The hyperglycemic effect of bronchial asthma

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Tأثير الربوع القصبي الرافع لمستوى الجلوكوز في الدم
محمد فصل لطفي، محمد يوسف سكر

Abstract
Background
Hyperglycemia could represent a physiological response to stress associated with asthma attacks and/or anti-asthma medications.
This study aimed to evaluate blood glucose concentrations in asthmatic patients and to identify the possible influences of anti-asthma medications on glycaemic control.

Materials and Methods
The study involved two groups: a control group of forty-one apparently healthy subjects and a test group of seventy-two known asthmatic patients. Asthma history and drug therapy were recorded to assess asthma activity at the time of examination. Patients were grouped according to the asthma control test (ACT), national asthma education and prevention program (NAEPP) classification and anti-asthma medication taken during the time of examination. Colorimetry was used for estimation of glucose concentrations and IQTQ Spirometer for assessing pulmonary function. Screening studied of variables for significant differences in the means between the groups was performed using analysis of variance. P < 0.05 was considered significant.

Results
The mean of RBG in non-asthmatic patients (M±SD = 86.9 mg% ±14.7) was significantly lower compared with those of well-controlled asthmatic patients (M±SD = 112.5 mg% ±10.7, P=0.000), poorly controlled asthmatic patients (M±SD = 106.2 mg% ±7.4, P=0.000), uncontrolled asthmatic patients (M±SD = 112.5 mg% ±10.7, P=0.000), and poorly controlled patients (M±SD = 105.3 ±7.7, P=0.000). The mean of RBG in non-asthmatic patients (M±SD = 106.2 ±7.4, P=0.000) was lower compared with those of well-controlled asthmatic patients (M±SD = 107.9 ±8.7, P=0.000), and poorly controlled patients (M±SD = 107.9 ±8.7, P=0.000). The mean of RBG in poorly controlled patients (M±SD = 105.3 ±7.7, P=0.000) was significantly lower compared with those of well-controlled asthmatic patients (M±SD = 112.5 mg% ±10.7, P=0.000), uncontrolled asthmatic patients (M±SD = 112.5 mg% ±10.7, P=0.000), and poorly controlled patients (M±SD = 105.3 ±7.7, P=0.000).

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105.3±7.7, P=0.000), patients suffering from mild intermittent asthma (M±SD = 109.9±11.4, P=0.000), mild persistent asthma (M±SD = 107.9±8.7, P=0.000), moderate persistent asthma (M±SD = 105.0±7.0, P=0.000) and severe persistent asthma (M±SD = 102.2±4.0, P=0.002) and those off-treatment asthmatic patients (M±SD = 106.0±9.1, P=0.000).

Conclusion
RBG of asthmatic patients was found to be significantly elevated compared with the control group even in off-treatment asthmatic subjects, suggesting that hyperglycemia is associated with asthma itself rather than its treatments.

Key words: hyperglycemia, stress, anti-asthma medications, ACT, NAEPP

Introduction
Stress hormones like cortisol and catecholamines may increase in stressful conditions like asthma and expected to induce hyperglycemia. Some anti-asthma medications increase blood glucose levels e.g. beta-blockers, while others are known hyperglycemic agents e.g. steroids. However, most medications are administered through the inhalation route and are less likely to cause systemic endocrinometabolic effects. Hyperglycemia could represent a physiological response to stress associated with asthma attacks. Excess stress hormone could ultimately induce insulin resistance. It has been hypothesized that insulin resistance may play a role in the development of asthma and allergy. There is evidence that insulin modulates the inflammatory component of asthmatic responses mainly by influencing production/release of tumor necrosis factor-alpha (TNF-α), interleukin-1beta (IL-1β) and others. Thuesen et al concluded that insulin resistance was associated with an increased risk of developing asthma-like symptoms. This finding supported the hypothesis that obesity and asthma might be linked through inflammatory mechanisms involved in insulin resistance. Reviewing the current understanding of the potential mechanistic links between obesity and asthma, there is an emerging interface between the metabolic syndrome and asthma.

On the other hand, the influences of anti-asthma treatments, namely beta agonists and steroids, on glycaemic control are well documented in the literature. However, anti-asthma medications are commonly used in small doses and by the inhalation route, which offer less endocrinometabolic effects. Moreover, stress hormones may be increased in stressful conditions like asthma attacks and are expected to induce hyperglycemia.

