treatment with these drugs. The drugs themselves appear to be responsible for the elevation of the uric acid in the treated hypertensive patients.

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CONTROLLED DOUBLE-BLIND TRIAL OF "PERSANTIN" IN TREATMENT OF ANGINA PECTORIS

BY

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The long-acting coronary arterial vasodilator drugs in use at present are disappointing, and the frequent appearance of new drugs testifies to the ineffectiveness of most of them. Search continues for an efficient drug of low toxicity that will give symptomatic relief in angina of effort.

Recently a new preparation, 2,6-bis-(diethanolamine)-4,8-dipiperidine-pyrimido-(5, 4-d) pyrimidine ("persantin"), has been shown to increase the coronary arterial blood-flow in dogs to a greater extent (Kadatz, 1959) and to have a more prolonged action (Bretschneider *et al.*, 1959) than either papaverine or theophylline after intravenous injections. Encouraging clinical reports on a small number of patients with coronary arterial disease and anginal pain have been made (Pabst, 1959; Jünemann, 1959; Hamm *et al.*, 1959) but no controlled trial has been carried out.

We report here the results of a controlled "double-blind" trial of persantin in 30 patients with angina pectoris.

Present Investigation

Material and Methods.—Thirty patients with typical angina of effort who had previously been seen in the department were selected; all were in a "static phase." The severity of symptoms was assessed before treatment, and each patient was requested to note any side-effects and the time at which improvement, if any, occurred. Patients receiving glyceryl trinitrate were advised to continue to take this if necessary for symptomatic relief, but other long-acting vasodilators were stopped. The dose of persantin prescribed was two tablets (25 mg.) four times daily with a tablet of lactose identical in appearance as a control. The tablets were dispensed by the hospital pharmacist on a "double-blind" basis, and neither patient nor physicians knew which tablet the patient was receiving at any given time. Each substance was given for one month. Every patient was interviewed two weeks and four weeks after starting each course, when the standing blood-pressure was recorded and improvement or otherwise in the angina noted. Finally, the response during each four-week period was compared.

Results.—Five patients died suddenly during the trial, presumably from further coronary vascular episodes, and one patient defaulted. These six patients are therefore not included in the results. At the time of death two patients were receiving persantin and three the control tablet. The remaining 24 patients completed the trial. They fall into one of four groups as shown in the Table. Nine patients (37%) did not improve with

Effect of Persantin on 24 Patients with Angina

Improvement with persantin alone	4 (17%)
,, ,, control alone	1 (4%)
,, ,, both persantin and control	10 (42%)
No change	9 (37%)

either tablet; 10 (42%) improved with both tablets (6 received persantin first and 4 the control first); 4 (17%) improved with persantin alone, and 1 (4%) improved with the control. Side-effects were slight and consisted of mild headache in two patients and constipation in one while on persantin. One patient complained of mild dyspepsia while on the control tablet. The blood-pressure fell slightly in two patients while on persantin.

Discussion

Four patients improved with persantin alone but the improvement was only slight in two; one patient improved with the control tablet, and 10 patients improved with both tablets. Therefore 14 patients (58%) improved on persantin as compared with 11 (46%) on the control tablet. Improvement in many patients was only slight and in none was there a dramatic change. It is a common occurrence for preliminary reports of new drugs in treatment of angina to be encouraging and for such claims not to be substantiated in subsequent controlled trials. Persantin seems to be no exception to this, and under the conditions of this trial and in the dosage used it did not give significantly better results than a control tablet.

Summary

A controlled "double-blind" trial of persantin has been made in 30 patients with angina pectoris. Five patients died and one other did not complete the trial. In the remaining 24 persantin did not give significantly better results than a control tablet.

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