The Use of Glifanan in Postoperative Pain*

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SUMMARY

A double-blind cross-over trial comparing the analgesic effect of Glifanan 200 mg, dextropropoxyphene 65 mg and placebo is reported. The degree of pain relief was significantly greater following Glifanan than that following dextropropoxyphene ($P<0{\cdot}005$) and that following placebo ($P<0{\cdot}005$).

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Glifanan (glyceryloxyaminophenaquine) became available in South Africa in 1967. The pharmacological evidence of its analgesic activity has been established[1] and early clinical reports have been favourable.[2-10] For this reason a controlled clinical trial seemed desirable.

The standard analgesic used in the Obstetrics and Gynecology Unit of H. F. Verwoerd Hospital is dextropropoxyphene in a dose of 65 mg and it was therefore decided to conduct a double-blind investigation comparing the analgesic effect of this drug with Glifanan, placebo being used as an additional control.

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METHOD

The 91 patients included in the trial were all suffering from pain of at least moderate severity following major obstetric or gynaecological operations. The trial began as soon as the patient could tolerate oral medication and usually commenced on either the first or the second postoperative day.

Identical capsules of Glifanan 200 mg, dextropropoxyphene and placebo were prepared and administered at random. Each patient received 2 of these 3 preparations at 4-hourly intervals. There were thus 6 possible treatment groups.

The patients were observed for a continuous period of 8 hours starting at 0800. Patients were only admitted to the trial if the preceding 4-hour period had been free of analgesic administration.

If analgesia was not produced within 1 hour of treatment, an 'escape analgesic' other than Glifanan or dextropropoxyphene was given and its use recorded. The second dosage of the trial was then given when pain returned following the fall-off in effect of the 'escape analgesic'.

Hourly pain levels were assessed by the patient, recorded by the observer, and scored as follows:

Pain level	*Score*
Severe	3
Moderate	2
Slight	1
None	0

Side-effects occurring during a period of 4 hours following each dosage were also recorded.

Pain relief scores were calculated by subtracting each hourly pain score from that recorded at the time of administration of the dose. Relief was taken as zero on administration of an 'escape analgesic'. The pain relief scores were summed up over 4 hours to produce total pain relief scores for each dose. Thus a maximum pain relief score of 4 × 3, i.e. 12, was possible if pain was reduced from severe to none for each of the 4 hours.

RESULTS

The mean initial pain scores for patients receiving each drug showed no statistically significant difference and are shown in Table I.

TABLE I. MEAN INITIAL PAIN SCORES

Glifanan	Dextropropoxyphene	Placebo
2·55	2·57	2·42

Of the 91 patients admitted to the trial, the records of 80 were available for final analysis, and were distributed as shown in Table II.

TABLE II. DISTRIBUTION OF PATIENTS WITHIN TREATMENT GROUPS

Dose 1	Dose 2	No. of patients
Glifanan	Placebo	13
Placebo	Glifanan	14
Glifanan	Dextropropoxyphene	12
Dextropropoxyphene	Glifanan	12
Dextropropoxyphene	Placebo	14
Placebo	Dextropropoxphene	15
Total		80

Of the 11 excluded, 6 received only one of the two doses; vomiting occurred in 2 patients and the severity or duration of pain was insufficient in 3 patients.

Table III gives the analysis of variance of the pain relief scores and Table IV gives details of the individual drug comparisons.

TABLE III. PAIN RELIEF SCORES: ANALYSIS OF VARIANCE

Source	d.f.	s.s.	m.s.
Blocks (eliminating treatments)	79	273·68	3·464
Treatment (ignoring blocks)	2	94·65	
Interblock error	78	565·91	7·255
Total	159	934·24	

d.f. = Degrees of freedom.
s.s. = Sum of the squares.
m.s. = Mean of the squares.

The differences in mean pain relief scores were analysed, using a balanced incomplete block design.[11] There was a statistically significant difference ($P<0.005$) between the mean pain relief score following Glifanan (3·25) compared with that following dextropropoxyphene (1·64) and compared with that following placebo (1·57).[12] There was no statistically significant difference between the mean pain relief score following dextropropoxyphene and that following placebo. The degree of pain relief plotted against time is shown in Figs. 1 - 3.

