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TO ASSESS THE CLINICAL SAFETY AND EFFICACY OF COMBINATION OF BISOPROLOL AND HYDROCHLORO-THIAZIDE IN STAGE I ESSENTIAL HYPERTENSION.

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ABSTRACT

Objective: To assess the clinical efficacy and safety profile of cardio selective beta blocker Bisoprolol (5 mg) and diuretic –hydrochlorthiazide (12.5 mg) in combination as monotherapy in patients with stage I essential hypertension.
Study Design: Cross Sectional Study
Place of Study: Medical OPD, Ghulam Mohammad Mahar Medical College Hospital, Sukkur
Duration of Study: From January 2010 to July 2010
Material and methods: 120 patients (90 males and 30 females), in the age group of 30-65 years, newly diagnosed hypertensives with stage I essential HTN (Sitting SBP 140-159 and DBP > 90-99 mmHg, JNC VII report) attending the medical OPD of Ghulam Mohammad Mahar Medical College Hospital, Sukkur, from January 2010 to July 2010 were included for the study after obtaining written informed consent. All the cases were given tab. Bisoprolol 5 mg and Hydrochlorthiazide 12.5 mg in combination once daily as monotherapy in the morning and BP was recorded every week for 4 weeks in the supine and standing position.
Results: The fall in BP (SBP and DBP) both in the supine and standing position at weekly intervals was significant ($p < 0.05$). BP was controlled in 80% of the cases. Side effects were reported in 5% patients in the form of weakness, lassitude, and muscle cramps. These side effects were mild in nature and did not warrant withdrawal of the study drug.
Conclusion: Low dose of cardio selective ?-blocker bisoprolol (5 mg) and diuretic – HCTZ (12.5 mg) provides greater additive effects with greater efficacy and tolerance, minimal side effects, and lower cost of therapy when used as monotherapy in case Stage I essential HTN.

Key words: Essential Hypertension; Systolic blood pressure; Diastolic blood pressure

INTRODUCTION:

Hypertension (HTN) is recognized as a major risk factor for coronary, cerebral, and renal vascular disease[1]. About 60 to 80% of deaths attributable to HTN occur in those with mild to moderate, now called Stage I HTN [2]. In India, the prevalence of HTN is about 3-15% in urban population and 1-5% in rural population[3]. A great stress has been laid on the importance of initiating antihypertensive treatment with monotherapy at the lowest effective dose and then titrating it upward if required, to control BP [4]. The combination therapies in low doses for HTN have been widely accepted due to their synergistic or additive effect, metabolic improvement, or both[5].
The present study was conducted to evaluate the safety and efficacy of combination of cardio selective ?-blocker – bisoprolol 5 mg and a diuretic - hydrochlorothiazide (HCTZ)

12.5 mg in patients Stage I essential HTN as once daily dosage. Low dose – HCTZ is known to contribute significantly to the efficacy, safety, and tolerability of low dose bisoprolol resulting in lesser side effects unlike conventional doses of diuretics and ?-blocker [6-8]

MATERIAL AND METHODS:

120 (90 males and 30 females in the age group of 30-65 years), newly diagnosed stage I essential hypertensives patients (sitting SBP > 140-159 mmHg and DBP > 90-99 mmHg, according to JNC VIIth report)[9-11], attending the medical OPD of Ghulam Mohammad Mahar Medical College Hospital, Sukkur comprised the subjects for the study after obtaining written informed consent. Study period was from January 2010 to July 2010. BP was measured 3 times in the left arm in the supine position after 10 minutes rest and in standing position after 3 minutes standing, using a standard mercury sphygmomanometer.

A wash-out period of 1 week was given at the outset prior to initiating therapy if the patients were taking any other antihypertensive medication(s). BP recorded (both SBP as well as DBP) at this point of time was taken as the baseline reading. Patients fulfilling the criteria for inclusion had a full work-up which included detailed history, clinical examination, laboratory investigations including Fasting Blood Sugar, Random Blood Sugar, Blood urea, Serum creatinine, Serum electrolytes, urinalysis, lipid profile, uric acid, Chest X-Ray, and 12 leads ECG. These parameters were repeated after 4 weeks of therapy to rule out any adverse event. Patients were excluded if they had any evidence of secondary/ malignant/ refractory HTN, congenital/ valvular heart disease, stroke, diabetes mellitus, chronic renal failure, known hypersensitivity to drugs, and those with concomitant severe illness necessitating other treatment. The cases were given tab. Bisoprolol 5 mg and HCTZ 12.5 mg in combination once daily in the morning and BP was recorded every week for 4 weeks. Side effects in the form of bradycardia, sick-sinus syndrome, muscle cramps, dizziness, syncope, diabetes mellitus, hyperuricaemia were recorded during each visit. Patients were considered to have responded satisfactorily if they achieved final DBP < 90 mmHg.

