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The Effect of Mometasone Furoate Nasal Spray on Blood Oxygenation in Allergic Rhinitis Patients

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ABSTRACT

Allergic rhinitis (AR) is a disease that presents with symptoms like nasal discharge, blockage, and itchiness, which impair the quality of life of most patients depending on its severity. The most common symptom in AR patients is a persistent bilateral nasal blockage, which may indirectly and potentially affect the airflow into the lung. However, the symptoms can be controlled using intranasal steroid spray (INS). This study investigated the role of nasal obstruction in lowering blood oxygenation and how INS improved blood oxygenation. This study included 33 patients with AR. Subjects with moderate-to-severe nasal obstruction were recruited based on the Visual Analogue Scale (VAS), and mometasone furoate nasal spray (MFNS) – two puffs twice a day for two weeks was given. Pre- and post-medication parameters compared included nasal obstruction VAS, partial oxygen arterial pressure (PaO2), partial arterial carbon dioxide pressure (PaCO2), and oxygen saturation (O2 saturation). All parameters were substantially different between pre- and post-medication. VAS, PaO2, PaCO2, and O2 saturation were significantly different before and after medicine ($p<0.01$). A comprehensive treatment of nasal obstruction using MFNS helps improve blood oxygenation and nasal obstruction in AR patients.

INTRODUCTION

Rhinitis is defined as inflammation of the nasal cavity and can be divided into allergic rhinitis (AR) and nonallergic rhinitis (NAR). AR is a combination of two or more nasal symptoms, such as rhinorrhoea, nasal congestion, nasal itchiness, and excessive sneezing. Signs of AR include hypertrophy of the turbinates, pale overlying nasal mucosa, especially over the turbinates, allergic shiners, the Dennie-Morgan line, and the nasal crease. AR is a symptom that results from IgE-mediated inflammation following exposure to allergens. AR can be classified into four types according to Allergic Rhinitis and its Impact on Asthma (ARIA) Guidelines (Hellings et al., 2019): mild AR, intermittent AR, persistent AR, and moderate to severe AR.

AR is a widespread condition affecting millions of people and is a known global health problem. The incidence of AR is steadily increasing within the general population, including adult and paediatric populations. According to the Allergies in Asia Pacific Survey (Katelaris et. al. 2011), AR is common across the Asia Pacific population, affecting approximately 10% of the population. In Malaysia, a study in the paediatric community showed the overall incidence of rhinitis symptoms at 27%, with a significantly higher prevalence in the 12 – 14 years age group (38.2%) than in the five to seven years age group (18.2%) (Asha'ari et al., 2010).

Among the most common troublesome symptoms for AR patients is a nasal blockage (DeShazo & Kemp, 2021). The allergen responses in the nasal mucosa, mediated by the various complex interactions among inflammatory markers, initiate the cascades of inflammatory mediator release (Passalacqua et al., 2007. As a result, it causes mucus gland stimulation and increases vascular permeability, resulting in nasal obstruction from increased secretions, oedema, and exudate formation (Chhabra & Houser, 2011). The enlargement of the nasal turbinates can also be due to mucosal or bony hypertrophy (Leong et al., 2010).

In AR patients, the duration of nasal obstruction symptoms is variable, but most commonly they occur in the morning and at night (Aoyagi et al., 1999). In severe AR, this symptom disturbs daily activities as well as causes the patient to mouth-breathe. Mouth breathing affects adults and children with chronic nasal obstruction by causing dry mouth and throat, eventually leading to sore throat and foreign body sensations, as well as hoarseness and postnasal drip due to the inability of nasal discharge to drain anteriorly (Chhabra & Houser, 2011; Leong et al., 2010). Apart from that, chronic nasal obstruction is believed to be related to chronic headaches, which occur more frequently in children with nasal obstruction and persistent rhinorrhea as compared to a normal child (Schoustra et al., 2022). Chronic nasal obstruction also has a role in determining the severity of sleep-disordered breathing (Passàli et al., 2004; Kim et al., 2013). Mclean et al. showed that by eliminating nasal obstruction and therefore reducing mouth breathing, a reduction in the severity of OSA might be achieved, if not totally resolving it (McLean et al., 2005; An et al., 2019).

