Original Article

Effects of β_2-agonist therapy on blood pressure, glycaemic control and electrolytes levels of asthmatic patients

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Abstract:

Introduction: the blood pressure, glycaemic control and electrolyte concentrations are influenced by autonomic nervous system and are expected to be affected by beta-2 agonist medications commonly used by asthmatic patients.

Objective: The objective of this study is to detect the possible effects of beta-2 agonist medications on blood pressure, blood glucose and electrolytes concentrations in asthmatic patients.

Methods: the study involved a control group of fifty-six healthy subjects matched for gender and age with the study group of one hundred asthmatic patients. Asthmatic patients were further subdivided into two according to whether they were taking beta2 agonists or not. Following verbal consent, blood pressures, blood glucose, sodium, potassium, calcium and magnesium concentrations were measured for each subject. Screening studied variables for significant differences in the means between the groups was performed using analysis of variance.

Results: the diastolic blood pressure of non-asthmatic was significantly lower compared with both asthmatic patients not taking beta2 agonist ($P = 0.036$) and asthmatic patients treated by beta2 agonist ($P = 0.003$). The mean of blood glucose concentration of non-asthmatic was significantly lower compared with the means of both asthmatic patients not taking beta2 agonist ($P = 0.002$) and asthmatic patients treated by beta2 agonist ($P = 0.000$). The mean of calcium concentration of non-asthmatic was significantly lower compared asthmatic patients treated by beta2 agonist ($P = 0.000$) while the mean of magnesium concentration of asthmatic patients not taking beta2 agonist was significantly lower compared asthmatic patients treated by beta2 agonist ($P = 0.000$). Sodium and potassium concentrations were not significantly different among studied groups ($P > 0.05$).

Conclusion: diastolic hypertension, hyperglycemia and hypercalcemia are likely to be associated with bronchial asthma itself, but are not because of beta2 agonist medications. However, hypomagnesaemia may be secondary to beta2 agonist therapy.

Key words: hyperglycemia, hypercalcemia, hypertension, hypomagnesaemia.

Pharmacologic intervention to treat established bronchial asthma is highly effective in controlling symptoms and improving quality of life. Approaches to asthma treatment in the Saudi Initiative for Asthma (SINA) are based on disease control by the utilization of Asthma Control Test for the initiation and adjustment of asthma treatment[1]. Asthma medications can be classified into controllers and relievers. Controllers are medications taken daily on a long-term basis to keep asthma under clinical control chiefly through their anti-inflammatory effects.

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Relievers are medications used when needed and act quickly to reverse bronchoconstriction and relieve its symptoms. The most important relievers are rapid-acting beta-2 agonists while long-acting beta-2 agonists act as controllers. However, like other drugs, repeated use of beta-2 agonists is expected to affect many physiological parameters in the body. Glycaemic control and electrolyte concentrations are influenced by autonomic nervous system and are expected to be affected by beta-2 agonist therapy[2-5]. However, most beta2 agonist medications are administered through the inhalation route and are less likely to cause systemic endocrinometabolic effects[6]. This study aims to detect the possible effects of beta-2 agonist

medications on blood pressure, blood glucose and electrolytes concentrations in asthmatic patients.

Materials and Methods

The study involved two groups: a control group of 56 healthy subjects matched for gender and age with the study group of 100 patients with a medical history of asthma but no other respiratory disease. Asthma history was recorded to assess asthma activity at the time of examination together with medications. Patients were classified into two according to whether they were taking beta2 agonists or not. As other asthma medications were taken by both groups in a similar manner, they were not considered in grouping of patients.

The non-invasive ausculatory method (Mercury in glass Sphygmomanometer – GOH Industries Limited - Japan) was used for measuring the systolic (SBP) and diastolic (DBP) blood pressures. Mean arterial blood pressure (MABP) was determined by the formula: MABP = DBP + [(SBP – DBP)/3]. Colorimetry was used for estimation of glucose concentrations (JENWAY 6051 Colorimeter - Bibby Scientific Limited – U.K), BS-200 Chemical analyzer (Shenzhen Mindray Bio-Medical Electronics – China) for measuring calcium and magnesium concentrations and flame photometry was used for estimation of sodium and potassium concentrations (Flame photometer 410 - Sherwood Scientific Limited – U. K).

