

Comparative study of analgesic effectiveness of single doses of paracetamol and ibuprofen in a dental pain model

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Abstract

Objective: The overall aim of this study is to evaluate the analgesic effectiveness of paracetamol and ibuprofen in the pharmacologic management of acute post-operative dental pain.

Method: This study employed the visual analogue scale to measure the effectiveness of single doses of ibuprofen and paracetamol over a six-hour period, following a third molar surgery in a homogenous study population, matched for age, body mass index (BMI) and gender. Alarms were set to remind patients to score pain intensity at time point 0.5, 1.0, 1.5, 2.0, 2.5, 3.0, 4.0, 5.0 and 6.0 hours, post-dosing. A measure of the difference between the pain scores at the various time interval and that at the basal level (time 0) is the pain intensity difference (PID) at the various time intervals. Data obtained were analysed, using the SPSS version 16.0. (Chicago, IL, USA). Inferential statistics used include Chi squared test and a two-way analysis of variance (ANOVA). $P < 0.05$ was considered significant.

Result: Ibuprofen showed a statistically significant superiority over paracetamol from time 2.5 hours to the sixth hour ($P < 0.05$). There is no significant difference between paracetamol and placebo ($P > 0.05$). The difference per dose prices of ibuprofen and paracetamol is negligible. Probability of developing significant pain following use of paracetamol is greater than 0.9, the relative risk is 1.10 and the odds 10.3, C.I. 95%.

Conclusion: This study concludes that ibuprofen is significantly more efficacious than paracetamol in the management of post-surgical dental pain and suggests that paracetamol should not be prescribed as a sole agent for analgesia after a third molar surgery.

Key words: Analgesic effectiveness, dental pain, pharmacologic management

Introduction

Dental pain has been described as pain originating from innervated tissues of a tooth or immediately adjacent to a tooth. It is a subjective oral health indicator, one of the most common reasons patients seek dental treatment. Dental pain is caused mainly by dental caries. Other causes include such conditions such as trauma (surgical trauma that is, post-operative pain inclusive), erosion and exfoliation of primary teeth^(1,2).

When dental postoperative pain is unchecked, it poses an important ethical and financial concern⁽³⁾. It leads to unnecessary suffering, sleep disturbances, diminished social activities, and increases school and job absenteeism. Therefore, dental pain potentially reduces the quality of life. Reducing the population level of dental pain and the number of days absent from school, employment, and work owing to pain of oral and craniofacial origin are targets of Global Goals for Oral Health 2020⁽⁴⁾ and, consequently, no efforts should be spared in a bid to effectively manage this pain and achieve these goals⁽²⁾.

The third mandibular molar surgery is widely used to evaluate the efficacy of drugs because this surgery causes acute post-operative inflammation and pain. It is the experimental dental pain model⁽⁵⁾; and has

been employed over the last thirty years to test analgesics, having proved to be a valid predictor of the efficacy of analgesics for treatment of other conditions of acute pain. This dental pain model has the advantage of involving healthy young subjects that are capable of complying with the study and in whom surgical removal of the mandibular third molars is indicated⁽⁶⁾. The analgesic efficacy of agents can be described through an assessment of subjective variables, pain intensity difference (PID) and total pain relief (TOPAR) as experienced by the subjects⁽⁷⁾.

Pain is a problem of global proportions with an increasing acceptance as the fifth vital sign at the same level of significance with blood pressure, pulse and respiration⁽⁸⁾ and defined by the International Association for the Study of Pain "...as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage"⁽⁹⁾. It is one of the most common reasons patients seek dental treatment. It may be due to many different diseases/conditions or it may occur after treatment. The presence of pain is perhaps the most common reason for an unscheduled visit to the dentist and most general dentists would probably see at least one or two patients with pain almost every working day⁽¹⁰⁾. Dental-related pain may also occur after treatment