This study aimed to evaluate blood glucose concentrations in asthmatic patients and to identify the possible influences of anti-asthma medications on glycaemic control.

Materials and Methods
The study involved two groups: a control group of 41 apparently healthy subjects (23 males and 18 females) recruited mainly from among university students and employees and a test group of 72 known asthmatic patients (37 males and 35 females) selected from chest clinics of the Khartoum, Khartoum North, Elshab and Omdurman teaching hospitals. Patients with past medical history suggestive of other chronic respiratory diseases apart from asthma, smoking, diabetes mellitus, hypertension and heart diseases were excluded.

Asthma history and drug therapy were recorded to assess asthma activity at the time of examination. Patients were grouped according to the asthma control test (ACT)\(^{10-12}\), national asthma education and prevention program (NAEPP) classification\(^{13,14}\) and anti-asthma medication taken during the time of examination. Colorimetry was used for estimation of glucose concentrations (JENWAY 6051 Colorimeter - Bibby Scientific Limited-UK)
IQ TQ Spirometer (Version 5.18 - Clement Clarke International Limited – U. K) was used for assessing pulmonary function according to ATS/ERS\(^{15}\) standards. Absolute values of FEV1\% was used in (NAEPP) classification\(^{16}\).

Screening studied variables for significant differences in the means between the groups was performed using analysis of variance. When significant differences were identified, individual groups were compared using the student two-tailed and unpaired T-test. In all of these statistical tests, only P < 0.05 was considered significant.

**Results**

The ages of both groups range between 20 - 40 years. The mean age was 25.0±4.8 (Mean (M) ± Standard deviation (SD)) in non-asthmatic patients and 29.7±5.4 in asthmatic patients. All spirometric measurements were significantly lower in the asthmatic patients as compared with the control group (P ≤ 0.006). Figure 1 shows the comparison of means and standard deviations of random blood glucose (RBG) concentrations in control subjects and different studied groups when classified according to ACT. The mean of RBG in non-asthmatic patients (M±SD = 86.9±14.7) was significantly lower compared with those patients suffering from mild intermittent asthma (M±SD = 109.9±11.4, P=0.000), mild persistent asthma (M±SD = 107.9±8.7, P=0.000), moderate persistent asthma (M±SD =105.0±7.0, P=0.000) and severe persistent asthma (M±SD = 02.2±4.0, P=0.002). As in ACT classes, one-way analysis of variance revealed no significant differences in the means when different classes of NAEPP were compared with each other (P ≥ 0.189 for all).

Figure 2 shows means and standard deviations of RBG concentrations of different studied groups when classified according to NAEPP. Other characteristics of NAEPP classes are summarized in Table 1. The mean of RBG in non-asthmatic patients (M±SD = 86.9±14.7) was significantly lower compared with those patients suffering from mild intermittent asthma (M±SD = 109.9±11.4, P=0.000), mild persistent asthma (M±SD = 107.9±8.7, P=0.000), moderate persistent asthma (M±SD =105.0±7.0, P=0.000) and severe persistent asthma (M±SD = 02.2±4.0, P=0.002). As in ACT classes, one-way analysis of variance revealed no significant differences in the means when different classes of NAEPP were compared with each other (P ≥ 0.189 for all).

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**Table 1**

<table>
<thead>
<tr>
<th>Class</th>
<th>Mean (M±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Asthmatic</td>
<td>86.9±14.7</td>
</tr>
<tr>
<td>Mild Intermittent Asthma</td>
<td>109.9±11.4</td>
</tr>
<tr>
<td>Mild Persistent Asthma</td>
<td>107.9±8.7</td>
</tr>
<tr>
<td>Moderate Persistent Asthma</td>
<td>105.0±7.0</td>
</tr>
<tr>
<td>Severe Persistent Asthma</td>
<td>02.2±4.0</td>
</tr>
</tbody>
</table>
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Table 1: Comparisons of number (N), means (M), standard deviations (SD), standard error of the means (SEM) and 95% confidence interval for mean between different groups (classified according to NAEPP)

