline abnormal | 7 (14)         | 14 (28)          |
| Abnormal        | 42 (84)          | 23 (46)          |
| BDI-II          |                  |                  |
| Normal          | 0                | 22 (44)          |
| Mild depression | 2 (4)            | 13 (26)          |
| Moderate depression | 29 (58)       | 15 (30)          |
| Severe depression | 16 (32)       | 0                |
| Dangerous depression | 3 (6)          | 0                |

BDI-II: Beck’s depression inventory-II, HADS: Hospital Anxiety and Depression Scale, NIV: Noninvasive ventilation

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**Nayebi, et al.: Comparing radiographic imaging and Raypex 6**

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**Nayebi, et al.: Comparing radiographic imaging and Raypex 6**
importance of depression in patients with OHS and positive effects of NIV in this issue.

Argun Baris et al. also evaluated 10 OHS and 10 OSAS patients in 2016. They showed that cognitive dysfunction, depression, and anxiety are important under-recognized comorbidities in OHS. It was also suggested that short-term ventilatory therapy could be associated with positive effects on neurocognitive functions, depression, and anxiety. It was also stated that further multicenter, prospective studies with large number of cases are required.\[24\] Another study was conducted by Hida et al. in 2003 on patients with OHS. Using the SF-36 questionnaire, they showed that patients with OHS and OSA have lower quality of life compared to normal population and also mentioned that the prevalence of depression and anxiety is higher among these patients. After 3–6-month treatments with NIV, they showed that the quality of life of patients improved significantly that was also associated with the improvement of daytime sleepiness.\[25\]

Our data also showed that the use of NIV was associated with significant improvements in clinical data and depression scores in patients.

These data suggest that NIV is an effective therapeutic method for patients with OHS that could also cause significant improvements in patient’s depression. Sivam et al. evaluated the resting wake and overnight sleep electroencephalography recordings, neurocognitive tests, and sleepiness, depression and anxiety scores in 15 OHS and 36 OSA patients and showed that positive airway therapies are associated with significant improvements in sleepiness, anxiety, and depression scores of patients within 3 months.\[9\] The results of our study were also consistent with these findings. A key point of our study was that we performed 1-month NIV treatments for OHS patients and observed significant improvements in blood gas levels and depression scores.

Bouloukaki et al. also investigated the long-term effects of positive airway pressure therapy on 252 patients with OHS. They evaluated patient’s depression levels using BDI-II

| Number | Question                                                                 | Often, n (%) | Sometimes, n (%) | Not often, n (%) | Very seldom, n (%) |
|--------|---------------------------------------------------------------------------|--------------|------------------|------------------|-------------------|
| 1      | I feel tense or “wound up”                                               | 20 (40)      | 10 (20)          | 20 (40)          | 0                 |
| 2      | I still enjoy the things I used to enjoy                                 | 17 (34)      | 15 (30)          | 5 (10)           | 13 (26)           |
| 3      | I get a sort of frightened feeling as if something awful is about to happen | 15 (30)      | 17 (34)          | 13 (26)          | 5 (10)            |
| 4      | I can laugh and see the funny side of things                            | 4 (8)        | 6 (12)           | 22 (44)          | 18 (36)           |
| 5      | Worrying thoughts go through my mind                                    | 22 (44)      | 24 (48)          | 2 (4)            | 2 (4)             |
| 6      | I feel cheerful                                                         | 7 (14)       | 8 (16)           | 18 (36)          | 17 (34)           |
| 7      | I can sit at ease and feel relaxed                                      | 3 (6)        | 10 (20)          | 21 (42)          | 16 (32)           |
| 8      | I feel as if I am slowed down                                            | 17 (34)      | 14 (28)          | 10 (20)          | 9 (18)            |
| 9      | I get a sort of frightened feeling like “butterflies” in the stomach    | 13 (26)      | 21 (42)          | 8 (16)           | 8 (16)            |
| 10     | I have lost interest in my appearance                                   | 11 (22)      | 13 (26)          | 14 (28)          | 12 (24)           |
| 11     | I feel restless as I have to be on the move                              | 12 (24)      | 14 (28)          | 10 (20)          | 14 (28)           |
| 12     | I look forward with enjoyment to things                                 | 13 (26)      | 12 (24)          | 12 (24)          | 13 (26)           |
| 13     | I get sudden feelings of panic                                          | 18 (36)      | 22 (44)          | 7 (14)           | 3 (6)             |
| 14     | I can enjoy a good book or radio or TV program                           | 15 (30)      | 18 (36)          | 10 (20)          | 7 (14)            |