RESULTS:

Positive family history of HTN was known in 30 (25%) of the subjects, absent in 18 (15%), and not clearly known in 72 (60%). Smoking was detected in 60 (50%) and all were males. Most of the patients were detected by chance – 90 (75%). Symptoms at presentation were headache –36 (30%), reeling of head – 18 (15%), epistaxis – 9 (7.5%), and palpitations – 9 (7.5%). Out of the 120 patients, the average SBP in Stage I HTN at baseline was 159.2 ± 7.3 and DBP 98.2 ± 2.6 mmHg. There were insignificant effects on potassium levels, lipid profile, and glucose tolerance when the investigations were repeated at 4 weeks.

TABLE I
AGE DISTRIBUTION

Age (yrs)	Males	Females
30- 39	12	3
40- 49	24	3
50- 59	45	21
60- 65	9	3
Total	90 (75%)	30 (25%)

TABLE II
SHOWING EFFECTS OF COMBINATION OF BISOPROLOL 5 MG AND HCTZ 12.5 MG ON SUPINE BP (MMHG) THROUGH 4 WEEKS

N= 120	Basal	Wk 1	Wk 2	Wk 3	Wk 4
Systolic	159.6	143.1	139.3	132.3	130.1
Diastolic	98.2	91.48	87.32	85.14	83.1

* p < 0.05 (significant) compared to baseline.

TABLE III
SHOWING EFFECTS OF COMBINATION OF BISOPROLOL 5 MG AND HCTZ 6.25 MG ON STANDING BP (MMHG) THROUGH 4 WEEKS

N= 120	Basal	Week 1	Week 2	Week 3	Week 3
Systolic	159.6	142.8	138.68	130.6	129.8
Diastolic	98.2	89.61	85.74	81.77	79.53

* p < 0.05 (significant) compared to baseline.

TABLE IV
SHOWING REDUCTION IN BP FROM BASELINE AFTER THERAPY WITH BISOPROLOL AND HCTZ IN COMBINATION

Position	BP (mmHg)	Week 1	Week 2	Week 3	Week 4
Supine	Systolic	16.50	20.30	27.30	29.50
	Diastolic	6.72	10.88	13.06	15.10
Standing	Systolic	16.80	20.92	29.00	29.80
	Diastolic	8.59	12.46	16.43	18.67

DISCUSSION:

Blood Pressure is the product of cardiac output and peripheral vascular resistance, both influenced by various factors[7]. The basal BP (SBP) in supine position fell from 159.6 to 130.10 mmHg at the end of 4 weeks and DBP from 98.2 to 83.10 mmHg at the end of 4 weeks. In this study the BP fall is sustained throughout 24 hrs period as reported by other workers also[8]. BP was controlled in 80% of subjects with tab. bisoprolol and diuretic – HCTZ in combination given once daily. So above findings are consistent with the workers reporting 80% efficacy [9]. The mean fall of BP (SBP) in supine position at 1, 2, 3, 4 weeks of therapy was 16.50, 20.30, 27.30, 29.50 mmHg respectively and fall in DBP was 6.72, 10.88, 13.06, and 15.10 mmHg respectively (significant fall). Similarly the mean fall of BP (SBP) in standing position at 1, 2, 3, 4 weeks of treatment was 16.80, 20.92, 29.00, 29.80 mmHg respectively and DBP fall was 8.59, 12.46, 16.43, 18.67 mmHg (significant fall). Side effects were reported in 5% of patients. In the form of weakness, lassitude, and muscle cramps. These side effects were mild in nature and did not warrant withdrawal of drug.[10-13] A very low dose of diuretic HCTZ 12.5 mg and cardio selective ?-blocker – bisoprolol 5 mg provides greater additive

effects than would be expected from each drug given separately[14],[15]. So a low dose, fixed dose combination of bisoprolol and HCTZ represents a valuable option to initiate the treatment with maximum efficacy, tolerability, and minimum dose related side effects[16]. (Tables I, II, III, IV)

CONCLUSION:

It is concluded that low dose combination therapy of bisoprolol (5 mg) and HCTZ (12.5 mg) is convenient to give as once daily dosing and produces significant reduction in BP with greater efficacy, fewer side effects, improved adherence to treatment, and lower cost of therapy when used as monotherapy in patients of Stage I essential HTN.

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