Antihypertensive Effect of Aliskiren as Related to BMI in Young Female Egyptian with Metabolic Syndrome

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Abstract: *Background*: In view of the potential benefit of direct renin inhibition, this clinical research article was designed to assess blood pressure lowering to the target blood pressure in 100 young (18-25 years) Egyptian female patients with metabolic syndrome (MS) and with body mass index of ≥30 kg/m^2 treated with aliskiren in multiple primary care units of female and child health all around Egypt.

Methods: At an initial visit, physicians assessed baseline blood pressure (BP), (HR), risk factors, signs of end organ damage and prior antihypertensive medication. Patients were prescribed aliskiren 40 mg/kg/day orally. Efficacy and tolerability were measured by assessing blood pressure, and side effects at a further visit after two months. Blood pressure target was defined according to the Seventh Report of the Joint National Committee on Prevention, Detection, evaluation and Treatment of High Blood Pressure (JNC7) that recommends a BP treatment goal of <130/80 mmHg for patients MS with diabetes mellitus (DM).

Results: Mean sitting systolic blood pressure/mean sitting diastolic blood pressure was lowered equally effectively (systolic/diastolic, p=1.0/0.8) in patients with metabolic syndrome (-22.0± 15.8/-10.9 ±9.6mmHg). Side effects were reported in 1% of all cases, none of them was life threatening.

Conclusion: Aliskiren administration for 2 months at a dose of 40 mg/kg/day orally was effective in young Egyptian female who were hypertensive with MS.

Keywords: Aliskiren, metabolic syndrome, obesity, blood pressure control.

INTRODUCTION

The metabolic syndrome (MS) is a clinical syndrome characterized by an impairment in both glucose and lipid metabolism (hyperglycemia, dyslipidemia), abdominal obesity with a marked increase in waist circumference and body mass index [BMI] [1-3]. Abdominal obesity is the major disorder constituting a base for the development of metabolic syndrome. BMI is the simplest, most practical, and most widely used system of indexing body weight. It is defined as body weight (in Kilograms) divided by the square of body height (in meters). According to this index, the patients are divided into 3 categories: under-weight, normal weight, overweight, and obese [4]. BMI is affected by sex, age, constitution, and training. It plays a very important role in the development of MS and in the assessment of cardiovascular risk. Abdominal obesity is identified as the waist circumference of ≥80cm in women and ≥94cm in men [5]. Patients with MS are at increased cardiovascular risk, they need antihypertensive treatment to reach the target level of the blood pressure according to JNC7. [6,7] It was found that patients with MS suffer from an increase in intracellular formation of angiotensin II in human adipocytes [8]. Renin-angiotensin-aldosterone system [RAAS] is particularly active in patients with MS that plays an important role in the patho-physiology of the associated hypertension in such disorder [9]. ACE-inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) were used as initial treatment options of hypertension in MS [10,11]. Direct renin inhibitors (DRIs), as aliskiren, have shown greater blood pressure reductions than irbesartan (ARB), amlodipine(CCB) or placebo [12]. No clinical studies examining the effective antihypertensive effect of a direct renin inhibitor, aliskiren, have yet been carried out in Egyptian patients with MS. This clinical study was primarily undertaken to assess whether the use of aliskiren leads to an effective blood pressure lowering in patients with MS compared to patients without MS. The target blood pressure in young Egyptian female patients with BMI ≥30 kg/ m^2 was <130/80 mmHg.

METHODS

Egyptian Physicians in multiple primary care units allover Egypt were contacted by me via the Department of Clinical Pharmacology in Faculty of Medicine Ain Shams University, Cairo, Egypt. They were asked to participate in a clinical study on the blood pressure lowering effect of aliskiren by recruiting:

Inclusion Criteria

100 young (18-25 years) Egyptian female with MS according to Table **1**: a BP ≥130 / ≥80 mm Hg, obesity [body mass index of ≥30 kg/m^2], dyslipidemia, impaired

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glucose tolerance as well as another 100 hypertensive (BP ≥130 / ≥80 mm Hg) patients (only hypertensive without prior medication or associated disease, they were recruited as congenital hypertension without MS at this age category), as a control group.

