tablets of virugon and the placebo.

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PARAZOLIDIN: A NEW COMPOUND ANALGESIC PREPARATION

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IN ACADEMIC CIRCLES THE USE of polypharmaceuticals is frowned upon. Whilst we do not deny the virtues of this purist approach and its validity under circumstances where patients are under constant supervision, we find that these conditions rarely apply in domiciliary medicine. This is particularly so when an elderly patient needs several different drugs

simultaneously. Through living in social isolation brought about by the death of relatives and friends, the intellectual grasp frequently slips and muddle over complicated treatment schedules is very liable to occur. In these circumstances, it is essential that the treatment regimen ordered by the general practitioner should be as simple as possible. As protagonists of useful polypharmaceuticals we were at once interested in a new compound analgesic tablet seemingly well suited to the needs of the elderly. Containing 50 mg. of phenylbutazone and 500 mg. of paracetamol, it promised the possibility of analgesic potentiation with a reduced risk of gastric irritation. Previous experience indicated this tablet combination to be effective and safe in a variety of painful conditions (McGuinness 1963).

The aim of this trial was to determine the range of usefulness and acceptability of this combination tablet and to determine the speed of relief obtained.

Materials and methods

The study began in October 1963, and continued for a year. The study was not double-blind and, therefore, without control since the therapeutic properties of the constituents were not in question. The following conditions were considered to be suitable. *Acute conditions:* fibrositis, lumbago, sciatica, sprains, tenosynovitis, thrombophlebitis and acute back strain. *Chronic conditions:* rheumatoid arthritis, osteoarthritis, spondylosis, ankylosing spondylitis, secondary carcinoma, Paget's disease and chronic back strain.

The suggested dosage of tablets was one three times a day or two twice a day according to the requirements of the patient. The results were recorded on a three point scale, pain and tenderness being noted as severe, slight or nil, and function as normal, slightly impaired or severely impaired. The preparation was given for short periods in acute conditions, and for a period of months where prolonged analgesic treatment was required. The results of therapy were noted on a special record card, each time the patient attended in the ordinary way for follow-up consultations. Observations were continued until the patient was pain-free in acute conditions or for a period of at least two months in the more chronic conditions. In the latter cases a full blood count was done in order to exclude the possibility of bone-marrow suppression.

Results

One hundred and twenty-five patients were treated and the results are summarized in table I.

From table I we see that results were most impressive in the cases of lumbago, fibrositis, tenosynovitis, thrombophlebitis and spondylosis but were very disappointing in the cases of rheumatoid arthritis and sprains and other painful conditions of joints.

In the fibrositis group, 13 of the 17 patients had complete relief within two weeks.

The group, lumbago and other back conditions, included cases of pro-

lapsed intervertebral disc and other conditions normally requiring longer periods of treatment. Twenty-five of this group of patients were symptom-free within two weeks and a further six recovered in a further two weeks. Two patients ceased treatment within two weeks because they had little relief of pain but the other patients, even those who had to take the treatment for longer remarked on the rapidity of relief from pain which in a number of cases was sufficient to enable the daily dose to be reduced. One patient took the tablets continuously for five months. He found that even at the end of this long period he was still getting rapid and effective relief of pain following each dose. The results in the treatment of osteo-arthritis were particularly good considering the chronic nature of the disease.

Side-effects

Twenty patients complained of side-effects, and these are detailed in table II.

Only where it is specified were the side-effects sufficiently serious or uncomfortable for treatment to be discontinued; thus eight of the 20 patients stopped treatment because of side-effect. Three of these would

TABLE I

Diagnostic group	*Number of patients*	*Dosage*	*Period of treatment*	*Effect*		
				Good	*Fair*	*Poor*
Acute conditions						
Fibrositis	17	1 tds to 1 qid.	From 5 days to 16 weeks	14	0	3
Lumbago and other back pains	39	1 bid to 1 qid.	From 4 days to 5 months	36	0	3
Sprains and other joint conditions	14	1 bid to 1 qid.	From 1 to 4 weeks	6	1	7
Tenosynovitis	11	1 bid to 2 bid.	From 2 days to 3 weeks	10	1	0
Thrombo-phlebitis	4	1 bid to 1 tds	From 3 days to 5 weeks	4	0	0
Neuritis	7	1 tds to 1 qid	From 2 days to 5 weeks	4	0	3
Chronic conditions						
Osteo-arthritis	18	1 bid to to 1 qid.	From 5 days to 1 year	14	0	4
Rheumatoid arthritis	12	1 bid to to 1 tds	From 6 days to 3 months	5	1	6
Spondylosis	3	1 tds to 2 bid	From 2 to 5 weeks	3	0	0

have continued had they not been advised to discontinue for good medical reasons.

