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COMPARISON OF THE ANALGESIC EFFECTS OF DIHYDROCODEINE TARTRATE, PARACETAMOL AND PHENYTON SODIUM

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ABSTRACT

One hundred and thirty five patients (age 18 –70 years) with baseline pain of varying degrees in the post operative period, had their pain treated with dihydrocodeine, paracetamol and phenytoin sodium. At the end of 48 hours from commencement of treatment, the patients were asked to give an assessment of pain relief, using the modified global rating scale as poor (1), fair (2) and good (3). The results showed dihydrocodeine to give 'good' relief in 86%; phenytoin in 47% and paracetamol in 34 % of patients with severe pain. Phenytoin is therefore a stronger analgesic agent than paracetamol but not as strong as dihydrocodeine.

KEYWORDS: Pain, Analgesia, Dihydrocodeine, Paracetamol, Phenytoin.

INTRODUCTION

Dihydrocodeine, paracetamol and phenytoin are drugs with proven analgesic activity (Agnew and Goldberg, 1976; Bond 1981) While paracetamol and codeine are listed as analgesic agents in the index of ethical preparations (BNF) and used as such; phenytoin is not so listed but has been so used (Smith et al, 1988). Dihydrocodeine being a narcotic is a potent analgesic whereas paracetamol is used predominantly to treat mild to moderate pain. There are sporadic reports in the literature of the use of phenytoin for its analgesic actions especially in the management of chronic pain (Swerdlow, 1984). The medication has also been shown to be effective in the treatment of acute pain (Essiet, 2002). Phenytoin is however primarily an anti convulsant drug. Experience with its analgesic actions is limited and its degree of analgesic activity is not very certain. This study compared the three drugs in patients with perceived baseline pain of different grades so as to appropriately categorise phenytoin as an analgesic agent. Postoperative patients were chosen for the study, as pain is an inevitable feature of the postoperative period (Cronin *et al*, 1973).

Approval for the study was given by the ethical committee of the University of Calabar Teaching Hospital where most of the work was done. Informed consent was obtained from all patients involved.

Patients and Methods

Consecutive surgical patients undergoing minor, intermediate and major surgical procedures to reflect three degrees of pain namely mild, moderate and severe; and meeting the criteria for inclusion in the study, were assigned to one of three treatment groups. Each group in turn comprised three subsets of 15 patients for each class of surgery. An 'open' non-cross over method was used to compare the outcome of treatment of postoperative pain in these patients using the drugs under study.

The drugs were assigned alphabets before the patients were selected. 'A' for phenytoin sodium, 'B' for paracetamol and 'C' for dihydrocodeine.

The highest tolerable and safe dose of each drug for naïve patients were used as follows: phenytoin sodium (epanutin, Parke-Davis) 100 mg. Three times /day; paracetamol (panadol, Smith Kline Beecham) 1gm. three times/day and dihydrocodeine tatrate (DF.118, Glaxomed) 80 mg. three times/day. The patients were made to score their baseline pain intensity (the first experience of pain after surgery) using the verbal rating scale (Sunshine *et al*, 1993) as follows: no pain - 0; slight pain - 1; moderate pain - 2; and severe pain -3. Their respiratory rate, pulse rate and blood pressure were noted. The study medication was then administered by a neutral person (the nurse). Subsequent pain intensity scores as well as vital signs were taken again after 30 minutes and thereafter hourly for 8 hours. In addition, the patients gave an indication of relief from baseline pain with scores as follows: no relief - 0; little relief -1; some (moderate) relief - 2; a lot of (good) relief –3 and complete (excellent) relief - 4. At the end of 48 hours each

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Table 1 Distribution of the means of some sociodemographic variables

