Captopril In The Management of Heart Failure

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Summary :

Seven patients in advanced refractory cardiac failure of different origin were given captopril in addition to the standard antifailure drug for varying periods. They were subjected to clinical examination and relevant lab investigation at weekly intervals. The objective being to identify the type of cases most likely to benefit from this drug and to asses if clinical and lab parameters suffice in monitoring patients on this form of therapy.

The cases which responded most (functional class IV to F.C. II) were those of low out put failures. Those suffering from corpulmonale' in which a state of vasodilation already existed, showed only limited response (from FC-IV to FC-III only) as the reduction of aldosterone was the only mechanism left for captopril to act. The clinical and lab parameters used in the study were adequate in monitoring both efficacy of the drug, as well as the early detection of side effects making the use of haemodynamic studies optional both in the selection and management of cases for this type of therapy.

Cardiac failure is a very common condition. Though no comparable figures are available for Pakistan its prevalance can be inferred to be about 1% among the adult United States population, judging from the prescription of digoxin in that country.

Left ventricular failure accounts for twenty five per cent of all heart patients in France. From therapeutic point of view, "Heart failure can be termed refractory when it persist or the patients condition deteriorates despite intensive therapy in contrast to Intractable cardiac failure which defies all known therapeutic measures".

The standard antifailure treatment in the present setup consist of rest, salt restricted diet, digoxin, diuretics. As such from our point of view, all those patient who failed to respond to the above regime were considered as refractory.

This study has been carried out with dual objectives.

1. The first one has been to ascertain the type of cases of refractory cardiac failure where "A.C.E." inhibitor "Captopril" is likely to be most effective.

2. The second one is to identify the most valuable "clinical parameters" which may be used as guide lines in the monitoring of the patients on this drug, as facilities for haemodynamic studies are not universally available in the country.

MATERIAL & METHODS :

Criteria for Selection :

1. Patients with correctable cardiac disease but in refractory stage (e.g. inoperable chronic rheumatic heart disease, coronary artery disease).
2. Patients with incorrectable cardiac disease e.g. cardiomyopathy.
3. Ischemic cardiac patients with associated incurable disease e.g. cor pulmonale with Ischemic heart disease and liver disease.

SOURCE OF CASES :

All patients conforming to the above criteria

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admitted in Medical Unit-III, National Institute of Cardiovascular Disease, during April/May, 1983 were included in this study. In all seven such patients were subjected to captopril therapy.

DOSAGE SCHEDULE :

The dosage schedule was variable depending the patients response and B.P. In general we followed the following routine. 1 Tab = 25 mg.

1st Day — 1/4 Tab. BD.
2nd Day — 1/2 Tab. BD.
3rd Day — 1/2 Tab. TDS
4th Day — 1 BD.

In none of the cases we had to give more than 2 tablets/day.

PARAMETERS USED :

(a) Subjectives : Patient's functional class were determined after close interogation of their activities and they were reassesed after a week from the initiation of chemotherapy.

(b) Objective : Routine checkup of heart rate, blood pressure, J.V.P. chest and examination for assessment of the extent of hepatomegally was done daily.

(c) Biochemical: invtigations were made to assess the affect of drug on liver kidney and blood gases.

(d) Radiological: assessment for the cardiac size was made before and one week after the initiation of treatment.

Table – I

AGE	SEX	F. C.		HEART RATE		Urea		B. P.	(m.m. Hg.)
		B.	A.	B.	A.	B.	A.	B. A.	B.A.
55	M	IV	III	110	94	28	41	110/70	120/80
25	M	IV	III	120	100	42	53	160/40	150/40
62	M	IV	II	94	80	34	46	110/80	118/80
50	F	IV	III	100	94	23	35	150/90	140/90
50	F	IV	II	130	96	24	38	140/120	120/90
62	M	IV	III	112	100	68	79	120/80	120/90
40	M	IV	II	120	80	63	72	130/100	110/70

Results :

From Table-I, the following inference can be derived.

AGE: The age varied between 25 to 62 year with a mean age of 50 years.
SEX: 66% of the patients were male.

Functional Class :

To start with all the patients belonged to Fe-IV. All cases derived benefit from the use of captopril as judged by their functional class before and after the initiation of treatment.

3/7 (40%) improved form functional class IV to functinal class II. These were suffering from Ischemic Heart Disease.

The rest of the cases which failed to improve beyond class-III were those, where a state of peripheral vasodialation already existed due to associated corpulmonale or hepatocellular failure. The mode of action of vasodialators has been only through reduction of volume due to inhibition of aldosterone secretion which accounts for the limited response in them.

Heart Rate :

Nearly all the patients had a heart rate greater than 110/min before the initiation of medication. One week after treatment with captopril, their heart rate decreased by 8% on average indicating stabilization in haemodynamic state.

Heart Sound & Blood Pressure :

No correlation could be found between pre-treatment and post-treatment blood pressure. S^3 disappeared in 5/7 cases further supporting improvment in hemodynamic state.

Chest :

The reduction of basal crepitations also confirmed the improvement in function of L.V.

Urea :

Blood Urea increased in all cases on the average by 12 mg%.

Blood Gases :

Blood gases were only done in corpulmonale.

While the control of failure by Captopril did reduce the acidosis. The increased Co^2 reduction and fall of oxygen may be due to slower breathing.

