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ORIGINAL ARTICLE

Comparative study of the therapeutic effects of brands of paracetamol (acetaminophen) on experimentally induced dental pain.

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Summary

Objectives: To compare the therapeutic effects of two brands of Paracetamol: Panadol® (paracetamol 1000mg) and Panadol-Extra®(paracetamol 1000mg and 60mg caffeine) on the perception of dental pain. **Method:** The setting for the study was the Oral Diagnosis Unit of the Dental Hospital, Obafemi Awolowo University Teaching Hospitals' Complex, Ile-Ife, Osun State, Nigeria. The Experimental design was a single blind quasi-experimental repeated measure. Twenty volunteers with healthy permanent upper right central incisors were the subjects of the study. Using the Digitest Pulp Vitality Tester as a stimulator, the pain thresholds of the right maxillary central incisors were detected. Subjects were then given 1000mg of paracetamol (Panadol®) or 1000mg of paracetamol and 60 mg caffeine (Panadol - Extra®) orally and the pain thresholds were again detected and recorded at 30. 60, 90 and 120 minutes after drug ingestion. At one-week interval, subjects' baseline pain thresholds were recorded and they were given the other brand of the drug. Pain thresholds were recorded at 30,60, 90 and 120 minutes intervals. The data were analysed using the SPSS for windows (Release 9.0 version), p-value ≤ 0.05 was considered significant. **Results:** Age and gender did not have any significant effect on the baseline or mean scores for both drugs. Overall, Panadol® and Panadol -Extra® individually demonstrated significant differences in tooth sensitivity when compared with the baseline. A comparison of the effects of both drugs however showed no significant difference in their effects on dental pain perception. **Conclusion:** Although both drugs had significant therapeutic effects on baseline dental pain perception, a comparison of their effects showed no significant difference in their effects on the pain.

Key words: Panadol, Panadol–Extra, Dental Pain.

INTRODUCTION

Pain is the most prominent symptom of diseases in man and analgesics are the most widely used drugs[1]. More than 90% of the analgesics being used belong to the so-called peripheral acting, non-opiod (non-narcotic) or mild analgesics. They are all derived from three types of compounds: aspirin and other acidic non-steroidal anti-inflammatory drugs (NSAIDs), aniline derivatives such as paracetamol (acetaminophen) and non-acidic pyrazole drugs like propyhenozole and dipyrone (metamizole)[1].

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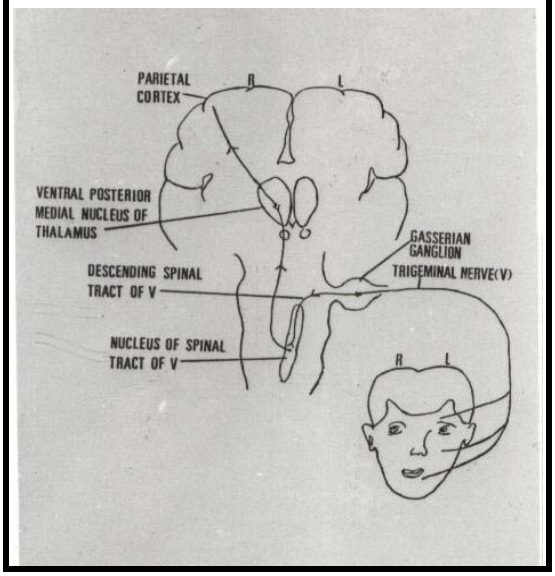
Analgesics are known to influence the transmission of pain impulses through the sensory pathways (Figure 1).

Figure 1. The pathway of pain fibres of the orofacial region



The analgesic action of a drug can be peripheral, central or both. A peripheral-acting analgesic such as aspirin, acts directly at the site of origin of pain to control it. This is done through anti-inflammatory effect or by vasodilatation. The central - acting drugs e.g. morphine act directly on the central nervous system (CNS) by inhibiting afferent activity or depression of the central mechanism. Such drugs may occupy the receptor sites to effect analgesia[2] . Paracetamol (acetaminophen) has both peripheral and central actions. Its mechanism of action is poorly defined however, it has been speculated that it selectively inhibits prostaglandin production in the CNS, which would account for its analgesic effect. Although a reasonably good antipyretic, it has very little anti-inflammatory activity[3]. Paracetamol is a valuable analgesic and anti-pyretic agent.

It is useful in the treatment of pain from everyday causes and for febrile infections with musculoskeletal pain, toothache or headache. It is practically problem-free when used correctly, however; its overdosage may cause hepatic damage. A dose of 8 to 10gm can be fatal in adult. In children the life threatening dose range from 2 to 8gm, depending on age, and in infants, only 0.5gm[3]. "Panadol® and Panadol-Extra® are registered trade names for Paracetamol 500mg B.P. and Paracetamol 500mg with Caffeine 30mg respectively. They are produced by SmithKline Beecham Drug Company. They are brands of Paracetamol and Panadol-Extra® is a combination drug. The use of two or more analgesics in combination (analgesic combination) is reasonable if their effects and their pharmacokinetics harmonize with one another. Caffeine is an alkaloid stimulant found in tea leaves and coffee beans[4].