Statistical evaluation was performed using the Microsoft Office Excel (Microsoft Office Excel for windows; 2003) and SPSS (SPSS for windows 17). 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, unpaired T-test. In all of these statistical tests, only $P < 0.05$ was considered significant.

Results

Figure-1 compares means (M) and standard deviations (SD) of blood pressures of studied groups. The DBP of non-asthmatic (M±SD = 75.0±10.0) was significantly lower compared with both asthmatic patients not taking beta2 agonist (M±SD = 79.7±8.6) ($P = 0.036$) and asthmatic patients treated by beta2 agonist (M±SD = 80.4±10.7) ($P = 0.003$). Concerning SBP and MABP, they were not significantly different among studied groups ($P > 0.05$).

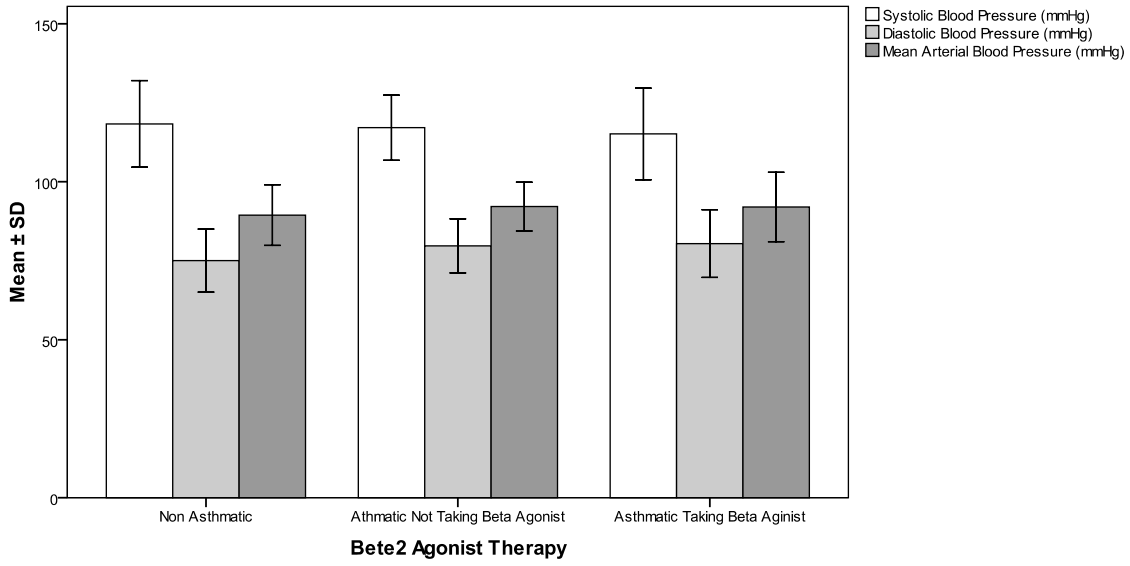

Figure1: Means and standard deviations (SD) of blood pressures of studied groups

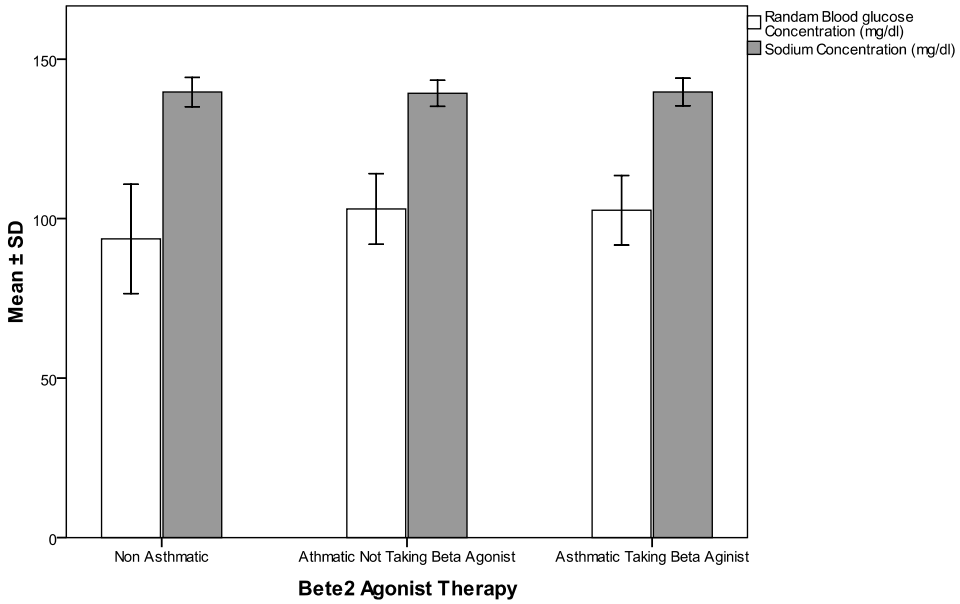

Figure2: Means and standard deviations (SD) of random blood glucose and sodium concentrations of studied groups

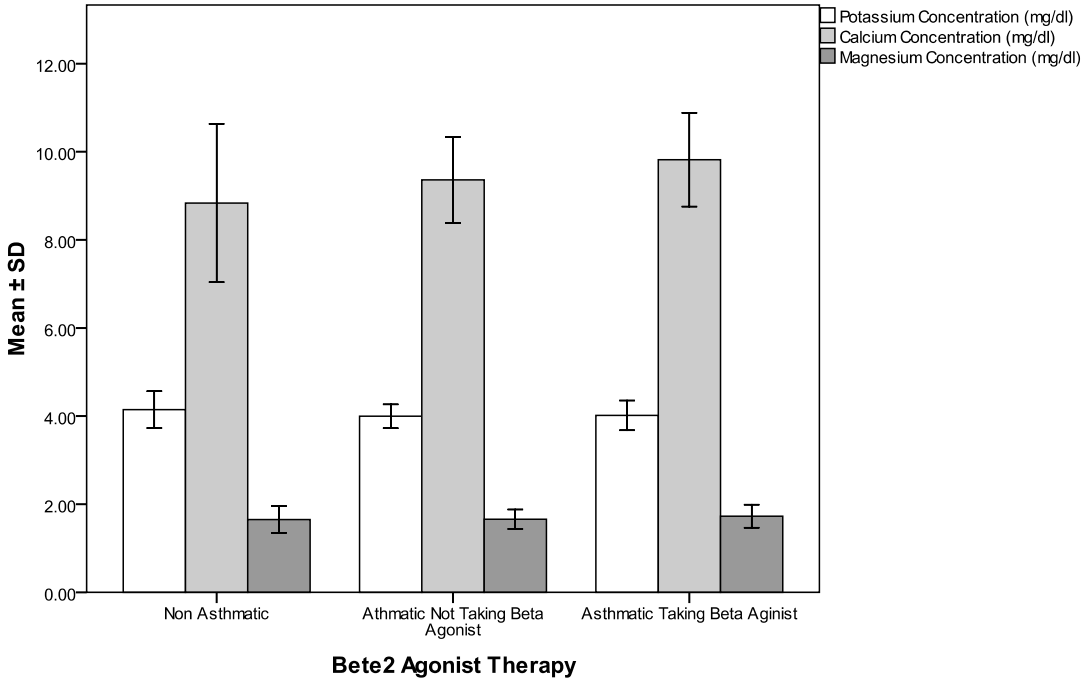

Figure3: Means and standard deviations (SD) of potassium, calcium and magnesium concentrations of studied groups

Figure-2 compares means and standard deviations of blood glucose and sodium concentrations of studied groups. The mean of blood glucose concentration of non-asthmatic (M±SD = 93.6±17.1) was significantly lower compared with the means of both asthmatic patients not taking beta2 agonist (M±SD = 103.0±11.1) (P = 0.002) and asthmatic patients treated by beta2 agonist (M±SD = 103.0±10.9) (P = 0.000). However, the means of blood glucose concentration of asthmatic patients not taking beta2 was not significantly different when compared with the mean of asthmatic patients treated by beta2 agonist (P = 0.884).

Figure-3 compares means and standard deviations of potassium, calcium and magnesium concentrations of studied groups. The mean of calcium concentration of non-asthmatic (M±SD = 8.8±1.8) was lower, but was not significantly different compared with the mean of asthmatic patients not taking beta2 agonist (M±SD = 9.4±1.0) (P = 0.078), however, it was significantly lower compared asthmatic patients treated by beta2 agonist (M±SD = 9.8±1.1) (P = 0.000).