Airway obstruction via nasal congestion can reduce arterial oxygen and induce hypoxia in tissues, especially if it is not properly compensated by mouth breathing (Bayrak et al., 2010). Studies have also shown that by creating nasal obstruction through nasal packing, which eliminates nasal breathing, the patient may suffer from pulmonary and cardiac problems along with complications such as hypoxia, myocardial infarction, cerebrovascular accident (CVA), and sudden death (Bayrak et al., 2010). The study also showed evidence of changes in blood gas values caused by alveolar hypoventilation, airflow obstruction, and a reduction in alveolar gas diffusion and ventilation/perfusion ratios (Bayrak et al., 2010). An experiment on dogs by Cavo et al., demonstrated that posterior nasal packing also induced arterial hypoxia and hypercapnia, which later returned to normal after packing removal (Cavo et al., 1975; Lin et al., 1979). In a study done by Zayyan et al., patients with total nasal obstruction showed no changes in partial arterial oxygen pressure (PaO_2) or oxygen saturation (O_2 saturation), but their partial arterial carbon dioxide pressure ($PaCO_2$) values decreased due to mouth breathing and increased breathing rate (Zayyan et al., 2010; Banglawala et al., 2013; Banglawala et al., 2014).

Clinically, there are two ways to measure the degree of nasal obstruction, which can be divided into subjective and objective measurements (Mohan, 2018). The subjective measurement includes the use of a visual analogue scale (VAS) and the physician's assessment of nasal obstruction following anterior rhinoscopy. Its measurement will determine the effect of treatment on nasal symptoms via scores given by the patient. VAS is one of the subjective methods for determining the degree of nasal obstruction. VAS is calculated using a 10-point scale or a 100-mm scale (Mora et al., 2009). Mora et al. concluded that clinically, VAS had good reliability to quantify nasal obstruction symptoms in the absence of rhinomanometry (Mora et al., 2009).

The use of objective measurement for nasal obstruction allows the physician to identify the location of the blockage and to evaluate the post-treatment effect on nasal airflow, volume, and physiology. Objective measurements include methods such as acoustic rhinometry, rhinomanometry, nasal inspiratory peak flow, rhinostereometry, radiographic techniques, and videoendoscopic documentation (Meltzer et al., 1998; Bernstein et al., 2012).

Medical treatment is the main option to treat AR. For temporary relief of nasal congestion symptoms, a nasal decongestant significantly reduced the nasal mucosal oedema associated with AR (Zicari et al., 2012). In their study, Zicari et al. discovered that after administering a nasal decongestant to patients with nasal obstruction, upper airway resistance decreased (Zicari et al., 2012). Aside from the temporary effect of a nasal decongestant, nasal steroid spray is more effective and long-lasting in reducing nasal obstruction in AR patients. Studies by Meltzer et al. and Bernstein et al. showed that MNS had an anti-inflammatory effect thus reducing the allergen's ability to cause an influx of basophils and mast cells into the airways. The dosage was according to the standard dosing in the treatment of AR practised in Hospital Universiti Sains Malaysia. (Meltzer et al., 1998; Bernstein et al., 2012). Apart from that, mometasone furoate is proven safe to be administered through the nose despite being highly potent, it is almost undetectable in plasma samples obtained after oral or intranasal administration in an adult due to its rapid and extensive metabolism. Meltzer et al. (1998) concluded that a daily dose of 50, 100, or 200 ug/dL did not affect the hypothalamus pituitary adrenal (HPA) axis in 96 paediatric patients (Brannan et al., 1997; Ow et al., 2022).

To determine the effect of nasal obstruction on blood oxygenation, arterial blood gases (ABG) were taken from the artery and analysed clinically. ABG is a useful parameter in assessing blood oxygen levels because it measures the partial pressure of oxygen (PaO_2) in arterial blood, which indicates how well the lungs are oxygenating the blood. ABG analysis can detect four major categories of acid-base disorders i.e., acidosis and alkalosis in respiratory and metabolic. Respiratory acidosis is an acid-base imbalance that can occur when the upper airway is obstructed. This kind of obstruction, if not compensated for by the body, will result in an acidotic pH, high carbon dioxide partial arterial pressure, and low partial oxygen pressure.