Cafffeine and other methylxanthines are believed to increase the absorption of acetylsalicylic acid in man. Similarly, simultaneous ingestion of phenacetin with caffeine not only delays the breakdown of caffeine but also potentates its effect [4] . Some bases for using caffeine in combination with analgesics may perhaps be found in the demonstrable efficacy of caffeine in migraine and headaches, an effect that may be due to its intrinsic power of raising vessel tone in the cranial area. A case can even be made for combining caffeine with paracetamol [5]."Panadol-Extra®" believed to be an improvement on "Panadol®", is an analgesic combination of Paracetamol 500mg BP and Caffeine 30mg. Its analgesic efficacy is expected to be superior to Panadol® (Paracetamol 500mg B.P).

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This study therefore sets out to evaluate and compare the therapeutic effects of "Panadol®" and "Panadol-Extra®" on experimentally induced dental pain in healthy volunteers.

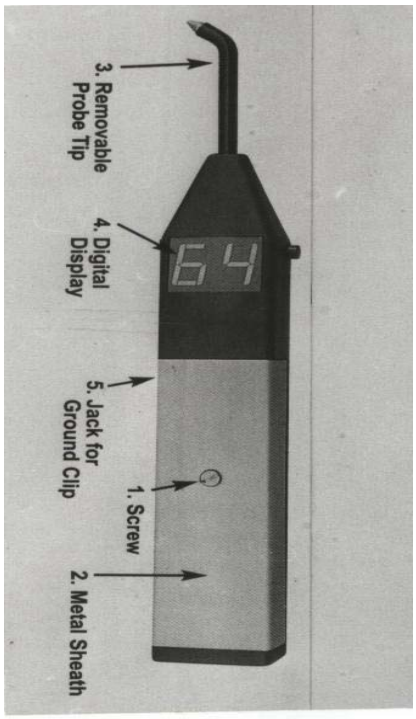
SUBJECTS AND METHODS

Twenty healthy volunteers (10 females and 10 males) with age range 17 to 44 years were used for this study. The volunteers were mainly Students and Staff of the Dental Hospital, Obafemi Awolowo University Teaching Hospitals' Complex, Ile-Ife, Nigeria. The criteria for selection for the study include the possession of healthy maxillary incisors, not previously restored in adults with no history of previous reaction to paracetamol or caffeine. The procedures of the study were explained to the volunteers and were assured of their safety after which their consents were obtained. The volunteers were expected to attend the two stages of the study carried out by only one of the authors (OO).

At the first visits, the volunteers were comfortably seated on dental chairs; their maxillary incisors were dried and isolated with gauze. With the aid of a Digitest Pulp Vitality Tester (Model No. D6260) by Parkell Electronics Division, Farmingdale NY 11735, (Figure 2) which was used as the stimulator, the pain thresholds on the right maxillary incisors were detected in all the volunteers. The tip of the sterile removable probe on the stimulator was smeared with some toothpaste, which acted as the conduction gel. The same brand of toothpaste was used for all the volunteers.

Obtaining the pain threshold involved applying the tip of the stimulator on the dried labial surface of the right maxillary incisor and stimulation was set on by continuously pressing on the button on the appliance with an ungloved hand. The stimulating intensity increased from zero to a maximum of 64 units.

Figure 2. Shows a digitest vitality tester (Model No. D6260)



The subject was expected to indicate by lifting up an index finger the moment he or she had the slightest sensation on the tooth. The button was then released and the intensity was read off from the tester. The reading appeared on the digital display for a few seconds before it disappeared. This was the pain threshold or baseline reading. The subjects were then randomly given 1000mg paracetamol (2 tablets of Panadol®) or 1000mg paracetamol and 60mg of Caffeine (2 tablets of Panadol- Extra) to ingest, single blind. Thirty minutes after the drug ingestion, the detection of pain threshold was repeated (P30 or X30). The same procedure was repeated after 60, 90 and 120 minutes post ingestion.

Subjects were recalled after one week for the second stage of the study during which they took the other brand of Paracetamol and the whole procedure was repeated recording the pain threshold at the stipulated time interval. The subject was not expected to ingest any brands of paracetamol during the one-week interval so as not to cause any interference with the study. All the data were recorded and analysed using the SPSS for windows (Release 9.0 version), p-value $\leq$ 0.05 was considered significant.

RESULTS

A logistic regression of the data showed that gender (sex) and age did not have any significant effect on either the baseline or mean scores for both Panadol® and Panadol-Extra®.