The mean of magnesium concentration of asthmatic patients not taking beta2 agonist (M±SD = 1.5±0.4) was significantly lower compared asthmatic patients treated by beta2 agonist (M±SD = 1.7±0.3) (P = 0.000). Sodium and potassium concentrations were not significantly different among studied groups (P > 0.05).

Discussion

The DBP of non-asthmatic was significantly lower compared with both asthmatic patients not taking beta2 agonist (P = 0.036). This fact suggests that high DBP is secondary to bronchial asthma itself. Stress hormones like cortisol and catecholamines, which may be increased in stressful conditions like asthma, are expected to increase both SBP and MABP alike[7-9]. Nevertheless, SBP and MABP were not significantly different among studied groups (P > 0.05). Therefore, a mechanism that predominantly increases peripheral vascular resistance and consequently diastolic blood pressure may exist to explain these findings[10].

Both bronchial asthma and hypertension are spastic disorders of smooth muscle. Moreover, the renin-angiotensin system was found to be activated in patients with asthma during severe acute attacks[11]. Angiotensin II is a potent vasoconstrictor, which may increase blood pressure in asthmatics. Therefore, these similarities between the pathophysiology of asthma and hypertension may predispose the patients with one disease to the other[10,12].

The DBP of asthmatic patients treated by beta2 agonist was not significantly different compared with those not taking beta2 agonist (P = 0.0491). Most beta2 agonist medications were administered through the inhalation route and are less likely to cause systemic endocrinometabolic effects[6]. The current study further supports this fact because DBP in asthmatic patients treated by beta2 agonist was still significantly higher when compared with non-asthmatic subjects (P = 0.003).

The mean of blood glucose concentration of non-asthmatic subjects was significantly lower compared with the means of both asthmatic patients not taking beta2 agonist (P = 0.002) and those treated by beta2 agonist (P = 0.000) suggesting that that hyperglycemia is secondary to bronchial asthma itself and not beta2 agonist. This implication is further supported by the finding that the mean of blood glucose concentration of asthmatic patients not taking beta2 was not significantly different when compared with the mean of the ones treated by beta2 agonist (P = 0.884). Bearing in mind actions of insulin per se on autonomic functions i.e. diminished parasympathetic and enhanced sympathetic tones[13,14], one can think of asthma activity, autonomic balance, hyperglycemia secondary to insulin resistance to be closely connected. Importantly, insulin resistance is associated with aeroallergen sensitization and allergic asthma, but not non-allergic asthma[15]. Furthermore, Al-Shawwa et al hypothesize that the pro-inflammatory state of insulin resistance may contribute to the pathogenesis of asthma in obese patients[16]. In addition,

insulin sensitivity was increased in asthmatic patients as a result of improvements in respiratory function noted following proper treatment[2]. Based on these studies and findings of present study, insulin resistance may explain hyperglycemia associated with bronchial asthma.

The mean of calcium concentration of non-asthmatic was significantly lower compared with those treated by beta2 agonist (P = 0.000). On the other hand, the mean of magnesium concentration of asthmatic patients not taking beta2 agonist was significantly lower compared with those treated by beta2 agonist (P = 0.000). Sodium and potassium concentrations were not significantly different among studied groups (P > 0.05).

Most previous studies on electrolyte disturbance in asthmatics have focused on asthma treatment as a contributing factor[4,17-19].

IV ß$_2$-agonists cause an increase in the urinary excretion of calcium[17]. This is also true in patients treated with IV aminophylline[18]. The findings of this study did not contradict previous studies, as none of asthmatic patients were receiving IV ß$_2$-agonists or IV aminophylline during the measurement of their electrolytes concentrations. On the other hand, studies of asthma patients indicate that dietary magnesium intake and serum magnesium levels are lower than healthy controls[20]. High magnesium intake was associated with improvement in symptom scores, though not in measures of airflow or airway reactivity[21]. The mechanisms for effects of magnesium on lung function include alteration in smooth muscle function[22], immune function[23] and oxidative stress. When magnesium is deficient, the action of calcium is enhanced and an excess of magnesium blocks calcium. These interactions are important to the respiratory patient because the intracellular influx of calcium causes bronchial smooth-muscle contraction[20].

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