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>M</th>
<th>SD</th>
<th>SEM</th>
<th>95% Confidence Interval for Mean</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Lower Bound</td>
<td>Upper Bound</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No Asthma</td>
<td>41</td>
<td>86.9</td>
<td>14.7</td>
<td>2.3</td>
<td>82.3-91.5</td>
</tr>
<tr>
<td>Mild Intermittent Asthma</td>
<td>9</td>
<td>109.9</td>
<td>11.4</td>
<td>3.8</td>
<td>101.2-118.6</td>
</tr>
<tr>
<td>Mild Persistent Asthma</td>
<td>32</td>
<td>107.9</td>
<td>8.7</td>
<td>1.5</td>
<td>104.8-111.0</td>
</tr>
<tr>
<td>Moderate Persistent Asthma</td>
<td>25</td>
<td>105.0</td>
<td>7.0</td>
<td>1.4</td>
<td>102.1-107.9</td>
</tr>
<tr>
<td>Severe Persistent Asthma</td>
<td>6</td>
<td>102.2</td>
<td>4.0</td>
<td>1.6</td>
<td>98.0-106.4</td>
</tr>
</tbody>
</table>

Figure 3 illustrates means and standard deviations of RBG concentrations of different studied groups when classified according to their medications. The mean of RBG in non-asthmatic patients (M±SD = 86.9±14.7) was significantly lower compared with those off-treatment asthmatic patients (M±SD =106.0±9.1, P=0.000), patients treated with beta-agonists only (M±SD = 109.8±9.7, P=0.000), patients treated with both beta-agonists and steroids (M±SD = 105.4±6.8, P = 0.000). One-way analysis of variance revealed no significant differences in the means when different classes of therapy were compared with each other (P ≥ 0.180 for all).

**Discussion**

It is evident from the results that RBG of asthmatic patients (M±SD=106.7±8.4) was significantly higher compared with the control group (M±SD = 86.9±14.7, P=0.000). This fact was true when different classes of asthma severity were compared with the control group (P ≤ 0.002 for all). Although there were no significant differences in the means when different classes of asthma severity were compared with each other (P>0.05), the means of RBG decreased gradually as asthma severity increased.

Hyperglycemic effects of asthma treatments, namely beta agonists and steroids, are well documented in the literature and should not be ignored when comparing blood glucose concentrations of control groups with other asthma groups. However, in the present study, the higher values of RBG in asthmatic patients seemed not to be secondary to anti-asthma medication. This is because the mean RBG of off-treatment asthmatic patients (M±SD =106.0±9.1) was significantly higher compared patients (M±SD =86.9±14.7, P=0.000). In addition, one-way analysis of variance revealed no significant differences in the means when on-treatment classes were compared with off-treatment patients (P>0.05). Absence of hyperglycemic effect of beta-2 agonists and steroids in patients taking these medications was probably attributable to the fact that most of these drugs were used in small doses and by the inhalation route. Little amounts will reach the general circulation and even then, it could easily be cleared or metabolized. Whether these findings are true or secondary to experimental error of using unpaired, rather than paired, t-test is questionable and need further randomized, double-blind, placebo-controlled studies. However, the present results regarding anti-asthma therapy are comparable with at least two previous studies on the endocrinometabolic effects of the aerosol therapy evaluated in asthmatic
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patients\(^7,^8\). Therefore, most of the findings in this study seemed to be associated with asthma itself rather than its treatments. Stress hormones like cortisol and catecholamines may increase in stressful conditions like asthma and are expected to antagonize insulin and therefore induce hyperglycemia. It has been hypothesized that resistance may play a role in the development of asthma and allergy\(^1,^17\). In addition, insulin sensitivity was increased in asthmatic patients as a result of improvements in respiratory function noted following successful treatment\(^18\). Based on these studies and findings of the present data, insulin resistance\(^19\) is likely to be involved in the pathophysiology of hyperglycemia of studied asthmatic patients. However, further studies are desirable to determine whether concomitant insulin resistance is a contributing factor of airways inflammation of asthmatic patients or it represents a physiological response to stress and/or anti-asthma medications.

In conclusion, RBG of asthmatic patients was found to be significantly elevated compared with the control group even in off-treatment asthmatic subjects, suggesting that hyperglycemia is associated with the pathogenesis of asthma rather than its treatments.

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**References**