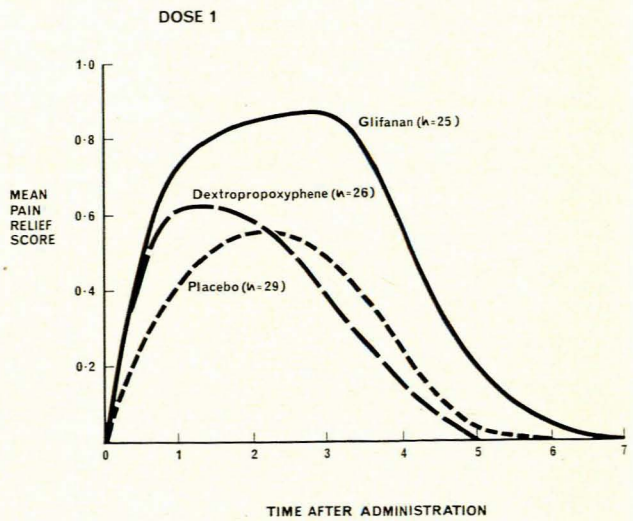

Fig. 1. See text.

TABLE IV. MEAN PAIN RELIEF SCORES

Comparison	Mean pain relief scores	Diff. in mean pain relief scores	Variance	t	d.f.	P
Glifanan vs. placebo	3·25 1·57	1·68	0·269	3·237	78	0·005>P>0·001
Glifanan vs. dextropropoxyphene	3·25 1·64	1·61	0·279	3·049	78	0·005>P>0·001
Dextropropoxyphene vs. placebo	1·64 1·57	0·07	0·266	0·136	78	0·8>P>0·8

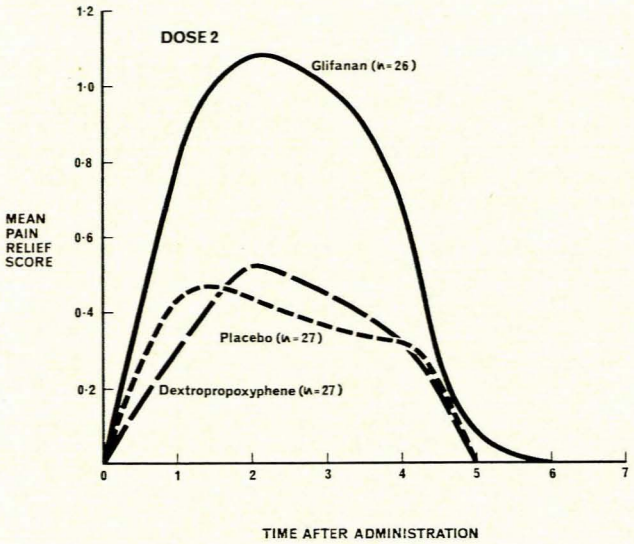

Fig. 2. See text.

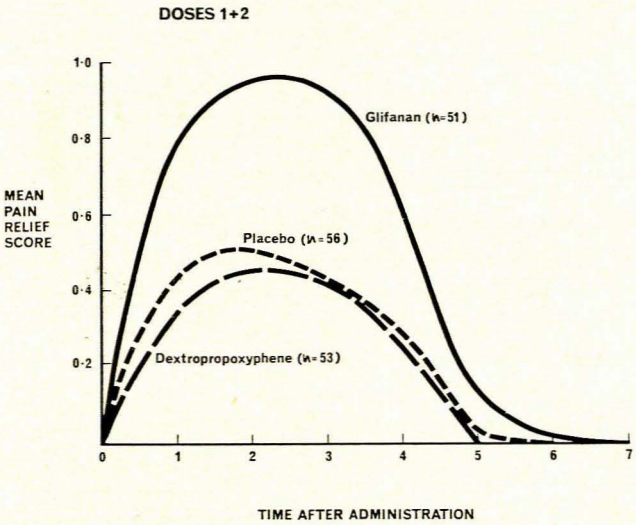

Fig. 3. See text.

'Escape analgesics' were necessary on 10 occasions following dextropropoxyphene, on 9 occasions following placebo and on 5 occasions following Glifanan.

The incidence of side-effects was low. One patient suffered from heartburn and 10 patients suffered from nausea. The incidence and distribution of side-effects are shown in Table V.

TABLE V. INCIDENCE OF SIDE-EFFECTS

Side-effect	Following administration of	No. of patients
	Glifanan	1
	Dextropropoxyphene	3
Nausea	Placebo	1
	Glifanan and placebo	1
	Dextropropoxyphene and placebo	4
Heartburn	Dextropropoxyphene	1
Total		11

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