Study of plasma orexin-A level in COPD patients during acute exacerbation

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Background: Orexin-A is a neuropeptide that regulates excitement, alertness and appetite.

Aim of the work: To study the plasma level of orexin-A in patients with COPD during acute exacerbation and its relation with both body mass index and body fat percentage in these patients.

Subjects, methods: This study included 80 subjects who were classified into two groups: Group (I): included 50 patients with COPD in acute exacerbation. Group (II): included 30 apparently healthy subjects as a control group. Plasma orexin-A levels, body mass index (BMI), body fat percentage (BFP), oxygen saturation (SaO2), partial pressure of arterial oxygen (PaO2) and partial pressure of arterial carbon dioxide (PaCO2) were recorded for all patients. Each group was subdivided according to their body mass index into: underweight with BMI less than 18.5, normal weight (BMI more than 18.5 and less than 25) and overweight (BMI more than or equal 25 and less than 30).

Results: Orexin-A was found to be higher in different COPD weight groups (underweight, normal weight and overweight) when compared with those of control group. Overweight patients in group I had higher values Plasma orexin-A when compared with underweight and normal weight in the same group. Orexin-A increased significantly with increased BMI, PaCO2 and BFP and had also significant negative correlation with PaO2 and SaO2.

Conclusion: Patients with COPD during acute exacerbation had higher values of plasma orexin-A when compared with normal subjects and plasma orexin-A correlated positively with BMI and BFP in these patients.

Introduction

Chronic obstructive pulmonary disease is common disease that can be prevented and treated. COPD progressively restricts airflow and is associated with chronic inflammatory reaction of the bronchi and the lung to harmful substances [1]. Lean body mass in COPD causes weakness in the respiratory muscles and this muscle weakness makes COPD patients at risk of respiratory failure [2]. Orexin-A is a member of a group of orexins which are present in the lateral hypothalamus [3]. Orexin-A administration causes a dose-dependent eating and accelerates metabolism [4]. Orexin-A promotes vigilance and regulate lipid metabolism and it also takes part in diabetes mellitus and obesity [5], with a strong and long lasting effect on appetite. Orexin-A can be measured in humans [3]. In animal studies orexin-A can pass to brain tissue, so elevation of its plasma level might lead to appetite control and energy loss [6]. Previous studies detected low values of orexin-A in COPD, with lower levels more prominent in underweight patients. However, plasma orexin-A is not yet studied in patients with COPD during acute exacerbation [7].

Aim of the work

To study the plasma level of orexin-A in patients with COPD during acute exacerbation and its possible relation with both body mass index and body fat percentage in these patients.
Subjects and methods

This case-control study included 80 subjects; classified into two groups. Group (I): 50 COPD patients in acute exacerbation, admitted in Damanhur Chest Hospital in the period from October 2016 to June 2017. Their diagnosis was based on history of exposure to risk factor, clinical examination, radiology and spirometry [8]. Group (II): 30 apparently healthy persons as a control group, all of them were nonsmokers. Each group was subdivided according to BMI into: those with underweight (UW) (with BMI less than 18.5), those with normal weight (NW) (BMI more than 18.5 and less than 25), and those with overweight (OW) (BMI more than or equal 25 and less than 30) [9]. Ethical Approval of this study was obtained from the Ethical Committee of the Faculty of Medicine, Benha University. Each subject signed a written informed consent before being enrolled in this study.

Inclusion criteria for group I: COPD patients with increased shortness of breath; the main symptom of exacerbation. Other symptoms include increased phlegm, along with increased coughing and wheezing [10].

Exclusion criteria: Patients with bronchial asthma, obstructive sleep apnea, malignancy, heart failure, diabetes mellitus, other endocrine diseases or patients with psychiatric problems.

All subjects were subjected to the following: 1- History taking. 2- Physical examination (general & local). 3- BMI calculation: BMI = weight in kilograms/(height in meters)². 4-BFP: in males = 2

Results

Out of fifty COPD patients (group I), 42 were males and 8 were females. The mean age in group I was (62.06 ± 7.59) years. The mean body mass index was (29.41 ± 8.81) kg/m². In group II (30 subjects), 28 were males while 2 were females. The mean age of controls was (61.93 ± 6.56) years. The mean body mass index was (24.88 ± 4.36) kg/m². There were statistically significant differences between group I and group II as regards body weight, BMI and BFP being statistically higher in group I, however, there was no statistical significant differences regarding age and sex (Table 1). Plasma orexin-A mean level was statistically higher in group I when compared with group II (77.03 ± 26.06 vs. 24.08 ± 10.03 ng/L respectively) (Table 2). In group I; patients were classified according to BMI into: UW nine patients; orexin-A ranged from 25.47 to 88.98 with Mean ± SD (49.19 ± 23.58), NW eight patients; orexin-A ranged from 56.23 to 96.49 with Mean ± SD (72.86 ± 12.31) and OW thirty-three patients; orexin-A ranged from 43.44 to 119.90 with Mean ± SD (85.63 ± 23.86). In group II (according to BMI), there were; two UW persons; orexin-A ranged from 19.55 to 25.07 with Mean ± SD (22.31 ± 3.90), fourteen NW persons; orexin-A ranged from 7.50 to 39.55 with Mean ± SD (23.41 ± 11.06) and fourteen OW persons; orexin-A ranged from 7.09 to 38.75, with Mean ± SD (24.99 ± 9.95). Overweight subjects in both groups (case and control) had higher values of plasma orexin-A levels when compared with those with normal weight, who in turn, showed higher plasma orexin-A levels when compared with those with under weight. Plasma orexin-A levels in OW, NW and UW of the case group were higher than their corresponding subdivisions of the control group (Table 3). In group I,
On the other hand, this work revealed that plasma orexin-A level was higher in patients suffering from COPD when compared with normal subjects. This result was in agreement with Zhu et al. who studied plasma orexin-A levels in patients with COPD suffering from type II respiratory failure; their study didn’t coincide with Adam et al. who revealed that plasma orexin-A levels might be affected by the underlying disease.