This study looked at nasal obstruction in AR patients and its impact on ABG. Even though nasal obstruction does not cause life-threatening acute airway obstruction in adults, the symptoms of nasal obstruction in AR patients are sometimes severe enough to disturb patients' daily activities. However, the literature available looking into the effect of blood oxygenation in nasal obstruction patients is a study that showed patients with nasal packing had mild hypoxemia and decreased oxygen saturation. The study showed that elimination of nasal obstruction improved pulmonary functions and oxygenation was significantly improved one-week postoperative following removal of the nasal pack (Sobh et al., 2021). The intranasal steroid nasal spray (INS) used in this study was mometasone furoate nasal spray (MFNS), which is widely available throughout Malaysia. One of the aims of this study was to find out the effect of MFNS on blood oxygenation in a patient using the maximum daily dose of 400 mcg per day. The authors hope that the improvement in blood oxygenation through reducing the symptoms of nasal obstruction may provide long-term medical benefits for AR patients.

MATERIALS AND METHODS

This was a prospective cross-sectional study of AR patients who attended the otorhinolaryngology clinic at HUSM in Kubang Kerian, Kelantan. Patients aged 18 to 35 were chosen as sample populations. The inclusion criteria included nasal obstruction symptoms with a VAS ranging from four to ten (the persistent group of AR) and recent use of INS for more than one month. The exclusion criteria were chronic medical disorders of the respiratory system, cardiac disease, haematological disorders, and neurological disorders. Subjects with a severely deviated nasal septum, an intranasal tumour, obstructive sleep apnoea, or who had undergone intranasal surgery were also excluded. The study was approved by the Universiti Sains Malaysia ethical research committee, and written consent was obtained from all the subjects.

A thorough history was taken for each subject, and the patient was subjected to a visual analogue scoring system to determine the severity of nasal obstruction symptoms. It ranges from zero (no obstruction) to ten (complete obstruction). The patient was asked to tick over the line corresponding to their perception of nasal obstruction. A physical examination involving anterior rhinoscopy and rigid nasoendoscopy was performed on patients with a visual analogue score of four or higher for nasal obstruction to rule out the presence of severe septal deviation, synechiae, nasal tumours, polyps, and adenoid hypertrophy.

ABG was taken from the patient prior to prescribing the INS. The ABG was taken from the patient's radial artery (the area was applied with a topical anaesthetic cream that contained a combination of lidocaine and prilocaine i.e., EMLA) using a pre-heparinized 23-gauge, 25 mm (1 inch) 2 ml syringe. The main parameters obtained from ABG were PaO_2, $PaCO_2$, and O_2 saturation. The patient was instructed to apply MFNS – two puffs per nostril, twice a day for two weeks. During the patient's follow-up, two weeks later, they were assessed again using the VAS regarding the nasal obstruction symptoms, and a repeat ABG sampling was taken. The chosen statistical method was the paired t-test, and the data analysis was performed using Statistical Package for Social Sciences (SPSS) version 20.

RESULTS

This study recruited a total of 33 subjects which included 28 Malays, two Chinese, two Indians and one Siamese (classified as others). There were 13 male (39.4%) and 20 female (60.6%) subjects involved and the patient's mean age was 28.21 years. The VAS post-medication showed marked improvement (Table 1). All the subjects showed improvement in their rhinitis symptoms including nasal obstruction. This also indicated that all the subjects were compliant with their treatment. The mean parameters obtained from the ABG in both premedication and post-medication showed a decrease in the mean except for $PaCO_2$ (Table 2).

