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Evaluation of the Relationship Between Substance P Serum Level with Gasometric Variables and Respiratory Test Indices in Patients with Asthma

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1. Abstract

Asthma is a chronic inflammatory disease damaged the respiratory system, which has recently been relatively prevalent in developing countries. The presence of inflammatory and intramuscular factors in the smooth muscles of the airway walls may lead to narrowing of these channels. Substance P is a member of neurokinin family with 11 amino acids that causes pain relief and has various effects on the smooth muscles of the respiratory airways. In this study, the level of substance P, spirometric parameters and arterial blood gases were analyzed in 60 patients with asthma (30 males and 30 females) with mean age 63.67 ± 14.61 years in 2018 at 17-e-shahrivar hospital (Mashhad, Iran). After completing the written consent and the information form, the levels of substance P, pH, O_2 and CO_2 pressure, bicarbonate, as well as vital capacity, forced vital capacity and FEV1 were evaluated. In comparison to normal range, the results demonstrate that the arterial oxygen pressure ($p = 0.0001$), arterial carbon dioxide pressure ($p = 0.058$), vital capacity ($p = 0.0001$), forced vital capacity ($p = 0.0001$), FEV1 ($p = 0.0001$) decreased significantly and the concentration of serum substance P ($p = 0.035$) increased significantly. Considering the above findings, it can be concluded that serum level of substance P in asthmatic patients is significantly increased and this factor may be used as a reliable indicator in predicting the state of asthma in patients.

2. Introduction

According to statistics from the World Health Organization, more than 1.5 million people worldwide suffer from respiratory problems and diseases, while 4% of deaths worldwide are due to respiratory diseases [1]. In recent years, chronic respiratory diseases account for the fourth highest rate of deaths, but are thought to increase with increasing levels of bio-pollutants, air pollution, deforestation and increased atmospheric volumes of greenhouse gases. Including carbon dioxide, the group will come in third in the next decade [2]. Asthma is one of the most common respiratory diseases in Iran and elsewhere in the world. According to statistics from the World Health Organization, more than 300 million people worldwide suffer from asthma and its complications, which will reach 700 million by 2024 [2].

It is one of the most common respiratory diseases in Iran and elsewhere in the world. According to statistics from the World Health Organization, more than 300 million people worldwide suffer from asthma and its complications, which will reach 700 million by 2024 [2]. The prevalence of asthma is increasing dangerously due to increasing levels of various pollutants. Studies in our country show that the prevalence of asthma in the population of children and adolescents has reached 13%, which has increased compared to the last decade. In general, it is the most common respiratory complication in children and adolescents [1].

Previously, this model was based on the assumption that asthma is caused by a series of immune responses due to an increase in sensitivity to an allergenic compound. By limiting exposure to these compounds and the use of anti-allergenic agents, asthma was again seen in many patients. Studies in immunology have also shown that asthma occurs for a variety of reasons, and the allergy-related effect on asthma is much more complex than previously believed [4]. Asthma is caused by inflammatory changes in the lung tissue, and asthma is a pulmonary response to inflammation. It is also worth noting that microbial agents, including viruses and bacteria, can interfere with the inflammatory response, causing infection and exacerbating inflammation in the tissue [3].

The role of the substance P neuropeptide and the nitric oxide synthase system is greater. By producing factors released from damaged cells, inflammation is intensified and, by affecting the smooth muscle of the bronchial wall, virtually hypertrophy and muscle hyperplasia are identified in the lung tissue as one of the main symptoms of asthma. Given these conditions, anti-asthma drugs are used that have two areas of activity. These drugs can dilate the bronchi or inhibit inflammation to reduce the effects of an asthma attack [6, 7]. Inflammation in the smooth muscles in the lungs of the lungs causes abnormal functioning of these muscles. When exercising a deep tail during respiratory congestion or bronchial stenosis, stretching the muscles decreases their ability temporarily while preventing or leading to muscle tension in asthmatic patients. Incomplete muscle tension and defects in the function of the muscles of the airway wall. In other words, in general, the major problem in patients with asthma is the inability to draw the smooth muscles of the bronchial wall and bronchioles in the tail, which in addition to reducing respiratory capacity puts pressure on various parts of the respiratory system [8].