SIDE EFFECT :

The incidence of side effects in present study was 42% (3/7) as compared to 34% reported in other trials.[2] Among the known side effects enlisted in table-II, only three were encountered in this series.

The most common was drowziness 2/7 (28%), both these cases were those of corpulmonale with normal renal function. Alteration of taste was encountered in a case of cardiomyopathy. The reported incidence has been 3%[2]. The dose used were the same as other patient. As such it cannot be accepted to be dose related.

All patients had transient rise of blood urea of almost 12 mgm%. A rise of 10—20 mgm% has also been reported previously.[2] This may be attributed to the direct nephrotoxic effect of drug and not due to renal ischemia from hypotension as no fall of "B.P." was noticed in them.

TABLE – II :

Cardiovascular, Dizziness, Hypotension, Asymptomatic, Orthostatic, Symptomatic, Renal Insufficency.

Cutaneous, Rash and/or pruritus, Pruritus, Rash, Rash/Pruritus.

Gastrointestinal, Abdominal Discomfort, Anorexia, Diarrhoea, Nausea, Taste Alteration.

Renal, Renal Insufficiency.

DISCUSSION :

For the management of refractory cardiac failures, who do not respond adequately to the conventional therapy of digoxin and diuretics, new therapeutic modalities have now become available.

It consists of control of venous return by decreasing "the preload" through the use of nitrates, or reduction of after load by hydrallazine which acts by peripheral arterial vasodilation.

Prazocin an alpha adrenergic blocking agent reduces both preload through venodilation and after load by arterial vasodilation.[3]

Its role could have been more beneficial if it were not limited by rapid onset of tachy phylaxis[4]

To the same group of drugs belong Capoten which not only has similar action to "PRAZOCIN" but the effect is even more sustained and devoid of the compensatory reflex tachycardia.

Captopril blocks the conversion of inactive peptide, "angiotension-I" to active peptide, "angiotensine-II. This results in decrease in systemic vascular resistance (after load) and venodilation (preload).

It also decrease the aldostrone induced sodium and fluid retention leading to even further lowering of the left ventricular filling pressure (pre load)[5].

The fluid retention by the kidney is of paramount importance in the altered physiology of heart failure though they are not appropriate because the failing heart responds rather poorly to further increase in filling. The correction of the renal fault is very effective in combating the difficult "HYPONATREMIA" seen in prolonged diuretic treatment[6].

The maximal haemodynamic response was seen at 6 hrs and 7 hrs after the 6.25 mg and 12.5 mgm respectively when stroke volume index has risen by 35% and mean pulmonary capillary wedge pressure had fallen to 49% from control[7]. Mean transit time and cardiopulmonary volume reduction was gradual over 1 month.

From this rather limited study it appears that, while some degree of benefit will be dervied in all cases of refractory cardiac failure essentially two types of therapeutic response may be expected from captopril.

In high out put failure as in that of Corpulmonale and aortic incompetence, a state of peripheral vasodilation already exists. The beneficial effect of Captopril is limited under these circumstances as it is being achieved through eldosterone inhibition only, there being no further scope of vasodilations. The low out put failure state is associated with increased level of circulating angiotensin due to reflex stimulation renin angiotensin system[8]. The enhanced response to Captopril in them may be atributed to both to vasodilation and reduction of aldosterone secretion.

Thus in this series the 3 (40%) patients who improved from functional classification IV to functional classification-II belonged to low cardiac out put. The four patients (60%) who improved from functional classification IV to functional classification III only also evidence of prexisting vasodilation, where the correction of fluid retention by the Kidneys was the only mode

of action.

The routine clinical + biochemical parameters will suffice in most cases as reliable guide lines both for selection and management of patients on this form of therapy.

Daily B.P. check-up, weekly estimation of blood urea, apart from patients subjective sense of well being, is all that was used in the monitoring of the drugs.

The reduced intensity of side effect not sufficient enough to warrant withdrawal of this drug in this series may be atributed partly to the absence of renal failure in this group. It is always desirable to withhold this drug where definite evidence of renal failure exists.

Mild proteinurea may subside despite continued treatment with Captoril.

In Nephrotic syndrome associated with gross albuminurea due to membranous glomerulphathy, which is clinically and histopathologically similar to other drug induced nephoropathy e.g. gold, caprotopril should be withdrawn.

The incidence of toxicity can be further reduced if the possibility of drug interaction is taken into account, which may occur under the following circumstances.

Orthostatic Hypotension results when captopril is administered with other antihypertensive particularly diuretics which deplete the volume. The risk of hyperkalemia may be increased with concomitant administration of potassium supplements or potassium sparing agent. Neurologic dysfunction has been reported in patients receiving captopril and cimetidine.[10].

Indomethacin has been shown to (attenuate) the reduction of blood pressure and increase in plasma renin activity in captopril treated patient[11]. Furthermore very few of the drugs idiosyncratic reaction have been reported in patients wih Congestive cardiac failure possibly because the dosage needed for the control of cardiac failure is considerably lower than THAT NEEDED, FOR BLOOD PRESSURE CONTROL[12]. This series consisted of only of patient suffering from cardiac failures, and the dose of the drug required by them was much less than that which usuals causes side effects.

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