Table 1 Premedication and post-medication VAS mean

Variables	n	Mean (SD)
Premedication VAS	33	7.15 (1.25)
Post-medication VAS	33	2.85 (1.12)

SD = Standard deviation, VAS = Visual Analogue Scale

Table 2 Premedication and post-medication mean of PaO_2, $PaCO_2$ and O_2 saturation

Variables	n	Mean (SD)
Premedication PaO_2	33	123.16 (15.13)
Post-medication PaO_2	33	111.89 (15.18)
Premedication $PaCO_2$	33	31.52 (3.53)
Post-medication $PaCO_2$	33	33.02 (3.36)
Premedication O_2 Saturation	33	97.90 (0.65)
Post-medication O_2 Saturation	33	97.46 (0.76)

SD = Standard deviation, PaO_2 = Partial pressure of Oxygen, $PaCO_2$ = Partial pressure of Carbon Dioxide, O_2 = Oxygen

A t-test was used to compare the premedication and post-medication differences between VAS, PaO_2, $PaCO_2$, and O_2 saturation. There were significant differences (p<0.01) between all the variables in the premedication and post-medication except for $PaCO_2$ (Table 3). It showed that only subjectively did the nasal symptoms improve, as all the variables and measures showed a significant difference.

Table 3 Comparison between premedication and post-medication results

Variables	Premedication mean (SD)	Post-medication mean (SD)	Mean difference (95% CI)	t-statistic (df)	*p*-value
VAS	7.15 (1.25)	2.85 (1.12)	4.30 (3.84, 4.77)	18.86 (32)	p< 0.01
PaO_2	123.16 (15.13)	111.89 (15.18)	11.26 (6.38, 16.15)	4.697 (32)	p< 0.01
$PaCO_2$	31.52 (3.53)	33.02 (3.36)	-1.50 (-2.83, -0.16)	-2.283 (32)	0.029
O_2 Saturation	97.90 (0.65)	97.46 (0.76)	0.44 (0.18, 0.70)	3.441 (32)	p<0.01

SD = Standard deviation, CI = Confidence interval, df = Degrees of freedom, VAS = Visual Analogue scale, PaO_2 = Partial pressure of Oxygen, $PaCO_2$ = Partial pressure of Carbon Dioxide, O_2 = Oxygen

DISCUSSION

In AR patients, nasal obstruction is one of the hallmark symptoms that may determine the severity of AR itself. Looking back at the pathogenesis of nasal obstruction in AR, which consists of three events; inflammation of the mucosa, congestion of nasal blood flow, and excessive secretions of mucous, these events do cause significant obstruction to the upper airway (Bousquet et al., 2020). This obstruction will reflect the respiration process. Theoretically, the arterial oxygen and carbon dioxide composition in the blood will be affected by any airway obstruction, alveolar hypoventilation, and reduced gas diffusion (Zayyan et al., 2010; Banglawala et al., 2013; Banglawala et al., 2014).

To maintain blood oxygenation, individuals with nasal obstructions prefer to breathe through their mouths. This is a physiologic compensatory mechanism in response to hypoxia due to nasal obstruction. The change of route of respiration from nasal to oral supposedly may or may not affect the blood gas parameters, which include PaO_2, $PaCO_2$, and O_2 saturation, as shown in a study by Zayyan et al. (2010) who evaluated the effects of nasal packing post-septoplasty and septorhinoplasty on cardiac function and blood arterial gases and found that there was no significant difference in pH, PaO_2, or O_2 saturation. However, he noted that there was a reduction in $PaCO_2$, and he later concluded that it was due to oral breathing because of nasal obstruction (Zayyan et al. 2010). Similarly, a study by Lin et al. (2015) and Yildirim et al. (2016) found that although nasal obstruction caused a decrease in oxygen saturation levels in the blood, the decrease was not significant enough to cause hypoxia or other adverse effects, and both studies concluded that these findings may vary depending on the severity and duration of the obstruction, as well as other individual factors such as rate of breathing, current lung function status, current metabolic status, and health condition (Lin et al., 2015, Yildirim et al., 2016). Our study also showed significant changes in the variables except for $PaCO_2$, which may indicate that the patient is breathing orally due to an obstructed nose.

