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Original Research Article

BLOOD BIOMARKERS AS A NOVEL SCREENING TOOL FOR OSA –AN INSTITUTIONAL STUDY

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ABSTRACT

Background: Laparoscopic cholecystectomy using low-pressure pneumoperitoneum (7–10 mmHg) may reduce postoperative shoulder tip pain and physiological complications compared to standard pressure (12–14 mmHg), although it may affect operative exposure and duration. This study compared postoperative shoulder tip pain between low- and standard-pressure pneumoperitoneum in laparoscopic cholecystectomy. **Materials and Methods:** This cross-sectional study was conducted in 100 patients at Government Theni Medical College over 1 year. Patients undergoing elective laparoscopic cholecystectomy were divided into two groups: low-pressure and standard-pressure pneumoperitoneum. The surgeries followed a standard technique with uniform anaesthesia. Postoperative pain, including shoulder tip pain, was assessed using a visual analogue scale at 6, 12, and 24 hours, along with analgesic requirements. **Result:** Patients in Group A reported significantly lower postoperative shoulder tip pain scores at all measured time points from 1 h to 3 days ($p < 0.001$). Group A also had a shorter mean hospital stay (2.36 vs. 3.12 days, $p<0.001$), although the mean duration of surgery was longer (93.2 vs. 83.6 min, $p=0.012$). The incidence of shoulder tip pain was significantly higher in Group B (84%) than in Group A (48%) ($p<0.001$). While both groups were predominantly female, Group A had more patients aged >50 years, whereas Group B had more aged <40 years ($p=0.038$). **Conclusion:** Lowering pneumoperitoneum pressure to 10 mmHg during laparoscopic cholecystectomy significantly reduced postoperative shoulder tip pain and analgesic requirements without affecting surgical outcomes. Although it slightly prolongs the operative time, it improves patient comfort without a significant haemodynamic impact.

INTRODUCTION

OSA is a disorder which is commonly associated with repetitive episodes of nocturnal breathing suspension where upper airway collapse is noticed with Nasopharynx being the commonest site of Obstructive sleep apnoea (OSA). The most common site of obstruction is nasopharynx. First description of the disorder was done in 1965.[1] Majority of the patients with clinical signs of OSA have never been diagnosed or treated.[2] The health consequences of obstructive sleep apnea are numerous and the highest prevalence was reported among middle-aged men when compare to women.[3] Symptoms of OSA are loud snoring, hyper somnolence (hallmark of OSA), feeling of chocking, restless and unrefreshing sleep, change in personality, and nocturia, It also includes features like excessive daytime sleepness, morning headache, impaired memory and concentration, reduced intellectual ability and disturbed personality and mood.[5,6]

The cause of this disorder includes a complex interplay between neuromuscular factors, anatomic and an underlying genetic predisposition,[7] Risk factors includes middle age, male gender, obesity, snoring, menopause in women and a variety of oropharyngeal and craniofacial features such as a low-lying soft palate, large neck circumference, micrognathia, macroglossia, adenoids, enlarged tonsils and nasal obstruction,[7] add to the severity of the disorder.

Diagnosis of OSA is based on history, physical examination, radiographs, polysomnography and blood bio markers. The American Academy of Sleep Medicine clinical practice guidelines stated that more accurate and user-friendly screening tools like numerous individual OSA blood biomarkers or combination can be used to diagnose OSA.[8,9]

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Abnormalities in endocrine systems and metabolic systems induced by OSA are associated with alterations in biomarkers. These biomarkers include erythropoietin (EPO), C-reactive protein (CRP), glycated hemoglobin (HbA1c), uric acid and interleukin-6 (IL-6).[10]

Aims and Objectives

The aim of the present study was to determine the relationship between OSA and the three blood biomarkers in patients with a clinical speculation of OSA. The main objective of the study was to specifically assess the circulating levels of three inflammatory biomarkers erythropoietin (EPO), C-reactive protein (CRP), glycated hemoglobin (HbA1c) in a small population of consecutively enrolled, untreated and otherwise healthy OSA patients

MATERIALS AND METHODS

Study Setting and Duration

This prospective observational study was conducted in the Department of Oral Medicine and Radiology, Meghna Institute of Dental Sciences, Nizamabad, Telangana, over a period of six months, from June 2020 to December 2020.

Study Population and Sampling

A total of 40 middle-aged male subjects were recruited through consecutive sampling. The study group consisted of 20 subjects with a clinical history suggestive of obstructive sleep apnea (OSA), and the control group comprised 20 healthy male subjects without any OSA symptoms.

Inclusion Criteria

Male patients in the middle-age group

For the study group: clinically suspected OSA based on presenting symptoms

For the control group: no clinical history or symptoms of OSA

Exclusion Criteria

Previously diagnosed and treated cases of OSA

Current use of chronic anti-inflammatory drugs, corticosteroids, or long-term analgesics

Clinical Assessment and Questionnaire

Participants completed a structured questionnaire addressing four symptom-related parameters:

Snoring

Elevated blood pressure

Daytime tiredness

Witnessed apneas

In addition, demographic details, age group, and body mass index (BMI) were recorded.

Sample Collection and Biomarker Analysis

Venous blood samples were collected from all participants during enrollment, prior to initiation of any therapy. Blood was drawn into EDTA tubes and serum separator tubes (SST). The following biomarkers were analyzed:

Erythropoietin (EPO)

C-reactive protein (CRP)

Glycated hemoglobin (HbA1c)

All assays were performed using standard laboratory protocols. Clinicians interpreting diagnostic sleep studies were blinded to biomarker results to avoid bias.