2.1. A Review of Studies

Cherniack et al. (2006) on 550 residents of Kashan including 295 males and 255 females showed that the FVC rate was calculated to be 4.79 liters. This study showed that the FVC index in Kashan residents is higher than that of Kurdistan residents, which somehow reflects the impact of living [12].

In 2006, Bhatia et al. Investigated the effects of compound P on inflammatory reactions induced by inhaled hydrogen sulfide. In this study, it was found that inhaling hydrogen sulfide can increase the concentration of substance P while exacerbating pulmonary inflammation. Pathological findings and histological staining also indicate that inhaling this gas can lead to serious lung injury and increase the activity of metalloproteinase in the lung. Pretreatment of animals tested with the neurokinin 1 receptor antagonist to protect mice against the inflammatory effects and damage caused by inhaled hydrogen sulfide gas. Also, the findings of this study showed that the use of receptors antagonists of other neuropeptides of neurokinin 2 and 3 showed no protective effect. Based on these findings, it was found that compound P could play a critical role in controlling the effects of inhaled hydrogen sulfide gas and its associated inflammatory damage on lung tissue and elaborate therapeutic strategies [13].

A study by Huang et al. In 2015 was conducted to evaluate the effect of substance P on the neonate of damaged pulmonary rats due to induction of pulmonary hyperoxidation. In this study of 32 rats, the animals were exposed to 95% oxygen for 14 days. After pathological studies, evaluation of various proteins and oxidative stress-related factors revealed that substance P composition could be tested by inducing antioxidant activities, reducing apoptotic process, reducing lung injury, oxidative stress and its damage in neonatal rats. Significantly decrease [14]. Nadel also found that inflammatory factors play a critical role in the onset and exacerbation of asthma. In this study, the status of cellular hyperactivity and regulation of inflammatory cascades in patients was evaluated. In general, inflammatory stimulants and their modulatory mechanisms have been shown to induce spasms in the airways and significantly exacerbate the potential for hypersensitivity in patients to allergens [15].

3. Method

As a pilot study, 30 women and 30 men with asthma participated in the study. Their asthma was confirmed by a specialist doctor. Inclusion criteria for the study were asthma, acceptance and completion of informed consent form, and no other diseases. To investigate the relationship between gasometric variables and serum level of substance P in patients with asthma, 60 patients completed spirometry tests and arterial blood gas tests after completing the data table. Then, 2–4 cc of venous blood was taken from each patient, centrifuged, and stored at -80 °C until completion of sampling. FRAP method was used to evaluate total antioxidant capacity and serum P was measured by ELISA method. Data were analyzed by SPSS software using independent t-test. In this study, experiments were carried out at three levels, including determination of serum P concentration, pH, oxygen (PO2) and carbon dioxide (PCO2) and bicarbonate (HCO3-) concentrations on arterial blood samples and capacity factor measurements. VC, FVC, and Forced expiratory volume in the first second (FEV1) were performed spirometrically. After performing various laboratory tests and completing the data collection forms, the data were analyzed in SPSS 20 software. Data were analyzed by Kolmogorov-Smirnov test and then by independent sample t-test. Results were considered significant with $p>0.05$. The normality of the data was evaluated by Kolmogorov-Smirnov test. Based on the results, oxygen and carbon dioxide pressures, vital capacity, forced vital capacity and FEV1 ($p>0.05$), while the results related to substance P, bicarbonate concentration and pH were abnormal ($p<0.05$) and subsequently. They will be analyzed with their own tests (Man-Whitney). Independent t-test was used to evaluate and compare the data obtained in this study

with normal values.

