Dihydrogenated Ergot Alkaloids in the Treatment of Essential Hypertension

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The effect of the oral and intravenous administration of the dihydrogenated ergot alkaloids on 25 cases of essential hypertension in the age group of 25 to 56 is reported with reference to (1) incidence of hypotensive effect, (2) degree of hypotensive effect, (3) duration of the hypotensive effect.

A NEW preparation, C.C.K.-179, a combination of equal amounts of dihydroergocristine, dihydroergokryptine, and dihydroergocornine, has recently been used in the treatment of hypertension. The theoretic and experimental basis for the trial of this preparation has been adequately elucidated by Nickerson. Conflicting results from clinical trials have been reported. Experimentally, certain hypotensive effects of the dihydrogenated ergot alkaloids have been demonstrated. The following theories have been postulated as to the mode of action of this group of drugs: (1) direct depression of the central vasomotor center with supposed concomitant stimulation of a vasodepressor center; (2) adrenergic blockade (so called adrenolytic and sympatholytic activity); (3) vagotonic action.

In “neurogenic hypertension” the adrenergic blockade activity would be most important. Unfortunately, we find this type of hypertension to be most unusual clinically. In essential hypertension all three mechanisms may be of varying relative importance. Of course, the dihydrogenated ergot alkaloids have other physiologic actions, some of which may tend to counterbalance the hypotensive mechanism. Prominent among the other actions is probably the smooth muscle constricting action, and possibly the depression of renal blood flow which has been reported.

We feel that therapy in the management of arterial hypertension, to be adequate, must not only lower blood pressure but must arrest or reverse the progressive pathologic lesions of the vascular tree. These lesions are far more significant than the height of the blood pressure and do not necessarily parallel blood pressure elevation. The best presently available objective means of detecting a therapeutic response in essential hypertension is probably a serial determination of the blood pressure and eye ground studies with an adequate pre- and post-therapy control period; at least, until the basic etiologic factors of essential hypertension are definitely known.

The 25 patients to whom we gave a trial on oral C.C.K.-179 have been followed by us, on an ambulatory basis, at frequent intervals for a period of 18 to 36 months. Most were seen in a special hypertension clinic. We are acquainted with the social and economic status of these patients, and with the individual variations of the blood pressure of each. Many have a good lay knowledge of the disease and can at times cite factors affecting the heights of their blood pressure. Compared with the usual untrained patient, these patients are less suggestible in reporting symptoms. In all patients the diagnosis of essential hypertension was adequately confirmed by physical findings and laboratory studies.

This group consisted of 17 Negro and 8 white patients; 8 males, 17 females. The average age was 40.4 years with extremes of 25 and 56. The average blood pressure of the group was 190/100. The extremes of blood pressure were 155/90 to 248/150.

The drug was administered in two forms: 1 mg. tablets and a liquid form containing 1 mg. of C.C.K.-179 in 1 cc. of vehicle. The individual patients were started on small doses...
which were gradually increased. The average maximum daily dose was 7.5 mg. in tablet form and 5.6 mg. in liquid form. The daily maximum dose was maintained for a minimum of one week. The extremes of daily dosage (tablets) were 3 mg. and 10 mg.; and (liquid) 2 mg. and 10.6 mg. Therapy was continued for from three weeks to three months. Alarming side effects were not encountered, probably because the dosage was not pushed to serious individual toxicity. Nevertheless, four patients had mild nausea, two had dizziness, and three experienced drowsiness. Because of these effects, several patients requested that the drug be discontinued.

One patient showed a significant blood pressure drop from 228/140 to 198/110 with a concomitant alleviation of headache. On discontinuing the drug the blood pressure slowly rose to pretreatment levels. This drop occurred on a dosage level of 8 to 9 mg. daily. A second patient had an equivocal drop in blood pressure (15 to 30 mm. Hg systolic, 0 to 15 mm. Hg diastolic). We could not maintain this drop in pressure because of drowsiness and “lack of energy” at the dose necessary for this effect, 10.6 mg. daily of the liquid form of C.C.K.-179. Twenty-three of 25 patients had no changes in blood pressure other than variations no greater than those noted prior to administration of the drug.

In addition to the above cases, two patients with hypertension were given 0.2 mg. of C.C. K.-179 intravenously over a five minute period. Both patients showed a fall in blood pressure within the first eight minutes, with a systolic drop of 50 mm. Hg and an average diastolic fall of 20 mm. Hg. However, both patients exhibited a return of blood pressure to pre-injection levels by the end of 45 minutes. Essentially the same results were obtained in two cases of chronic glomerulonephritis and one case of acute glomerulonephritis with hypertension. Subjective manifestation in all of these cases consisted of warmth, tingling of skin of the face and extremities, and headache which began within the first two minutes of injection and lasted approximately 10 minutes.

**Conclusion**

We do not doubt that the dihydrogenated ergot alkaloid preparations are capable of lowering blood pressure when given in sufficiently large doses, intravenously and orally. However, from a clinical standpoint we do not feel that the particular compounds we used have any practical application in the management of an individual with essential hypertension because of

1. the extreme low incidence of hypotensive effect;
2. the minimal degree of hypotensive effect when this result was obtained; and
3. the short duration of the hypotensive effect of the intravenous form of the compound.

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**REFERENCES**

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