Variables	Phenytoin group n=45			Dihydrocodeine group n=45			Paracetamol group n=45		
	Mild pain	Moderate pain	Severe pain	Mild pain	Moderate pain	Severe pain	Mild pain	Moderate pain	Severe pain
Total valuable patients (n)	15	15	15	15	15	15	15	15	15
Mean Height (cm)	F=159.1 M=165.0	F =159.7 M =164.5	M=163.9	F=159.5 M=163.6	F=159.1 M =164.0	M =162.9	F=160.1 M=163.5	F = 160.2 M =164.2	M =71.0
Mean weight (kg)	F =64.8 M =70.2	F =64.2 M =69.6	M =68.9	F = 65.1 M =70.4	F =64.9 M =71.2	M = 69.9	F=63.4 M=69.8	F = 65.2 M =71.0	M =70.5
Mean age (Years)	F =38.3 M =49.2	F =37.1 M =50.4	M =61.1	F=39.3 M=49.5	F =39.1 M =51.0	M = 61.2	F=39.4 M=50.7	F =40.2 M =49.5	M = 61.5

patient was asked to give a rating of the post operative pain management as; poor -1, fair - 2 or good –3. All drugs were given orally on demand by patients but in accordance with the prescribing information. Any patient that did not have significant pain relief after two doses was given a more potent analgesic (intramuscular pethidine 100mg 4 - 6 hourly as appropriate). For purpose of statistical analysis, such patients had the score for their 'baseline pain intensity' taken as their observed pain intensity and zero entered for pain relief in all subsequent hourly observations. Care was taken not to allow any medications that may interact with the test drugs (giving false results) during the duration of the study and during anaesthesia.

The differences in hourly pain intensity scores (PID) for each drug in different treatment groups were noted. The sum of the values for each group gave the SPID (sum of pain intensity difference). The sum of hourly pain relief values weighted by the time lapse between readings, gave the total pain relief score (TOTPAR). Peak percentage PID (the maximum pain relief score achieved divided by the maximum attainable score, multiplied by 100) was worked out for each drug in the different treatment groups. Data obtained were analyzed and the results are presented in tabular and computer generated graphic forms.

RESULTS AND DISCUSSION

One hundred and thirty five patients, 89 male and 46 females (M: F = 1.9:1) were entered in the study. There was not much difference among the female patients in age, weight and height in the different 'grade of pain' groups, while in the males mean age for the severe pain group was 61.2 years and for the other groups 50.1 years. The means of the various demographic variables are shown in Table 1.

Table 2 shows the results for various pain assessment parameters; the sum of pain intensity difference (SPID) for phenytoin in mild pain was 8.55; dihydrocodeine 8.60 and paracetamol 7.55. For moderate pain; phenytoin 8.97; dihydrocodeine 9.01; paracetamol 8.37. In the severe pain group the difference was marked, with score for phenytoin 10.26; dihydrocodeine 12.39 and paracetamol 10.1.

Total pain relief (TOTPAR) scores are also shown in Fig 1. In the mild pain group, the scores were 16.28, 16.32 and 15.70 for phenytoin, dihydrocodeine and paracetamol respectively. For moderate pain; phenytoin 13.91; dihydrocodeine 13.90 and paracetamol 12.29. For severe pain, dihydrocodeine scored the highest 13.00 while the results for phenytoin and paracetamol were 10.68 and 10.31 respectively. Phenytoin was

TABLE 2:Comparison of analgesic parameters of phenytoin with those of dihydrocodeine and paracetamol