Statistical Analysis

Data were analyzed using the independent sample t-test to compare biomarker levels between the study and control groups. Statistical significance was set at $p < 0.05$.

Ethical Considerations

Approval was obtained from the Institutional Ethics Committee of Meghna Institute of Dental Sciences before study initiation. Written informed consent was obtained from all participants after explaining the study objectives and procedures in their local language.

RESULTS

40 male subjects were enrolled in the study with range of 40 to 60 years age, with 20 in the study group and 20 in control group. Study result showed that the most significant associations of biomarkers with obstructive sleep apnea severity indices were for erythropoietin (EPO) followed by C-reactive protein. Specifically statistical significant correlations were observed in study group compared to control group for EPO as the p value of <0.01 and CRP; p value of <0.05 statistically non significant correlations was observed for HBA1C with the p value of >0.05 among study and control group. And the study also proved that individuals with increasing BMI showed significant increase in OSA compared to control group with the mean difference of 5.553.

Table 1: Shows mean comparison between control and study group of BMI

VARIABLES	GROUP	MIN	MAX	MEAN	SD	MEAN±SD difference	t value	P value
BMI	CONTROL	18	24.9	22.81	1.98	5.53±0.21	8.379	--
	STUDY	23.6	31	28.34	2.19			
EPO	CONTROL	4	9	5.89	1.58	9.43±3.39	8.093	0.001 Significant
	STUDY	6	23	15.32	4.97			
HB A1C	CONTROL	4.1	6	5.1	0.56	0.3±0.02	1.214	0.06 Not Significant
	STUDY	5	6.8	5.4	0.58			
CRP	CONTROL	0	0.1	0.03	0.04	0.07±0.05	5.702	0.04 Significant
	STUDY	0.6	0.6	0.1	0.09			

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DISCUSSION

A perfect biomarker should possess some critical characteristics, such as disease specificity, mandatory presence in all affected patients (i.e., high sensitivity and specificity), and reversibility following proper treatment, and delectability before patients develop obvious clinical manifestations. Ideal biomarkers should reveal not only the severity of the disease, but also be indicative about the cumulative history of the disease, as well as allow a cut-off value with minimal intersection between normal and disease.[13] In addition, an ideal diagnostic biomarkers would be relied upon to diminish the expense and weight of diagnosing a patient,[14] Most of the studies evaluated blood biomarkers, with only few studies having evaluated either urine, saliva and/or EBC, although such methodologies are noninvasive and effectively gathered, and especially appropriate for kids and youngsters.

In our study EPO biomarker was obtained more significant in study group when compared to control group followed by CRP biomarker. There was no significant difference in the levels of HBA1C in control and study group. OSA-induced hypoxia is associated with increased EPO concentrations, and EPO decreases after continuous positive airway pressure (CPAP) therapy in those with OSA.[17,18] Healthy people exposed to hypoxia show expanded EPO.[19] EPO promotes the formation of red blood cells; the mild EPO elevations (≥8mIU/mL) observed in OSA patients in this study may represent a response to hypoxia.

Therefore, there is a biological plausibility for including EPO in the biomarker panel for OSA. As a part of routine dental examinations dentist can recognize a small upper airway and other anatomic risk factors for OSA, and have an opportunity to under diagnosis of OSA through use of simple questions. Both sleep physician and dentist have essential roles in the treatment of OSA with oral appliance therapy (OAT).[20]

The results of the present study are in accordance with studies conducted by Wesley elonfleming et al, with respect to EPO and CRP but not with HBA1C. This non-significant result of HBA1C can be attributed to the method of selection in our study group. The OSA patients in our group were selected based upon the clinical symptoms and BMI, a thorough evaluation of the patient based on sleep studies and including patients only with moderate to severe OSA would have given a much clear and better results.[21]

Studies have reported independent association between OSA, insulin resistance and diabetes with mild to moderate elevation of HBA1C (≥ 5.7%) level suggestive of prediabetes. Patients with increased BMI were found to show insulin resistance which would further contribute to the onset of Prediabetes. Since OSA patients had increased BMI, the increased levels of HBA1C might be due to insulin resistance.

A number of studies have observed increased serum CRP levels in OSA. This correlation is attribted to the reason that long-term sustained hypoxia in OSA patients will lead to activated inflammatory responses resulting in elevated levels of proinflammatory cytokines.[22]

Studies in large cohorts need to further validate our study findings and to evaluate the diagnostic utility in additional patient subgroups including women, further studies correlating combination biomarkers and OSA should be conducted. Cost effectiveness of these screening tools and their result, follow up should also be done.

In non-obese subjects, the biomarker combination was superior to BMI in predicting OSA. The target of this planned examination was to assess the utilization of blood biomarkers, exclusively to screen OSA in grown-up men. This validation study was conducted in order to replicate findings from a prior feasibility study.[15] The AASM reports that blood biomarkers may be useful in identifying individuals at risk for OSA. Implementing OSA biomarker screening by primary care providers in high-risk populations could significantly improve the accuracy of sleep specialist referrals and ultimately improve patient outcomes.[16] The biomarker associates with OSA seriousness, with attendant rise of EPO and CRP showing a high likelihood of moderate/extreme OSA.

CONCLUSION

Hence we conclude that OSA is related with trademark signature group of biomarker changes in men. Hence concurrent elevation of EPO level should generate high suspicion of OSA and may have utility as an emerging diagnostic tool. Therefore, these may assist sleep centers in identifying and triaging high risk patients for sleep study diagnosis and treatment.

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