4. Results

4.1 Evaluation of Serum Level of Substance P in Participants

The results of this study showed that the serum level of substance P in men was 6.33 ±14.13 ng/ml and in women 11.44 ±28.23 ng/ml.

The results obtained from the analysis of data on serum substance P level in the participants showed no significant difference between the participants. Studies have shown that the amount of substance P is 2.86±1.47 ng/ml [16, 17]. Considering the normal range of substance P, the amount of this compound in the study participants was significantly higher than normal (p = 0.035). (Table 1)

Table1: Evaluation of the serum level of substance P in participants (ng / ml) in the study by sex

Max	Min	Standard Deviation	Average	Number	Gender
60	*0	14.01	6.33	30	**Male**
115	0	28.23	11.44	30	**Woman**

*Serum levels of less than 0.1 ng / ml were diagnosed by the device as undetermined and -0

4.2. Arterial Blood Analysis

The participants' arterial blood analysis is reviewed. The findings of this study showed that the arterial blood pH was 7.35±0.06 in men and 7.36±0.05 in women. There was no significant difference between participants.

Analysis of data and comparison of mean bicarbonate concentrations in arterial blood of men and women showed no significant difference between the two groups (p = 0.141). Studies have shown that bicarbonate concentrations in the arterial blood are 22-28 mEq [18, 9]. Regarding the normal bicarbonate range and comparing it with the data obtained in this study, there was no significant difference (p = 0.372) (Table2 and Table3).

Table 2: Evaluation of arterial blood pH in participants by sex

Max	Min	Standard Deviation	Average	Number	Gender
7.5	7.2	0.06	7.35	30	**Male**
7.4	7.2	0.05	7.36	30	**Woman**

Data on arterial bicarbonate concentrations show that this compound is 26.2±5.1 mmol / l in men and 27.69±4.43 mmol / l in women

Table 3: Evaluation of arterial blood bicarbonate ion content (in milli-valency per liter) in participants by gender

Max	Min	Standard Deviation	Average	Number	Gender
43.5	19.4	5.10	26.2	30	**Male**
37.6	20.2	4.43	27.69	30	**Woman**

4.3. Evaluation of Arterial Blood Pressure

The data obtained in this study show that oxygen pressure in men is 50.87±19.15 mmHg and in women is 49.91±20.2 mmHg.

Studies on the data from the analysis of arterial blood gas in the participants showed that there was no significant difference between men and women in this factor (p = 0.851). Studies show that the normal arterial oxygen pressure is 75-100 mmHg [19]. In this case, the level of oxygen pressure in the study participants was significantly lower than its normal level (p = 0.0001) (Table 4).

Table 4: Arterial Oxygen Gas Pressure Evaluation in Participants (in mm Hg) by Gender

Max	Min	Standard Deviation	Average	Number	Gender
96	12	19.15	50.97	30	**Male**
92.6	13	20.20	49.91	30	**Woman**

4.4. Evaluation of Arterial Carbon Dioxide Gas Pressure

The data show that arterial carbon dioxide gas pressure in men is 42.46±14.29 mmHg and in women is 45.09±11.66 mmHg.

Analyzes also showed no significant difference in arterial carbon dioxide gas pressure between the opposite sexes (p = 0.438). According to studies, the normal range of arterial carbon dioxide pressure in a healthy adult is 38-42 mm Hg. Regarding this case, the level of carbon dioxide pressure in the study participants was higher than its normal level while there was no significant difference (p = 0.058) (Table 5).

Table 5: Assessment of carbon dioxide gas pressure (in millimeters of mercury) in participants by gender

Max	Min	Standard Deviation	Average	Number	Gender
96	12	19.15	42.46	30	**Male**
92.6	13	20.20	45.09	30	**Woman**

4.5. Evaluation of Spirometric Data

The data obtained for the evaluation of the participants' vital capacity indicate that this rate is 2.92±0.87 liters in men and 2.61±0.65 liters in women.