Parameters	Phenytoin group	Dihydro-codeine group	Para-cetamol group
(i) SPID scores			
Mild pain	$8.55^{xy} \pm 0.02$	8.60 ± 0.02	7.55 ± 0.5
Moderate pain	$8.97^{xy} \pm 0.02$	9.01 ± 0.02	8.37 ± 0.02
Severe pain	$10.26^{xy} \pm 0.01$	12.39 ± 0.01	10.10 ± 0.01
(ii) TOTPAR scores			
Mild pain			
Moderate pain	$16.28^{xy} \pm 0.01$	16.32 ± 0.02	15.70 ± 0.03
Severe pain	$13.91^{xy} \pm 0.01$	13.90 ± 0.01	12.29 ± 0.02
	$10.68^{z} \pm 0.02$	13.00 ± 0.01	10.31 ± 0.02
(iii) Global Rating scores			
Mild pain	$2.93^{xy} \pm 0.04$	2.97 ± 0.03	2.50 ± 0.06
Moderate pain	$2.82^{xy} \pm 0.06$	2.85 ± 0.04	2.21 ± 0.05
Severe pain	$2.06^{z} \pm 0.07$	2.78 ± 0.06	1.85 ± 0.05
(iv) Time of PID (Hours)			
Mild pain	4.07 ± 0.13	3.03 ± 0.03	2.00 ± 0.04
Moderate pain	4.13 ± 0.13	3.03 ± 0.04	2.03 ± 0.01
Severe pain	4.20 ± 0.10	3.11 ± 0.05	2.03 ± 02
(v) Peak PID percentage			
Mild pain	96.5 ± 0.11	97.3 ± 0.09	84.5 ± 0.12
Moderate pain	88.5 ± 0.15	89.4 ± 0.17	73.1 ± 0.21
Severe pain	56.0 ± 0.02	81.8 ± 0.25	45.0 ± 0.25

Above results show mean ± SEM; n = 15

Key:

SPID = Sum of pain intensity difference
TOTPAR = Total pain relief
PID = Pain intensity difference

X = Statistically, no significant difference between it and dihydrocodeine at $P \leq 0.05$.

y = Statistically, there is a difference between it and paracetamol in favor of pheytoin at $P \leq 0.05$.

z = Statistically, there is a difference between it and dihydrocodeine in favour of dihydrocodeine, at $P \leq 0.05$.

rated higher than paracetamol in all grades of pain.

Global rating scores were higher for dihydrocodeine in mild pain (2.97) and severe pain (2.78) than for phenytoin (2.93) and paracetamol(2.50) in the mild pain group as well as for phenytoin (2.06), and paracetamol (1.85) in the severe pain group. The scores for dihydrocodeine and phenytoin were not statistically different ($p > 0.05$). Again the scores were significantly higher than for paracetamol in all grades of pain. Results for phenytoin and dihydrocodeine are comparable for mild and moderate pain while in severe pain; phenytoin was not as effective as dihydrocodeine.

There was variation in the time of peak 'pain intensity difference' (PID) in the different treatment groups. Average time of peak PID for phenytoin sodium was 4.13 hours, which is higher than for dihydrocodeine (3.06 hours) and paracetamol (2.02 hours). Table 3 shows pain relief ratings in different grades of pain for the three drugs. Dihydrocodeine gave 'good' relief in all grades of pain. Phenytoin sodium gave 'good' relief mostly in the mild and moderate pain groups and scored higher than paracetamol. It was not as effective as dihydrocodeine in severe pain. While dihydrocodeine led to 'good' relief in 86% of cases, phenytoin sodium gave 'good' relief in 47% which is however better than the result for

