"Catapres In The Management Of Hypertension"

BY

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Introduction:

The trend in hypertension to-day is to treat it early, even when the patient is free of symptoms. By this means one is able to avert deaths due to heart failure and cerebrovascular accidents. Deaths due to myocardial infarction are unaffected, while deaths from renal failure will commonly occur when treatment is started where renal insufficiency is already severe. (A. Ebringer et al). Many of the drugs currently used in hypertension have side effects that discourage patients, particularly the asymptomatic ones, from taking them. There is an urgent need, therefore, for a drug that will be effective over a wide range of blood pressures and yet be relatively free of side effects.

The aim of the trial was to test the efficacy of Catapres in hypertension and to note whether its use was attended by any serious side effects. Catapres is the proprietary name for Clonidine:– 2 (2,6 - dichlocophenylamino) imidazoline hydrochloride. It is an imidazoline derivative, closely related to tolazoline (Priscol) and phentolamine (Regitene). It has probably several mechanisms of actions. It may be centrally inhibiting sympathetic activity. It has central sedative and anticholinergic actions. It probably reduces venous return, produces a fall in cardiac output and therefore a fall in blood pressure as the peripheral resistance does not fall in response to the reduced cardiac output. Given acutely intravenously to control hypertension in labour produces a transient and slight rise in blood pressure. Catapres is available as 0.15 mgm tablets. We report here our experience with this drug for the mangement of all grades of hypertension.

Patients and Methods:

Altogether 38 patients were selected for the trial. The trial was commenced in early June 1973 and came to an end on 31st. March 1974 when the last patient in the trial had completed 6 months of continous therapy with Catapres. The patients were picked from the admissions to the medical unit of the Kangar General Hospital. Any new case of hypertension seen for the irrespective of age, sex or severity of hypertension; however in cases of hypertensive emergencies patients were sometimes left out and treated with routine drugs for ethical reasons. In addition patients who were known hypertensives but responding poorly to their current drugs were also admitted to the trial. In this manner patients were selected on a first come basis till the 38th patient had entered the trial. Thereafter no new cases were admitted to the trial.

As far as possible, all patients had a running-in period of one week before they were started on Catapres. During this time the blood pressure was watched several times to note its level. All patients were admitted to the ward to initiate treatment. The blood pressure was taken in the standing and lying positions. All doctors and staff-nurses concerned in taking blood pressures were specificaly instructed to take lying blood pressure after 5 minutes of lying down and standing blood pressure after standing 1 minute. The level of the diastolic blood pressure was indicated in all cases by the disappearance of the sounds on auscultation.

The patients' blood pressure was classified into the following grades:-

Mild	Diastolic blood pressure . .	90 - 110 mm
Moderate . .	-do-	. . 110 - 120 mm
Severe	-do-	. . 120 - and above.

A detailed clinical history was taken from each patient and the following investigations were done for all the patients: Hb, T.W.D.C., Platelet Count, Peripheral Blood Film, Urine FEME, Blood Urea, Blood Uric Acid, Serum Electrolytes, Blood Sugar, Serum Cholesterol, Liver function test. In addition every patient had an ECG and an X-ray chest. When indicated, plain X-ray of the abdomen and IVP were also done. By these means we tried to assess the patients' complications and to determine whether the hypertension was essential or secondary.

(1. TWDC: Total White and differential count.)

(2. Urine FEME: Urine for full and microscopical examination.)

At the end of about 3 months, all patients had the following investigations repeated:-

Hb., TWDC., Platelet Count, Peripheral Blood Film, Blood Urea, LFT., ECG., X-ray Chest. The aim of these tests was to see whether any deterioration occured in them either as a result of the drug or of the disease itself.

The patients were initially started on Catapres ½ tablet tds. The dosage was then altered in either direction till the blood pressure was controlled. The maximum dose of Catapres given was 8 tablets a day. In those instances when control was unsatisfactory with Catapres alone, Aldomet or Chlorothiazide was added to the regime.

After the patients had been stabilised in the ward they were discharged and followed-up in the Medical Unit follow-up clinic. During this period the dosage of the drug was altered if needed.

All throughout the patients were closely watched for any side effects of the drug. Their incidence and persistence were noted down carefully. The patients were impressed upon to maintain a regular attendance at the clinic. Defaulters were immediately traced by post or messenger. However, those who defaulted for too long were dropped from the trial.

The response of the patients was graded as follow:-

Excellent response	Diastolic Blood Pressure	80 – 95 mm
Good Response	–do–	96 – 99 mm
Fair Response	–do–	100 – 110 mm
Failed	–do–	110 –, though reduced: or no change in BP; or therapy stopped because of side-effects.

Results: No. of Patients Completing Trial.

Out of a total of 38 patients only 22 completed the trial. Out of the remaining, 10 patients defaulted treatment and were dropped from the trial. One patient had to be changed over to Inderal. He had very marked sedation after taking Catapres and therefore could not tolerate the drug. He also had mild postural hypotension when on Catapres (BP - 100/80 on standing). Another patient had drug fever with Catapres - with rashes, fever and an increase of his blood Eosinophils from 3% to 12%. This was relieved when Catapres was stopped and he was discharged on Aldomet alone. Another elderly Malay patient who was asthmatic as well died of myocardial infarction after 5 months of treatment with Catapres. His control of blood pressure had been excellent up to the time of death. The last patient who dropped out of the trial was a 53 year old lady. She had severe hypertension of several years' standing that had been poorly controlled in the past. She had had past episodes of CCF also; she was also a known case of Bronchial Asthma and used to have frequent attacks. She was admitted to the trial in June 1973 due to her poor control of hypertension. She was put on a combination of Aldomet and Catapres, but her BP control was very poor (110 mm). In January she was admitted for Bronchial Asthma; in the ward she also developed a left hemiplegia. Her condition was poor and she took a discharge at her own risk; we have not seen her since then.