Analysis of data on the survey of the critical capacity of participants showed that this factor did not have a significant difference among the opposite sexes (p=0.121). According to studies by Pemberton et al., Normal levels of vital capacity in the adult are 3-5 liters [20, 21]. Concerning this case, our data show that the vital capacity of the participants in this study was significantly lower than its normal value (p=0.0001) (Table 6).

Table 6: Critical capacity (in liters) of participants by gender

Max	Min	Standard Deviation	Average	Number	Gender
5.4	1.8	0.87	2.92	30	**Male**
4.3	1.5	0.65	2.61	30	**Woman**

4.6. Evaluation of Mandatory Vital Capacity (FVC) Data

The analysis of data on this factor showed that FVC was 2.8±0.84 liters in men and 2.48±0.63 liters in women.

Evaluation of the data shows that there is no significant difference in the critical capacity factor among the opposition movements (p=106). Studies have shown that the range of normal forced vital capacity ranges from 5.5 to 3.6 L in healthy and healthy adults [22]. According to this finding, our findings show that the amount of mandatory critical capacity in the study participants was significantly lower than the normal level of this factor (p=0.0001) (Table 7).

Table 7: Mandatory Critical Capacity (in Liters) by Participants by Gender

Max	Min	Standard Deviation	Average	Number	Gender
2.92	5.4	1.8	2.8	30	**Male**
2.61	4.3	1.5	2.48	30	**Woman**

4.7. Evaluation of FEV1 Levels in participants

Evaluation of data from factor FEV1 (the air that exits the lungs during the first second of forced expiratory pressure) shows a rate of 2.31±0.71 liters in males and 2.07±0.54 liters in females is.

Evaluation of the data showed that there was no significant difference between the data obtained from the FEV1 between men and women in the study (P=0.148). Findings from various studies have shown that the normal FEV1 suffering in healthy and healthy individuals is 3.2 to 4.7 liters [22]. With this in mind, our findings show that FEV1 levels in the study participants were significantly lower than normal (p=0.0001).

In general, the data show that there is no significant difference between men and women in the tested factors. Comparison of the above data with their normal values in healthy samples indicates that there is a significant difference between our findings and their normal values. Correlation statistical tests were used to evaluate the relationship between the indices studied with substance P. These tests are based on the normal distribution of data and parametric-non-parametric indices including Pearson and Spearman tests (Table 8).

Table 8: Evaluation of FEV1 (in liters) in participants by gender

Max	Min	Standard Deviation	Average	Number	Gender
4.2	1.2	0.71	2.31	30	**Male**
3.4	1.15	0.54	2.07	30	**Woman**

5. Discussion

The results showed that substance P was inversely and positively correlated with arterial oxygen content (pO2) (r = -0.30, p = 0.82), and arterial carbon dioxide carbon (pCO2) positively and positively (r = 0.13, P = 0.299), VC positive and weak relationship (r=0.15, p=0.233), mandatory (FVC) positive and weak relationship (r=0.15, p=0.23), FEV1 positive and weak relationship, (r=0.15, p=0.238). Also, based on the evaluation of correlation using nonparametric test, the relation of substance P with negative and weak pH (r = -0.14, p = 0.286) and inverse and weak relationship with bicarbonate ion (HCO3-) (r = 0.018, p = 0.89) has it.

In other words, based on the analyzes performed with the above tests, our data show that the serum P content in the study participants is directly related to spirometric parameters (vital capacity, mandatory vital capacity, and FEV1).

Also, the association of substance P with arterial blood parameters including bicarbonate ion (HCO3-) and oxygen pressure (pO2) was inversely and poorly evaluated. These findings indicate that changes in serum P levels were inversely related to these two variables and had little effect on their changes. Also, the relationship between the serum level of substance P and the pH was inverted and weak, so that as the substance P increases, the pH of the arterial blood becomes highly acidic. Also, the relationship between substance P and carbon dioxide was direct and weak, with increasing amount of substance P increasing carbon dioxide and decreasing CO2.