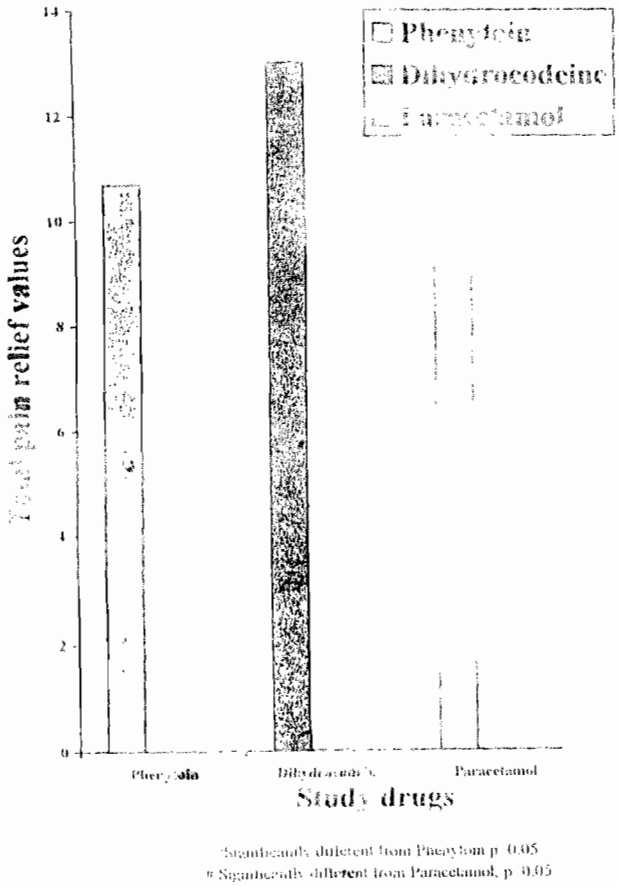

Fig. 1: Total pain relief values for severe pain in different groups

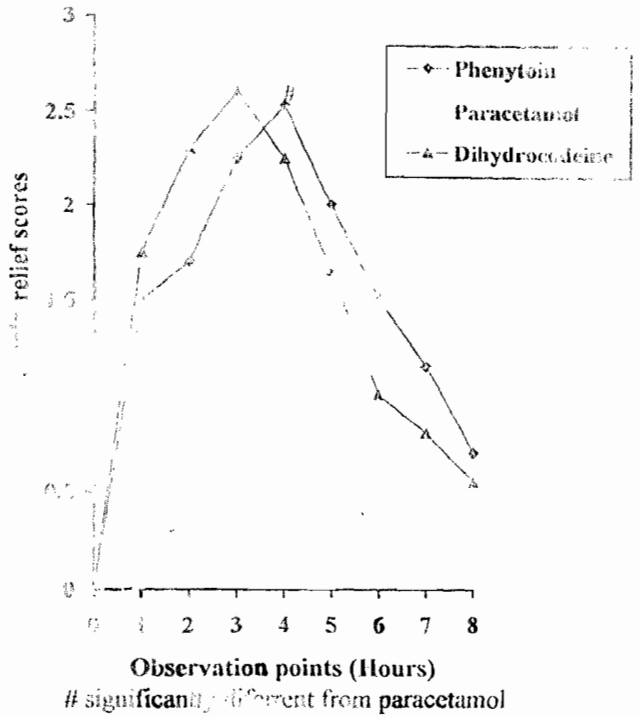

Fig. 2: Time-effect curve for mean pain relief of moderate pain in the different study drugs

TABLE 3: Comparison of the grade of pain relief following administration of drugs in the different pain groups.

Study groups	Poor (1)	Fair (2)	Good (3)
Phenytoin			
Mild pain (n = 15)	-	1 (7%)	14 (93%)
Moderate pain (n = 15)	1 (7%)	2 (13%)	12 (80%)
Severe pain (n = 15)	6 (40%)	2 (13%)	7 (47%)
Dihydrocodeine			
Mild pain (n = 15)		1 (7%)	14 (93%)
Moderate pain (n = 15)	-	2 (13%)	13 (87%)
Severe pain (n = 15)	1 (7%)	1 (7%)	13 (86%)
Paracetamol			
Mild pain (n = 15)	2 (13%)	2 (13%)	11 (74%)
Moderate pain (n = 15)	4 (27%)	3 (20%)	8 (53%)
Severe pain (n = 15)	7 (46%)	3 (20%)	5 (34%)

Note: Percentages are in bracket.

paracetamol (34%). Findings in this study suggest that phenytoin sodium is an effective analgesic agent in some forms of acute pain. It is not as strong as dihydrocodeine, but clearly stronger than paracetamol. It can therefore be used effectively in the treatment of mild to moderate pain.

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