| Number | Question                                                                 | Often, n (%) | Sometimes, n (%) | Not often, n (%) | Very seldom, n (%) |
|--------|---------------------------------------------------------------------------|--------------|------------------|------------------|-------------------|
| 1      | I feel tense or “wound up”                                               | 10 (20)      | 4 (8)            | 30 (60)          | 6 (12)            |
| 2      | I still enjoy the things I used to enjoy                                 | 16 (32)      | 10 (20)          | 10 (20)          | 14 (28)           |
| 3      | I get a sort of frightened feeling as if something awful is about to happen | 12 (24)      | 6 (16)           | 15 (30)          | 15 (30)           |
| 4      | I can laugh and see the funny side of things                            | 12 (24)      | 18 (36)          | 7 (14)           | 13 (26)           |
| 5      | Worrying thoughts go through my mind                                    | 16 (32)      | 14 (28)          | 12 (24)          | 8 (16)            |
| 6      | I feel cheerful                                                         | 18 (36)      | 15 (30)          | 10 (20)          | 7 (14)            |
| 7      | I can sit at ease and feel relaxed                                      | 13 (26)      | 17 (34)          | 8 (16)           | 12 (24)           |
| 8      | I feel as if I am slowed down                                            | 13 (26)      | 11 (22)          | 14 (28)          | 12 (24)           |
| 9      | I get a sort of frightened feeling like “butterflies” in the stomach    | 8 (16)       | 14 (28)          | 16 (32)          | 12 (24)           |
| 10     | I have lost interest in my appearance                                   | 10 (20)      | 12 (24)          | 15 (30)          | 13 (26)           |
| 11     | I feel restless as I have to be on the move                              | 11 (22)      | 10 (20)          | 13 (26)          | 16 (32)           |
| 12     | I look forward with enjoyment to things                                 | 11 (22)      | 9 (18)           | 11 (22)          | 19 (38)           |
| 13     | I get sudden feelings of panic                                          | 14 (28)      | 17 (34)          | 11 (22)          | 8 (16)            |
| 14     | I can enjoy a good book or radio or TV program                           | 13 (26)      | 12 (24)          | 12 (24)          | 13 (26)           |
We also suggest that physicians pay more attention to this finding, as it is in line with the previous studies emphasizing the importance of NIV in patients with OHS and depression.

The levels of depression also decreased after the treatments that were confirmed by psychiatrists. These were performed for 1 month. The limitations of the present study were restricted study population and lack of proper long-term follow-up of patients. Another limitation of our study was not to conduct any structural interview for clinical examination of the participants. These points should be considered for further studies.

The key point of the current study was that we used both BDI-II and HADS questionnaires to evaluate the depression levels of patients and also their depression levels. It was also mentioned that physicians should suggest this therapeutic technique in OHS patients suffering from poor quality of life and depression. Based on the results of our study, usage of NIV is associated with significant reduction in depression scores that were also indicated in former studies.

The questionnaire along with quality of life of patients and their daytime sleepiness. Finally, they reported that usage of positive airway pressure therapy was associated with significant improvements in clinical data of patients and also their depression levels. It was also mentioned that physicians should suggest this therapeutic technique in OHS patients suffering from poor quality of life and depression. Based on the results of our study, usage of NIV is associated with significant reduction in depression scores that were also indicated in former studies.

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The key point of the current study was that we used both BDI-II and HADS questionnaires to evaluate the depression levels of patients and also performed the NIV treatments for 1 month. The limitations of the present study were restricted study population and lack of proper long-term follow-up of patients. Another limitation of our study was not to conduct any structural interview for clinical examination of the participants. These points should be considered for further studies.

**CONCLUSION**

Taken together, we showed that NIV therapies are associated with improvements in blood oxygen and CO₂ of patients with OHS. The levels of depression also decreased after treatments that were confirmed by psychiatrists. These findings were in line with the previous studies emphasizing the importance of NIV in patients with OHS and depression. We also suggest that physicians pay more attention to this technique.

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**Conflicts of interest**

There are no conflicts of interest.

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