The evaluation of nasal obstruction can be done subjectively and objectively. Rhinomanometry, acoustic rhinomanometry, nasal peak flowmeters, and rhinostereometry are the objective measurements for nasal obstruction. These types of measurements will help the surgeon determine the severity of the obstruction (Moubayed & Most, 2022). The objective instrument requires a measurement instrument. In Malaysia, not all otorhinolaryngology clinics have this form of facility. This equipment is expensive, and the cost of maintenance is high. A subjective measurement of nasal obstruction includes patient-reported symptoms such as nasal congestion, stuffiness, and difficulty breathing through the nose (Baraniuk, 2011). The advantage of subjective measurement is that it provides insight into how the patient is feeling and how their symptoms are affecting their quality of life. However, it is subjective and can be influenced by factors such as anxiety, depression, and other psychological factors (Keeler & Most, 2016). A surgeon will rely on the patient to describe the severity of nasal obstruction symptoms in the subjective measurement, and it is more cost-effective. In this study, we used a subjective measurement via VAS to classify the severity of the nasal obstruction symptom due to the unavailability of the instruments mentioned above.

There are a few studies that verify the suitability of VAS results in conjunction with objective assessment i.e., rhinomanometry or acoustic rhinometry findings. Among others is a study by Mora et al. that utilised the VAS to quantify the subjective feeling of the nasal obstruction symptom in patients following turbinectomy, and in their study, they found that there was a significant and strong relationship between the VAS for nasal obstruction and nasal airflow resistance (measured by rhinomanometry) pre and post turbinectomy (Mora et al., 2009).

Another study, that aimed to investigate the correlation between VAS and acoustic rhinometry in children with no nasal symptoms, found a significant correlation between VAS and minimal cross-sectional area at baseline, but no correlation was found between VAS and acoustic values after decongestion and concluded that VAS showed potential as a subjective tool to investigate nasal obstruction in children over seven years of age (Haavisto et al., 2011). VAS may also be used as a surrogate for rhinomanometry, with adequate reliability. The study aimed to evaluate the relationship between VAS and nasal obstruction in patients with persistent allergic rhinitis and concluded that it was a reliable tool (Ciprandi et al., 2009).

Our study also investigated the effect of MFNS on nasal obstruction symptoms via three blood gas parameters: PaO_2, $PaCO_2$, and O_2 saturation. Zayyan et al. (2010) evaluated the effects of nasal packing post-septoplasty and septorhinoplasty on cardiac function and blood arterial gases and found that there was no significant difference in pH, PaO_2, or O_2 saturation. However, he noted that there was a reduction in $PaCO_2$, and he later concluded that it was due to oral breathing because of nasal obstruction. (Zayyan et al., 2010; Banglawala et al., 2013; Banglawala et al., 2014). These findings were similar to ours, which also noted that only the $PaCO_2$ had a significant difference ($p > 0.01$). Our study had control subjects that compared whether the changes in arterial blood gases were significant or not, therefore allowing us to establish any intranasal anomalies or patients already experiencing nasal blockage symptoms. Based on this study, we conclude that some arterial blood gas parameters, especially the PaO_2 and O_2 saturation, may remain the same even in a patient with chronic nasal obstruction.

Premedication

Our study showed that during the premedication period, the PaO_2 was higher than normal (mean PaO_2 = 123.16 mm Hg). The $PaCO_2$ mean was low at 31.52 mm Hg, and the oxygen saturation means stood at 97.9%, which was within the normal range. During this period, the results suggest that the patients were having hyperventilated ABG results due to a high oxygen intake and high carbon dioxide washout. The mean value of the VAS for the nasal obstruction symptom was high at 7.15, which suggests that patients were having nasal obstruction and breathing orally during this premedication period.

Nasal obstruction does contribute to low oxygen intake, which may cause hypoxia. This hypoxia will be compensated by the physiological response of the body to facilitate more air intake through oral breathing. A large volume of air intake explains why, during the premedication phase, patients have a higher PaO_2 value than normal. The same compensatory mechanism through oral breathing is also responsible for causing hypocapnia. In hyperventilation, more oxygen will be inspired, and at the same time, more carbon dioxide will be exhaled. This results in hypocapnia or carbon dioxide washout, which will cause a low reading of $PaCO_2$.

