A CONTROLLED CLINICAL TRIAL OF 'PERSANTIN' (R A 8) IN ANGINA PECTORIS*

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'Persantin' (R A 8) is the trade name for 2,6-bis-diethanolamino)-4,8 - dipiperidino - pyrimido - (5, 4 - d) pyrimidine.

It is a synthetic substance whose basic structure is a double ring consisting of 2 condensed pyrimidine rings.

* Based on a paper presented at the Second Scientific Meeting of the Association of Physicians of South Africa (M.A.S.A.), Johannesburg, July 1960.

The compound has been reported to increase coronary blood flow in dogs and to be twice as potent in this respect as papaverine.[1-4]

The drug was tried clinically in ischaemic heart disease, and several reports from Germany mentioned 'good results' in 50 - 75% of cases.[5-7]

We have conducted a controlled clinical trial of

persantin** in 15 patients with chronic angina pectoris seen in private practice in Johannesburg.

CLINICAL TRIAL

Methods

The investigation was conducted as a 'double-blind' trial. The patients received persantin and placebo tablets (of indentical appearance and taste) for periods of 2 weeks alternately, and it was hoped that each patient would have at least 2 periods on each form of tablet. The tablets were issued by the receptionist and the patients were not informed that a placebo was to be used. The first course was either placebo or persantin, and the authors were unaware which tablet the patient was receiving, until analysis at the end of the study.

Of the 15 patients entering the study, only 5 completed at least 2 courses of each tablet, while 9 others completed at least 1 course of each tablet. One patient failed to complete 1 course of each tablet and he has been excluded from the results.

The patients were given forms on which they were asked to document, each day, the number of anginal attacks they experienced, the number of trinitrin tablets used, and their general remarks on the efficacy of the drug.

Patients were considered improved if there was a noteable reduction both in the average number of anginal attacks and the average consumption of trinitrin, while those in whom angina became no longer evident were considered to be markedly improved.

The patients received 12·5 mg. of persantin 3 times daily.

Material

There were 10 males and 5 females. Their ages ranged from 50 to 77 years, with an average of 59. Eleven patients had had previous myocardial infarctions (2 infarctions in each of 2 patients), while of the remaining 4 patients, 3 showed ischaemic changes on the electrocardiogram taken after effort and, in 1, the resting electrocardiogram revealed ischaemia. All the patients experienced frequent angina of effort, and all had been accustomed to use trinitrin for the relief of pain. In no case had there been any significant variation in the severity of the angina over the preceding few months.

Results

Of the 5 patients who completed 2 courses of both persantin and placebo, 3 experienced no change in their angina during any period of therapy. Two patients were improved on both persantin and placebo, 1 of the 2 being markedly improved (Table I). It is of interest that this patient has now taken 4 courses of *each* tablet, and his improvement is maintained.

TABLE I. RESULTS IN 5 PATIENTS WHO COMPLETED AT LEAST 2 COURSES EACH OF PERSANTIN AND PLACEBO

Result	*Patients*
No change	3
Improved on persantin and placebo	2 (1 slight) (1 marked)
Improved on persantin alone	0
Improved on placebo alone	0
Total	5

** Supplied by C. H. Boehringer Sohn, through Pfizer Laboratories South Africa (Pty.) Ltd.

Of the 14 patients who completed at least 1 course of persantin and 1 course of placebo, 7 experienced no change in their angina during therapy. Three patients were improved on both forms of medication (1 patient markedly improved). Two patients improved on persantin but not on placebo (1 markedly improved), while 2 patients improved on placebo, but not on persantin (Table II).

TABLE II. RESULTS IN 14 PATIENTS WHO COMPLETED AT LEAST 1 COURSE EACH OF PERSANTIN AND PLACEBO

Result	*Patients*
No change	7
Improved on persantin and placebo	3 (1 marked)
Improved on persantin	2 (1 marked)
Improved on placebo	2
Total	14

Side-effects

Nausea was reported by 1 patient while on persantin, but this did not reappear with the second course of persantin. No other side-effects were noted.

DISCUSSION

It is well known that the severity of angina varies considerably from time to time in an individual patient.

Placebo reactors among anginal subjects are not uncommon and many reports of one or another medication being efficacious do not allow for 'spontaneous' variation or placebo response. We have not been able to trace a previously reported *controlled* clinical trial of persantin, and we embarked on the present trial as a pilot study.

The results in this small group have shown no significant difference between persantin and the placebo used. It is conceded that a trial in a considerably larger number of patients may reveal differences between persantin and placebo, but it is felt that if the differences were to be really significant, some pattern would already have shown itself in our 14 patients. It is further conceded that larger doses may have shown an effect. However, in view of the negative results in our series, and the difficulties of conducting a controlled trial in private practice, we did not feel justified in continuing the trial further. Two patients who failed to respond were subsequently given 25 mg. of persantin 3 times daily, but again there was no improvement.

When we embarked on this study it was hoped that each patient would receive at least 2 courses each of persantin and placebo, so that we could determine if any effect shown was reproducible. As mentioned previously, only 5 patients (33%) completed the full trial. Of the 10 patients who stopped the trial before the full period, 4 discontinued the tablets because they felt they were not helping; 1 patient 'noticed a difference' when changed from persantin to placebo, and was therefore given persantin again for continuous therapy. The remaining 5 patients did not complete the trial or return to report their reasons for stopping.

We believe that patients who would accept a full trial at hospital are rather more suspicious of such a trial conducted in private practice and that the high

incidence of failure to complete the trial may be a result of these suspicions. We have had past experience of controlled therapeutic trials in hospital practice,[8] where far greater cooperation from the patients was obtained. As a result of our experience in this study, we shall not embark on a controlled clinical trial in private practice again and would not recommend such a trial to other private practitioners.

SUMMARY

A new vasodilator (persantin) was administered to 15 patients with angina pectoris. Placebo control periods were used and the trial was conducted as a 'double-blind' study. In the dosage used (12·5 mg. *t.i.d.*), no difference was found between the effects of persantin and placebo.

The difficulties of conducting such a trial in private practice are mentioned.

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