Comparison between underweight, normal weight and overweight subdivisions of the studied groups regarding plasma orexin-A level.

There were statistical significant positive correlations between plasma orexin-A level from one side and BMI, PaCO2 and BFP from the other side but statistical significant negative correlations between plasma orexin-A level and both PaO2 and SaO2 (Table 4).

**Discussion**

In the current study, there was statistical significant difference between group I (cases) and group II (controls) regarding BMI distribution as it was statistically higher in group I (p < 0.05). Our result was not matched with that of Maria et al. who revealed that underweight and normal weight were more common in COPD patients than overweight [14]. Our study disagreed with Zhou et al. who performed 2 population-based studies (a cross-sectional study and a subsequent four-year cohort study); they revealed that low BMI is a systemic manifestation of COPD and an important risk factor for the disease [15]. These different results could be explained by the fact that the present study had fewer numbers of cases which may be non-representative. Our study showed that there was a highly statistical significant difference between cases and controls as regards BFP distribution (p < 0.01) as it was statistically higher in group I. Increased BFP in group I might be due to increased plasma orexin-A level in group 1 which stimulated glucose influx in 3T3-L1 adipocytes in group 1 might be due to increased plasma orexin-A level in group 1 which stimulated glucose influx in 3T3-L1 adipocytes and the increased energy absorption was stored as lipids, orexin-A thus increased lipid formation [19]. It also might inhibit lipid catalolism [20]. Our study showed that there was statistical significant difference between UW, NW and OW subjects in both case and control groups regarding plasma orexin-A level and it was significantly higher in COPD patients (p < 0.05). These results were in agreement with Zhu et al. who revealed that plasma orexin-A level in UW, NW and OW subgroups of COPD patients were higher than the corresponding subgroups of normal subjects [16]. The current study coincided also with those of Kawad et al. who revealed that plasma levels of orexin-A and leptin were elevated in overweight children when compared with those who have normal weight. Their study was performed to measure plasma orexin-A and to evaluate its relationship with other anthropometric and metabolic markers. Forty-seven overweight children were included in their study. Plasma orexin-A level was higher in OW children (17.0 ± 0.4 ng/L) than in NW children (13.5 ± 1.1 ng/L) [21]. Our study didn’t coincide with Adam et al. who revealed that plasma orexin-A had lower values in overweight persons. In their study, plasma orexin-A and leptin levels were studied in people with BMI between 19.8 and 59 kg/m². Obese subjects had lower values of Plasma orexin-A [22]. As an explanation for this difference, plasma orexin-A levels might be affected by the underlying disease.
in different studies. In the present study, plasma orexin-A level showed significant positive correlation with BMI in patients with COPD. This result was in concordance with Zhu et al. who revealed that plasma orexin-A level increased significantly with increased BMI in COPD patients with type II respiratory failure [16]. Similar result were obtained by Matsumura et al. who found that orexin-A levels correlate positively with BMI and fat mass values in COPD patients [7]. In the present study, there was statistical significant positive correlation between plasma orexin-A levels and BFP in COPD cases. This result agreed with Zhu et al. who revealed that plasma orexin-A levels correlate positively with BFP in type II respiratory failure COPD patients [16]. This result could be explained by that: 1- In obesity, elevated lipids and triglyceride in peripheral blood led to increased hypothalamic orexin-A gene expression [23]. 2- The presence of orexin-A receptors in fatty tissues with its role in lipid formation [19]. In the present study, there was a statistical positive correlation between plasma orexin-A levels and PaCO2 in COPD patients, a finding that didn’t coincide with Zhu et al. [16] and Igarashi et al. [24] who revealed no correlation. Also, Igarashi et al. found no correlation between plasma orexin-A levels and PaCO2 in patients with obstructive sleep apnea [24]. These different results could be explained by different patient categories included in these studies. In the current study, there was statistically significant negative correlation between plasma orexin-A levels and both partial pressure of arterial oxygen and partial pressure of arterial carbon dioxide in patients with COPD. Our results were in agreement with Zhu et al. who revealed a negative correlation between orexin-A and both partial pressure of arterial oxygen and oxygen saturation in COPD patients with type II respiratory failure [16]. This result could be explained by the fact that orexin-A has a role in respiratory control by accelerating ventilation [25].

Conclusion

Patients with COPD during acute exacerbation had higher values of plasma orexin-A when compared with normal subjects and plasma orexin-A correlated positively with BMI and BFP in these patients.

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References