Tables 1 and 2 show that for Panadol®, there were significant differences in tooth sensitivity at baseline (Wilcoxon Signed Ranks Text) compared with measurements taken at 30 mins (Z = - 2.416, P = 0.010), 60 mins (Z = - 2.644, P = 0.008), 90 mins (Z = - 2.713, P = 0.006) and 120 mins (Z = - 2.699, P = 0.007). The overall effect of Panadol® was also found to be significant using Friedman's test (P = 0.001). Similarly for Panadol-Extra®, there were significant differences in tooth sensitivity at baseline (Wilcoxon Signed Ranks Test) compared with measurements taken at 30 mins (Z = - 3.379, P = 0.01), 60 minutes (Z = - 3.558, P = 0.00), 90 mins (Z = - 3.837, P = 0.00) and 120 mins (Z = - 3.442, P = 0.001). The overall effect of Panadol-Extra® was also found to be significant using Friedman's test (P = 0.00). When Panadol® was compared with Panadol-Extra®, no significant differences were observed at baseline (Z = - 0.26, P = 0.026), 30 mins. (Z = - 1.431, P = 0.153) 60 mins. (Z = - 1.930, P = 054), 90 mins. (Z = - 1.403, P = 1.61) and at 120 mins. (Z = - 1.356, P = 0.175).

Table 1. Effect of the gender on drug action

Variable (Gender)	B	SE	Wald	df	Sig
Panadol-Mean	0.3921	0.3169	1.5311	1	0.2160
Panadol-Extra-Mean	0.0154	0.2620	0.003C	1	0.9534
Baseline-Pan Ext	0.1821	0.4751	0.146C	1	0.7015
Baseline-Pan	0.3409	.3156	1.1671	1	0.2800
Constant	0.0368	1.7120	0.0005	1	0.9828

Table 2. Effect of age on drug action

Variable (Age)	B	S.E.	Wald	df	Sig
Panadol – Mean	0.0352	0.2617	0.0181	1	0.8929
Panadol Extra Mean	0.1913	0.2506	0.5828	1	0.4452
Baseline- Panadol Extra	0.0807	0.4366	0.0304	1	0.8617
Baseline- Panadol	0.1616	0.2702	0.3576	1	0.5498
Constant	0.3376	1.7552	0.0370	1	0.8475

DISCUSSION

This study showed that the age and sex of the subjects did not have any significant effect on the analgesic functions of Panadol® and Panadol-Extra®. Similarly, in a study on the search for sex differences in response to analgesia, Averbuch and Katzper[6] reported that gender had no effect on analgesic response to ibuprofen, a mild analgesic like Panadol® or Panadol-Extra®. This was irrespective of the generally accepted view that males and females respond differently to painful conditions and that females demonstrate a lower pain threshold and a lower tolerance of painful stimuli. Females were also reported to have experienced greater analgesic efficacy than do males after the administration of narcotic analgesics[6].

Our finding that age had no effect on the analgesic function of Panadol ®and Panadol-Extra® support the various reports in the literature that paracetamol equally relieved mild to moderate pain in children as well as in adults[7-10]. Panadol® was found to have produced significant differences in tooth sensitivity at baseline compared with measurements taken at 30, 60, 90 and 120 minutes.

The differences were most prominent at 90 and 120 minutes post-ingestion of the drug. Similarly, Panadol-Extra® produced significant differences in tooth sensitivity at baseline compared to measurements taken at 30, 60, 90 and 120 minutes and the differences were most prominent at 60 and 90 minutes post-ingestion of drug. This study therefore confirmed the analgesic efficacy of paracetamol (acetaminophen) for mild to moderate pain as already proposed by experts, [3,7,11,12]. However in severe pain, paracetamol could offer a significant additive analgesic effect to the opiates[7] . It has been speculated that paracetamol selectively inhibit prostaglandin production in the CNS, which could account for its analgesic effect[3,12].

When Panadol® was compared with Panadol -Extra® (an analgesic combination of paracetamol 500mg B.P. and caffeine 30mg) no significant differences were observed at baseline, 30, 60, 90 and 120 minutes post - ingestion of drugs. The combination of paracetamol and caffeine was proposed by Laska et al[5]. Caffeine is believed to be capable of potentiating the effect of an analgesic by increasing its absorption[4] hence Panadol-Extra® is expected to be a more potent analgesic than Panadol®.

This study however showed that even with the combination of caffeine with paracetamol in Panadol-Extra®, its analgesic effect in relieving dental pain was not significantly different from that of Panadol® (Paracetamol).

CONCLUSION

Panadol® and Panadol-Extra® had significant effects on the relief of dental pain. However, when their effects were compared, Panadol-Extra® did not seem to have any significant superior effect on the relief of dental pain compared with panadol®.

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