The results showed that the serum levels of substance P in the study participants were significantly higher than the normal level, while there was no significant difference between the participants in terms of gender. In other words, these results suggest that in patients with asthma, substance P levels increase and gender does not affect them.

6. Conclusion

In this study, spirometry parameters in asthmatic patients were significantly decreased compared to control group. It was also found that S P increases the production and secretion of reactive oxygen species from macrophages and neutrophils and significantly reduces antioxidant capacity in these patients. In this study, lavage fluid from patients compared to control group showed higher S P concentration in patients than control group.

Our study also found that the level of S P in asthmatic patients was significantly higher than in their normal range. Also, in line with the findings of the above article, the vital capacity and FEV1 in asthmatic patients were significantly reduced compared to normal suffering. Taking these results into account, it can be seen that both studies have been performed in one way and the results are consistent [10].

A study by Springer and colleagues showed that oxidative stress and its damage could be due to activation of S P. In a study of A549 lung cancer cells, we identified the transcription factor AP-1 that induces inflammatory processes and the production of cytokines and chemokines that induce inflammatory processes during oxidative damage and increase in reactive oxygen species. Activates pro-inflammatory and pro-inflammatory cells has a direct relationship with SP.

Based on the findings of this study, S P could be effective on the expression of AP-1 and its downstream proteins, which induce the expression of inflammatory cytokines and chemokines. These findings indicate that SP has been shown to be effective in the development and inflammation of inflammatory responses, and is probably one of the reasons for the increase in inflammatory and fluid lavage tissue obtained from asthmatic patients with an effect on the persistence of inflammation and associated oxidative damage. With it [11].

In our study, it was also found that the serum level of SP in patients significantly increased compared to normal subjects. Overall, our findings suggest that SP may increase significantly in inflamma-

tion cases, leading to a sustained inflammatory response and the production of pro-inflammatory and inflammatory cytokines.

What has been studied so far about S P and its effects was the effects of this compound on induction of oxidative stress and persistence of inflammatory responses. In other words, until this part of the study, S P has been shown to induce and induce oxidative responses and, as a neuropeptide, stimulate the expression of pro-inflammatory and pro-inflammatory cytokine genes. Our study also found that the level of SP in patients with asthma was significantly higher than its normal level.

In a 2016 study by Sang-Min Baek and colleagues, significant results were obtained that challenged the interpretation of the effect of SP compound on physiological responses. In this study, SP was found to be able to repair oxidative damage. In other words, this compound, as it causes inflammation and increases expression of inflammatory cytokines, can reduce the damage caused by oxidative damage and ameliorate these damages [23]. In summary, in this study H2O2 was used as an oxidant for corneal granule cells to evaluate the role of SP. The findings of this study showed that SP can modulate the damage induced by oxidative stress and H2O2 by activating the Akt/GSK-3β signaling pathway and induce remission [23].

Based on the findings of this study, it was found that the serum SP level in the study participants was significantly higher than the normal level. On the other hand, spirometer results showed that the vital capacity, mandatory vital capacity and FEV1 in the participants were significantly decreased and were inversely related to SP. Arterial blood parameters showed a significant decrease in oxygen gas pressure and carbon dioxide and were inversely correlated with serum SP levels.

Considering the findings and various studies, it can be concluded that the level of SP in asthma patients is increased and this increase may be in order to continue the inflammatory reactions that require protection of the body against harmful factors. On the other hand, increased SP according to recent studies could be related to the repair of oxidative damage, suggesting the role of this substance as a factor in tissue homeostasis.

In general, the composition of SP in asthmatic patients increased while spirometric and arterial parameters decreased. Based on these findings, it can be concluded that SP may be a factor in assessing and predicting asthma status in patients.

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