by a dentist. Hence, dentists must be able to diagnose the source and nature of the pain and must also be familiar with strategies for the management of dental, oral, facial and post-operative pain. The dental profession, since its infancy, has been a pioneer in the fields of anesthesia and pain control and this stems from the need to render pain free dental care in an anatomic region that is profusely innervated by the second and third divisions of the trigeminal nerve^(11,12). Pain has a dramatic physiologic impact that can adversely affect the health and well-being of dental patients. It is a problem of global proportions, and postoperative pain is one of the most common types of pain. Postoperative pain is acute although it is preventable and/or treatable, it is often undertreated. Lack of appropriate analgesic management has significant impact on clinical and economic outcomes⁽¹²⁾. Negative clinical outcomes of inadequately managed acute postoperative pain include extended hospitalization, compromised prognosis, higher morbidity and mortality, and the development of a chronic pain state resulting in neuronal plasticity and can have a profound effect on the cardiovascular, pulmonary, endocrine and gastrointestinal systems^(11,12). It is difficult to estimate the economic burden of postoperative pain but this burden is considerable and results from direct costs due to excess health-care resource use, as well as indirect costs due to reduced patient functionality and productivity. Therefore adequate pain control is a medical and dental necessity and not merely an issue of patient comfort as dental surgeons has a duty to provide, and patients have a right to expect, adequate and appropriate pain control⁽¹²⁾.

The major cause of pain is thought to be due to there lease of inflammatory mediators that activate sensitivenociceptors (**Figure 1**). Given the mechanisms that are occurring at the per'phery, anti-inflammatory agents should be used to control this process. The non-steroidal anti-inflammatory drugs, readily comes to mind in these situations amongst these are Paracetamol and Ibuprofen and these are widely prescribed. It is therefore logical to reason that frequently, a choice must be made between these agents and evidence based decision are invaluable when occasion call for such decisions^(1,13).

The management of pain is the raison de'taire of dentistry. Over the years, dentists have remained in practice mainly to manage pain arising from intra-oral and peri-oral tissues as well as associated structures such as the temporomandibular joint (TMJ) among others. It is unfortunate therefore that some of these dental procedures in themselves cause post-management pain and knowing the consequences of pain to the overall wellbeing and quality of life, the need to develop an effective protocol to its management cannot be overemphasized.

The most prescribed analgesic in the many Dental Centers is paracetamol for mild to moderate pain. Other less prescribed analgesic agents include tramadol, diclofenac and in some other cases benzodiazepines are employed for moderate to severe pains⁽¹³⁾. Elsewhere ibuprofen and paracetamol are widely prescribed agents for same condition⁽¹⁴⁾. Prescriptions have had to be changed severally on

phone due to the lack of conviction, varying opinions, unverifiable personal experiences, weak anecdotal evidences and myths, particularly for females presumed to be the weaker sex. This irrational drug use has consequent health and economic burdens on the patients in particular and the society at large⁽¹³⁾ and it is therefore unacceptable. This study was therefore designed to scientifically assess the effectiveness of paracetamol and ibuprofen (two commonly used analgesic agents) on patients in our environment, with a view to establishing the difference, if any and grading them in the management of dental pain rather than employing them without scientific evidence. In evaluating the analgesic effectiveness of paracetamol and ibuprofen in the pharmacologic management of acute post-operative pain in our environment and carrying our study, the following hypotheses were formulated for assessment, by statistic testing:

- (i) Null hypothesis-1 (HO-1): No significant difference between the effectiveness of paracetamol and ibuprofen in the management of acute dental post-operative pain. Alternate hypothesis-1 (HA-1): There is significant difference in the potency of paracetamol and ibuprofen in the management of dental post-operative pain.
- (ii) Null hypothesis-2 (HO-2): There is no significant difference between intensity of pain felt by both sexes for similar stimuli. Alternate hypothesis-2 (HA-2): There is significant difference significant difference between intensity of pain felt by both sexes for similar stimuli.

The objective of this study is therefore to compare the analgesic effectiveness of paracetamol and ibuprofen in the management of acute post-operative pain following disimpaction of third mandibular molars and to assess the difference, if any in the amount of pain felt by both genders.

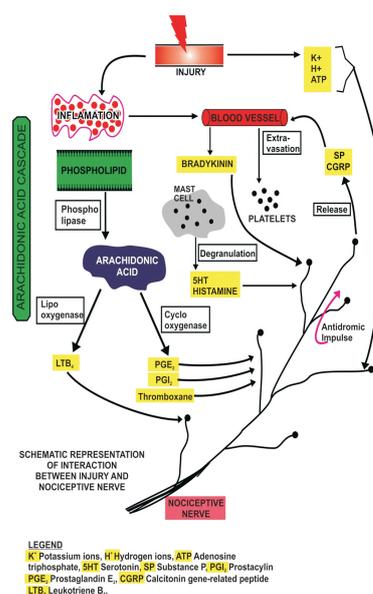


Figure 1. Diagrammatic representation of release and interaction of mediators with nociceptors.