Results: Age and Sex Distribution:

Out of the 22 patients who completed the trial, there were 15 male and 7 female patients, with the age distribution as shown in the table 1.

Age	Male	Female
20 – 29 years	1	0
30 – 39 years	3	1
40 – 49 years	5	2
50 – 59 years	4	2
60 – 69 years	2	2
Total:	15	7

Severity of Hypertension:

The classification of the severity of hypertension in the 22 patients was as follows as Table 2:–

Mild (90 – 110 mm)	7 patients
Moderate (110 – 120 mm)	7 patients
Severe (120 and above)	8 patients

All patients in the study had essential hypertension.

Effectiveness of Therapy:

One of the aims of the trial was to see how effective Catapres was in reducing the diastolic blood pressure of patients with different severities of hypertension. We noted that Catapres was effective in lowering the blood pressure satisfactorily in all types of patients. Table No. 3 gives the responses of patients with mild, moderate and severe hypertension and demonstrates that the majority of patients could be satisfactorily controlled with Catapres.

Severity of Hypertension.	No. of Patients.	Types of Response Excellent. (80-95mm)	Good. (96-99mm)	Fair. (100-110mm)	Failure. (– –)
90 – 110 mm	7	6	–	1	–
110 – 120 mm	7	6	–	1	–
120 – and above	8	5	1	2	–

For the purpose of assessing the response, the mean of these patietns' lying and standing blood pressures was noted in each case.

ECG Changes During Therapy:

ECG's of the patients were done at the start of the trial and once again about 3 months later. 11 patients had normal ECG's at the start of the trial. Of these patients, 10 patients had normal repeat ECG's. The remaining one patient showed mild ischaemic changes in his repeat ECG.

The patients had ischaemic changes in their ECG at the start of the trial. Their repeat ECG's 3 months later were normal.

Two patients had evidence of left ventricular hypertrophy in their ECG at the start of their treatment; their repeat ECG's after 3 months showed the same pattern. Five patients had minor ischaemic changes at the start of therapy: their repeat ECG's did not show any significant changes. Two other patients had ischaemic changes in their ECG's at the start treatment; however, no repeat ECG's were available in their case.

Thus out of 20 patients who had repeat ECG's, only one patient showed a deterioration of his ECG. Two showed a marked improvement and 7 severe had initial changes of ventricular hypertrophy or ischaemio that persisted. The remaining 10 patients had normal ECG's that did not deteriorate.

Changes in the Chest X-ray During Therapy:

14 patients showed cardiomegaly on their chest x-ray at the start of therapy; 8 patients had hearts of normal size. A repeat x-ray was done for the patients after about 3 months. One patient showed a reduction in the heart size at this stage. No changes were noted in any of the other patients.

Effects on Renal, Hepatic and Haemopoetic Systems:

Laboratory investigations done at the srart of the trial and about 3 months later did not reveal any deterioration in the kidney and liver functions or any adverse effects in the blood.

Incidence of Side-Effects:

The incidence of side-effects in the 22 patients during the trial was noted. None of these effects were permanent.

Side Effects:	No. of Patients:
Rashes	2
Sedation	4
Postural Hypotension	3
Paraesthesiae	2
Asthenia	5
Nausea	1
Anorexia	1
Dry mouth	1

In none of the 22 patients was it necessary to stop the drug because of side effects. In one patient, however, sedation was found to be troubesome and the dosage schedule had to be altered to obviate the effect during working hours. This list does not include the patients who were taken off Catapres because of drug fever and of marked sedation and postural hypertension (Vide Supra).

Adjuvant Drugs for Controlling Hypertention:

20 patients were controlled with Catapres alone. The other two patients were long standing servere hypertensives who had been poorly controlled in the past with other drugs. One of them was on Aldomet and Chlorothazide before the trial; the other was on Aldomet and Ismelin. Both were given Catapres in addition be their previous drugs and had fair control of their blood pressure.

Tolerence to Catapres:

7 patients developed early tolerence to Catapres and needed an increase in the dosage 1 – 2 weeks after initial stabillisation to attain proper control of the blood pressure. The other 15 patients remained well stabilised on the initial doses.

Complication of Hypertension During Therapy:

One patient had congestive cardiac failure. There was no incidence of angina pectoris; left ventricular failure or renal failure in particupants during the period of the trial. One patient died of myocardial infarct after 5 months of good control with Catapres. Another patient had a stroke - but his blood pressure was well controlled.

Discussion:

The trial showed that Catapres is an effective and safe drug for the control of all grades of hypertension in all age groups. The majority of patients had an excellent response to Catapres. In 20 patients, Catapres was sufficient to control the blood pressure alone and in two other patients who had been poorly in controlled with other drugs in the past, Catapres was a useful adjuvant in controlling the blood pressure.

The incidence of side effects was not very high and mostly the side effects were transients. No patient complained very severely about the side effects. Only two patients were taken off Catapres because of a side-effects. However, tolerence to the drug was noted in 7 (32%) of the patients after initial stabilisation; with further increases of dosage, the blood pressure could be well controlled.

It was significant that the ECG deteriorated in only one patient during the trial and definitely improved in another two. This is perhaps a good sign to indicate slowing down of complications though our findings differ from those of other workers (W.B. Jackson). No patient showed increased heart size after treatment, though in one patient the heart size was reduced. One case each of myocardial infarct, stroke and congestive cardiac failure occured during the course of the treatment.

There were no adverse effects on the kidney, liver or blood due to the drug.

Summary:

Catapres is a safe and useful drug for the management for all grades of hypertension, either alone or as an adjuvant to other drugs. The incidence of side effects is low and does not prevent the patients from taking the drug.

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