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# Antihypertensive Therapy with Diuretics Without Potassium Supplement

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## INTRODUCTION

Compliance is a major problem in maintaining optimum anti-hypertensive therapy, particularly in a asymptomatic mild hypertensives. Drugs with single dose regimen and minimum of side effects have the maximum chance of compliance.

The present investigations assesses the efficacy and safety of Furosemide (Lasix) and hydrochlorothiazide in low single dose without potassium supplement.

## SUBJECTS AND METHODS

Forty out patients with mild Essential Hypertension (Diastolic  $> 95$  to  $< 110$ ) participated in this twenty four week double blind study. Patients for inclusion in the study were selected during a pretreatment period of two weeks on placebo. During this period physical Examination, base line laboratory value, including a full blood count, urinalysis, ECG and clinical chemistry were evaluated. The placebo period also served to assess base line blood pressure which was recorded in supine position in the right

arm. The Diastolic pressure was recorded as the fifth phase of Korotkoff sounds. Patients were examined in the hypertension clinic at the same time of the day. Any patient with Cardiac, renal, endocrine, cerebral and fundal changes more than grade II (Keith, Wagner, Barker classification) or who was under treatment for hypertension was automatically excluded from this study.

Table I summarises the composition of the two patient groups. Mean base line values for clinical chemistry and serum electrolytes were comparable and within normal limits for the two groups.

carefully monitored for symptoms and signs of clinical hypokalemia, E.C.G. for arrhythmias and GTT.

Treatment was considered successful if the supine Diastolic Blood Pressure continued to remain below 95mmHg. Patients who did not satisfy the criterion were excluded from the study at six weeks, Table IV.

**RESULTS**

Both Furosemide and Hydrochlorothiazide significantly lowered the mean supine Blood Pressure from the base line levels Table III. There was no

**TABLE I  
SUMMARY OF TREATMENT GROUP CHARACTERISTICS**

Treat ment Group	Race		Sex		Age						Pulse Rate			
	Negro	Asian	Male	Female	30	30-40	40-50	50-60	60	Average	70	70-80	80	Average
F	17	3	16	4	2	9	5	3	1	40	3	12	5	75.4
M	18	2	12	8	3	7	8	2	0	43	1	16	3	76.8

**TABLE II  
SUMMARY OF UNTREATED BLOOD PRESSURE**

Treatment Group	Placebo Treated Supine Diastolic Pressure				Placebo Treated Supine Systolic Pressure			
	100	100-105	105	Average	140	140-160	160	Average
F	1	7	12	104.4	0	9	11	162.0
H	1	5	14	106.1	0	10	10	163.0

**TABLE III  
SUMMARY OF TREATED \*MEAN AVERAGE BLOOD PRESSURE VALUES**

Groups	Placebo Treated	Drug Treated
Furosemide	123.8 S.D. 4.19	112.5 S.D. 9.26
Hydrochlorothiazide	125.0 S.D. 5.79	113.4 S.D. 11.06

\*Mean - Diastolic + 1/3 puls pressure.

Treatment with either Furosemide or Hydrochlorothiazide was administered orally according to double blind design with random allocation of the patient to the drug. The dose of Furosemide was 40mg once a day and of Hydrochlorothiazide 50mg once a day. No other antihypertensive therapy or potassium supplement was permitted.

Hypokalemia was defined as a serum potassium below 3.6mEq/L. Potassium supplement was not allowed even in cases of hypokalemia, but were

**TABLE IV  
NUMBER OF PATIENTS AT EACH EXAMINATION POINT**

	Post Placebo	6 week	12 week	18 week	24 week
Lasix	20	*12	12	11	10
Hydrochlorothiazide	20	*14	14	12	11

\*Non responsive patients withdrawn

**TABLE V  
COMMULATIVE INCIDENCE OF HYPOKALEMIA**

Treatment Group	Total Patients	6 week	12 week	18 week	24 week
Furosemide	20	0	1	0	1
Hydrochlorothiazide	20	1	2	2	3

statistical significant difference between the two patient groups.

70% in the Chlorothiazide group and 60% in the Furosemide group responded favourably, Table IV.

Serum potassium tended to decrease in both drug groups. The incidence of hypokalemia was variable at various time points. The lowest reading of serum potassium (3.3 mEq/L) recorded was in a patient on hydrochlorothiazide at 18 weeks. Com-

mulative incidence of hypokalemia is given in the Table V.

At 24 weeks, one patient on Furosemide and three on hydrochlorothiazide became hypokalemic. None of the patients of chemical hypokalemia showed any evidence of clinical hypokalemia.

As regards other Laboratory values, Viz Blood Sugar, Uric Acid, Creatinine, Urea, Sodium and Chloride. There were sporadic instances when individuals in either drug group had single value outside the normal limit but no persistence of any such change was observed.

### DISCUSSION

Through Furosemide and Chlorothiazide act upon different parts of the renal tubules and cause degree of sodium and water loss during the acute stage of the treatment. There was no significant difference between the effects of these two diuretic upon Blood Pressure in this study. Similar has been the observation of other studies too.

The protocol called for a fixed dosage regimen for both drugs and the drugs were not individualized according to patient response.

More patients became hypokalemic during hydrochlorothiazide than during Furosemide treatment.

The amount of kaliuresis produced by a diuretic is most likely related to the duration of action of the drug. It is not surprising therefore to have more hypokalemic in hydrochlorothiazide group as compared to Furosemide group. Hydrochlorothiazide has a long duration of action than Furosemide and makes available more sodium for exchange with potassium in the distal renal tubules over each 24 hour period.

Many of the serious adverse effects of Furosemide on serum electrolytes concern patients being treated with high doses of drug for congestive cardiac failure, cirrhosis or azotemia with secondary change in renal Haemodynamics and electrolytes 2,3. Such effects on serum electrolytes are therefore not necessarily applicable to hypertensive patients, who have intact renal functions and receiving low dose of diuretics as in our patients.

Mild chemical hypokalemia in our patients had no clinical significance as none of the patient complained of the symptoms directly attributable to it nor any of them showed E.C.G. or G.T.T. changes.

This mild hypokalemia produces very little fall in total body potassium<sup>4</sup>. It is doubtful if the potassium supplement can neutralise this drop. As increased intake of potassium is balanced by an increased urinary excretion and no change in total body potassium occur<sup>5-6</sup> Potassium supplement

complicates treatment, compliance falls and can result in hyperkalemia which is more dangerous.

The compliance of the patient to therapeutic regimen appears to be directly related to the daily frequency of drug administration, its simplicity and side effects. Gatley et al<sup>7</sup> notes 67% of patient compliant with once daily medication as compared to 22% who were receiving Q.I.D. medication. In this study we achieved excellent compliance by keeping the regimen very simple.

It is concluded from this study that both Furosemide and hydrochlorothiazide cause a comparable fall of blood pressure even at low dosage in those hypertensive patients who respond to drugs. This sustained fall in blood pressure is accompanied by negligible incidence of hypokalemia during Furosemide treatment. The degree of chemical hypokalemia produced in such situation is of doubtful clinical significance and potassium supplement as a Routine is unwarranted in these cases.

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