In addition to the above there was one patient who complained of

TABLE II

Patient No.	*Sex*	*Age*	*Diagnosis*	*Dosage*	*Period of treatment*	*Side-effect*
1	M	49	O.A. of right hip	1 tds	1 month	Epigastric pain and tenderness. (Previous D.U.)
(Treatment stopped on medical advice)						
8	F	25	Acute muscle strain	1 tds	1 week	Legs "felt like jelly". Faintness.
(Treatment stopped by the patient)						
10	F	24	Tenosynovitis	1 tds	1 week	Nausea.
23	F	62	Rheumatoid arthritis	1 tds	1 month	Dyspepsia.
31	F	45	Fibrositis of shoulder	1 tds	5 weeks	Felt depressed, bloated and had headaches.
33	F	43	Fibrositis	1 qid	2 weeks	Indigestion.
38	F	62	Rheumatoid arthritis	1 tds	2 weeks	Abdominal pain and vomiting.
(Treatment stopped on medical advice)						
46	F	50	Subacute rheumatism	1 tds	6 days	Nausea and indigestion.
(Treatment stopped by the patient)						
47	M	69	O.A. of left hip	2 bid 1 bid	3 months	Slight dyspepsia.
49	F	55	Thrombophlebitis	1 tds	5 weeks	Complained of a "hot sensation"
(Treatment stopped by the patient)						
56	F	73	Rheumatoid arthritis	1 tds	3 months	Granulocytopenia (previous blood dyscrasia).
(Treatment stopped on medical advice)						
59	F	30	Tenosynovitis	1 tds	1 week	Depression and tiredness.
61	M	53	Rotator cuff tear	1 tds	1 week	Diarrhoea.
65	F	45	O.A.	1 tds	2 months	Nausea.
(Treatment stopped by the patient)						
80	F	45	Rheumatoid arthritis	1 tds 1 qds	2 weeks	Drowsiness.
(Treatment stopped by the patient)						
85	M	50	Acute lumbago	1 qds 1 tds	5 days	Indigestion on the higher dose.
88	F	50	Rheumatoid arthritis	1 tds	1 month	Constipation.
92	F	50	Sacro-iliac strain	1 tds	6 days	Nausea.
96	F	48	Fibrositis	1 tds	5 days	Diarrhoea.
122	M	62	Rheumatoid arthritis	1 tds	3 weeks	Slight indigestion.

difficulty in swallowing the tablets and two who complained of the tablets having a bitter taste. These were not considered to be side-effects.

It will be noticed from this table that the commonest side-effects relate to the digestive system—14 out of the 20, there being 11 patients complaining of nausea, indigestion or dyspepsia, two of diarrhoea and one of constipation. Two patients complained of depression, one noticed that her legs " felt like jelly " and that she felt faint, another complained of drowsiness, and one of a hot sensation. It is interesting to note that although rheumatoid arthritis represented less than ten per cent of the total patients in this investigation, 30 per cent of the side-effects occurred in this group of patients. This figure is remarkably close to that (29.5 per cent) reported by Sperling (1959) who also noted that rheumatoid patients had a higher incidence of side-effects with phenylbutazone. The only other case with a side-effect was a patient who was found to have a granulocytopenia. This elderly lady was found to have a borderline neutropenia when a routine blood count was carried out after more than a month of treatment. Subsequent blood counts showed only slow improvement. The patient volunteered the information that she had had extensive investigations of a blood condition over a period of four years some 20 years previously. Attempts to trace the records of this investigation have failed as the hospital records were incomplete prior to 1948. It would seem, however, almost certain that the condition was not drug induced.

Discussion

The analgesics phenylbutazone and paracetamol have been used separately for many years. Phenylbutazone occasionally produces undesirable effects but this is usually related to high dosage (Bruck *et al.* 1954 and Sperling 1959). Toxic agranulocytosis due to hypersensitivity cannot be foreseen, but gastric irritation may be expected in the elderly who seem less tolerant to the drug.

Paracetamol is relatively free from side-effects, although dyspepsia is not uncommon especially if high doses are given (Hajnal *et al.* 1959). One case of agranulocytosis is on record (Lloyd 1961).

A combined preparation containing small doses of each has been subjected to clinical trial over the period of a year and strikingly low incidence of side-effects encountered (15 per cent). Coupled with this has been the surprising potency and speed of action of the combination, which seem greater than would be accounted for by a simple addition of analgesic action. Possibly the explanation lies in potentiation, though potentiation was not shown in pharmacodynamic studies on animals (Harper 1964).

Nine patients volunteered a comparison of effect with other analgesics, two patients compared the combination tablet with ethoheptazine, three compared it with aspirin, one with tab. codein co., one with phenylbutazone alone and two with " other pain relieving tablets ". In all cases in which patients volunteered a comparison the new combination tablet was stated to be better. We are left with the impression of a useful addition

to the pharmacopoea and a preparation worthy of further study.

Summary

A new compound tablet containing 50 mg. phenylbutazone and 500 mg. paracetamol was evaluated in 125 patients with musculoskeletal pain. Satisfactory analgesia at an unusually low dose-level was attained in 75 per cent. Side-effects, mainly of a minor degree insufficient to interrupt treatment were encountered in 15 per cent. The new preparation is held to be rational, a useful therapeutic tool and worthy of further more formal study.

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HOSPITAL PRACTICE

THE GENERAL PRACTITIONER BED UNIT, EAST BIRMINGHAM HOSPITAL

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THIS UNIT WAS OPENED IN September 1964 and is unique in that it is the first ward opened within the bounds of a general hospital, in an urban area, for the sole use of general practitioners. The ward (Beauchamp Ward) is in two halves, consisting of six male and female beds.

During the first year 36 doctors admitted patients. The number varied per doctor from one to 30. Two hundred and eight patients were admitted during this time.

Special investigations and treatment included X-ray, pathology, ECG,