In oral breathing, the breathing rate is maintained in the normal range of 15 to 18 times per minute. However, the amount of inspired oxygen is increased, and less inspired air is trapped in the anatomical dead space because an oral breather bypasses the nasal cavity and nasopharynx. Oral breathing allows a greater amount of carbon dioxide to be washed out of the lungs as less restriction of airflow is encountered due to reduced nasal resistance.

Blood oxygen saturation, by definition, is a relative measure of dissolved oxygen that is carried in the blood. The oxygen percentage indicates that all available heme-binding sites in the blood haemoglobin level have been saturated with oxygen. This is why oxygen saturation levels never exceed 100%, and the normal range of oxygen saturation is around 96 to 100%. In our study, the mean premedication oxygen saturation was 97.9%, which was within the normal range.

Post-medication

After two weeks of using MFNS, we found that our patient demonstrated a lower VAS score with a mean of 2.85. The difference between pre- and post-medication VAS was significant. This indicates that our patient was experiencing a reduction in nasal obstruction symptoms, suggesting that MFNS did improve the subjective nasal obstruction symptom. This could be because there is less mucosal oedema on the nasal cavity surface, particularly along the lateral walls, allowing for a better laminar flow of air during inspiration. Vaidyanathan et al. (2021) noted that mometasone nasal spray effectively reduced nasal mucosal oedema and therefore nasal obstruction. The authors found that mometasone nasal spray significantly improved nasal obstruction compared to placebo or other intranasal corticosteroids, as measured by various symptom scores and objective measures of nasal airflow.

On assessing the post-medication arterial blood gases, we found that there was a reduction in the PaO_2 reading. The reading was still above normal, but there was still a significant difference between pre- and post-medication arterial pressure. It proves that by breathing through the nose, adequate oxygen can be inspired for normal respiration. We also noted that our patient had an improvement in $PaCO_2$ post-medication, where the mean was 33.02 mm Hg. This may be explained by the fact that when patients start to breathe through the nose, less carbon dioxide is expelled into the atmosphere due to the presence of nasal resistance. This will cause slight carbon dioxide retention in the lung. Apart from that, the slow release of air during expiration allows the lungs to maintain compliance and reduce the risk of lung atelectasis.

The post-medication oxygen saturation result showed that our patients had a normal oxygen saturation mean of 97.46%, which was within the normal range. Although the t-test analysis showed a significant difference between pre- and post-medication results, we believe that the oxygen saturation difference was not directly influenced by the transition from oral to nasal breathing. It is because it only measures how much the heme-binding sites of haemoglobin are saturated with oxygen. This value is under the influence of haemoglobin level, which was not measured during this study.

It appears that most of our patients were having less inspired oxygen and lower expired carbon dioxide washout from the lungs after two weeks of treatment with MFNS. Based on the VAS after medication, our patients started to breathe normally through the nose. This study showed that with an intensive course of MFNS treatment lasting two weeks, there was a reduction in the nasal obstruction symptom. Furthermore, this study showed a significant difference between pre- and post-medication parameters of PaO_2, $PaCO_2$, and VAS, demonstrating that nasal breathing had been achieved.

The usage of objective measurements such as acoustic rhinometry and rhinomanometry can further improve the data outcome. A larger sample size can increase statistical power and reflect more representative results in this study. Other modes of treatment, whether it be a single mode or in combination, can also be used to optimise the effect and therefore show a more reliable result.

CONCLUSION

The treatment with MFNS alleviates symptoms of nasal obstruction in AR patients by reducing mucosal oedema and therefore improving blood oxygenation. The parameters measured initially showed an adaptation of the AR patient to their current symptoms, which later showed significant improvement at a later stage of the treatment. These improvements in blood oxygenation showed a positive effect that would provide long-term medical benefits for AR patients.

CONFLICT OF INTEREST

The authors declare that they have no conflict of interest in publishing this article.

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