Table 1: Inclusion Criteria for Patients with Metabolic Syndrome according to [13]

Women Waist circumference >102 cm	Metabolic syndrome has to be considered if 3 or more criteria apply in the present study
Elevated triglycerides ≥1.7 mmol/l	
Low HDL <1.0 mmol/l	
Elevated BP ≥130 / ≥80 mm Hg	
Diabetes mellitus ≥5.6 mmol/l	

Schedule of Visits and Measurements

At the initial (1^{st}) visit, blood pressure (measured seated), demographic data (age, weight, height). Standard sphygmomanometer for blood pressure measurement were available in these units. Waist circumference, blood glucose and lipid levels were measured for all recruited patients in the study (Table **1**).

The second visit was arranged exactly after two months from the initial visit. The efficacy of aliskiren as an antihypertensive treatment was assessed by measuring blood pressure. No prior medication of any type even contraceptive drugs was included in this study. Any unexpected side effect (s) was documented in the case report form (CRF) of each patient. Side effects were recorded and forwarded to the pharmacovigilance section of our faculty.

Serious Adverse Events

Death, hospitalization, life-threatening condition as hypertensive emergencies. Once, anyone was reported, it leads to withdrawal of the patient from the clinical study.

The efficacy and tolerability of aliskiren's regimen in all patients was assessed using two 4-item Likert scales (very good, good, sufficient, and insufficient). The design of this clinical study was approved by the Ethics Committee of Faculty of Medicine, Ain shams university, Cairo, Egypt. Target blood pressure was defined according to JNC7 <130/80mmHg as patients with MS suffer from diabetes mellitus as shown in the inclusion criteria (Table **1**).

Statistical Analysis

A descriptive statistical analysis using Prism GraphPad 5.00 software. For the subsequent analysis, parametric methods (ANOVA and Tukey's post-hoc-test) were used. Correlation analysis was performed using a two-sided Pearson co- efficient and a significance level of p <0.05.

RESULTS

200 young (18-25 years) patients were included within six months (January 2012 to June 2012), 100 of whom were diagnosed with MS for the first time according to (Table **2**) [13]. Another 100 young female were recruited without MS from these units according to randomization table prepared with the statistical dept. of our Faculty of Medicine, Ain Shams University.

Written consent were obtained from all the recruited females in this clinical study.

Table 2: Baseline Characteristics of the Patients included in the Analysis

Parameter	Patients without metabolic syndrome (n=100)	Patients with metabolic syndrome (n=100)
Age	22.6 ± 2.2 yrs	22.4 ± 2.4 yrs
Weight	78.6 ± 13.7 kg	89.1 ± 19.4 kg
Height	170.5 ± 8.5 cm	169.3 ± 9.1 cm
BMI	27.0 ± 4.2 kg/m^2	31.0 ± 5.9 kg/m^2
Mean sitting SBP	159.6 ± 15.5 mm Hg	161.0 ± 16.6 mm Hg
Mean diastolic DBP	94.4 ± 10.0 mm Hg	95.6 ± 9.2 mm Hg
	76.6 ± 9.9 bpm	78.2 ± 10.1 bpm

Change in Blood Pressure and Target Blood Pressure

At the second visit, systolic (SBP) and diastolic (DBP) blood pressure reduction of -22.0±15.6/ -11.0 ± 9.3 mm Hg was recorded. (At initial visit: 160.1±15.9/94.3±9.7mmHg) and an equally marked blood pressure reduction (p < 0.05 for SBP and p = 0.05 for DBP) was found in both patient groups (Figure **1**). A large number patients with MS attained blood pressure targets (85%). The same for patients without MS reached their targets at a high percentage (80%) (Figure **2**).

BP reduction was correlated positively with BMI (Pearson =0.069 /0.071).

Adverse events Side effects were reported in 1% of all cases included in the analysis, although none of the side effects were serious. The most commonly reported side effect was nausea (0.3%), headache (0.2%), diarrhea (0.2%) and fatigue (0.1%). There was no statistical difference between patients with or without MS. 90% of participating physicians rated the tolerability of aliskiren as very good. Dose adjustment (10%) was necessary at visit 2, it was modified to 30 mg/kg/day in patients suffering from nausea. Bisoprolol and Amlodipine were chosen as an alternative treatment in this 10% of both groups.

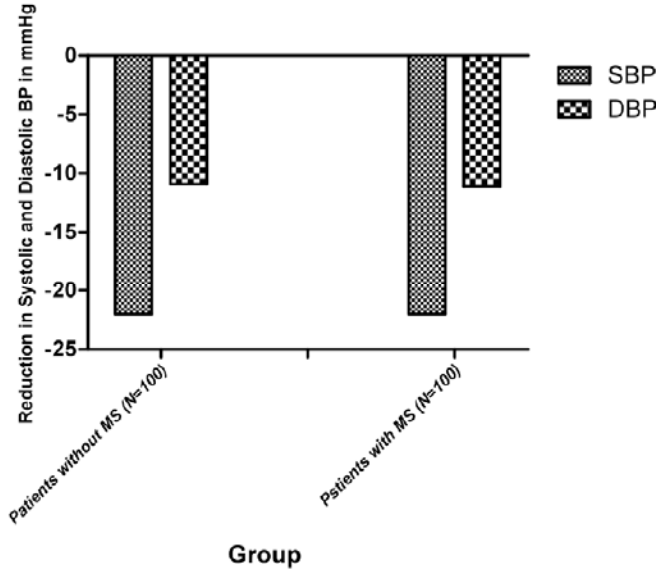

Figure 1: Reduction of systolic/diastolic blood pressure in patients with and without metabolic syndrome and patients with BMI <30 kg/m2 and BMI ≥30 kg/m^2.

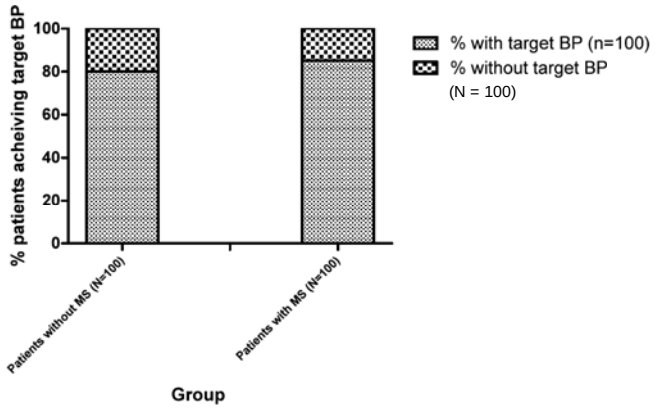

Figure 2: Percentage patients achieving target BP.

DISCUSSION

Metabolic syndrome (MS) is a serious life-threatening public health problem worldwide and its occurrence is increasing. In population studies, MS includes a serious social problem with an increase in the risk of cardiovascular diseases especially hypertension and dyslipidemia [14].

This present clinical study provides an apparent evidence of the potential anti-hypertensive effect with minimum adverse effects when orally administered to young hypertensive Egyptian females with MS and elevated BMI ≥30 kg/m^2. Aliskiren as a direct renin inhibitor, DRI, is most likely to inhibit the genesis of angiotensin I in the vascular cell and various studies have shown the superiority of DRIs compared to ARBs in patients with MS [15].

Our findings suggest a possible benefit of the direct renin inhibition in obese patients with MS. However, the achievement of the target blood pressure leads to the conclusion that DRI, being one of RAAS-blockers, could be useful for patients with MS with minimum adverse effects, randomized controlled trials are needed to assess its beneficial effect on both blood glucose and LDL in patients with obesity and MS [16].

DISCLOSURE

The author reports no conflicts of interest in this work.

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