Materials and method

Study Design and Setting:

The study was a placebo-controlled comparative study. The cohorts were matched for age, sex and body mass index.

Study Location:

The Study was carried out in the Department of Oral and Maxillofacial Surgery of the University of Benin Teaching Hospital, Benin-city, Edo state, Nigeria.

Study Population:

The study involved patients attending the dental center for the management of impacted third molars and who gave an informed consent for inclusion in the study. The age range of participants was eighteen (18) to thirty-five (35) years. Patients with impacted third molars indicated for disimpaction meeting inclusion criteria and consenting to participate were matched for age, sex and BMI and randomly allocated to the cohorts.

Inclusion Criteria:

Criteria for recruitment into the study population include:

- a. Minimum age: 18 years.
- b. Maximum age: 35 years.
- c. Gender: Male and female.
- d. Body Mass Index (BMI): 19.0 - 24.0
- e. Presence of impacted mandibular molar indicated for disimpaction
- f. Patients who gave informed consent.
- g. Patient with no systemic diseases e.g. diabetes mellitus, hypertension, acquired immunodeficiency syndrome (AIDS), chronic renal failure, bleeding disorders.
- h. Non-gravid/breast feeding females.
- i. Patients who had not used analgesics within three (3) days prior to the day of surgery.
- j. Patients without any known hypersensitivity for the agents used.
- k. Those for whom surgery was concluded within 30 min.
- l. Those for whom anesthesia was achieved with 3.6 ml of 2% lignocaine hydrochloride with 1:80,000 adrenaline.
- m. Non-smokers

Exclusion Criteria:

- a. Patients who objected to participating in the study.
- b. Patients in whom there was proximity of the impacted tooth to the inferior alveolar nerve.
- c. Presence of systemic diseases, e.g. diabetes mellitus, hypertension acquired immunodeficiency syndrome (AIDS), chronic renal failure, and bleeding disorders.
- d. Pregnant/breast feeding females.
- e. Patients who had used analgesics within three (3) days prior to the day of surgery.
- f. Patients with known active ulcers or gastrointestinal bleeding.

g. Patients with any known hypersensitivity for the agents used.

h. Those in whom there was failure to achieve anesthesia with 3.6 ml of 2% lignocaine hydrochloride with 1:80,000 adrenaline.

i. Smokers.

j. Patients with surgery time exceeding 30 min.

Pre-Operative Data and Patients' Preparation, Surgery and Pain Assessment:
Ages, sex, medical and social status of patients were obtained by interview and clinical observations. Body mass index was calculated from the patients, height (cm) and weight (kg), and patients with a BMI of 18.6-24.9 who met other inclusion criteria were recruited. A meter rule was used to get the patients' heights while a scale (Hanson® made in the United Kingdom) was used to measure weight of the patients.

Pre-operation preparations included all clinical protocols to ensure that a right diagnosis had been made and appropriate treatment prescribed. This was achieved by undertaking a detailed history, systematic general physical, extra-oral and intra-oral examination, and appropriate radiological investigation of each individual tooth for disimpaction. Periapical radiographs were used for the investigation of these cases. Attention was paid to asepsis. All instruments used were sterilized in the central sterilizing unit of the University of Benin Teaching Hospital Central Supply System Department (CSSD) except for the gloves, blades and suture materials, which were pre-sterilized by the manufacturers, using gamma rays and ethylene oxide as appropriate. All patients had a prophylactic scaling and polishing done, 3-5 days before surgery.

The individual cases were classified following a review of standard periapical radiographs based on spatial orientation of the tooth relative to the second molar, amount of space between the distal aspect of the second molar and the ascending ramus, and degree of eruption relative to the fully erupted second molar.

The Akinosi mandibular block technique, a closed-mouth intraoral approach to the nerve block anesthesia of the mandibular nerve was used to achieve anesthesia. A volume of 3.6 ml of 2% lignocaine hydrochloride with 1:80,000 of adrenaline was delivered into the superior aspect of the pterygomandibular space via 3.5 cm long 27 gauge hypodermic needle in a standard dental syringe (all are products of Henry Schein®, France). This resulted in the anesthesia of the inferior alveolar, lingual and long buccal nerves.

The degree of pain perception was indicated by the patient, about 5 min after the injection of the local anesthetic using a visual analogue scale (VAS). This is a scale of ten levels indicating the varying degrees of pain from 0 to 10 corresponding to no pain and the most intolerable/most severe pain respectively (Walls and Melzack, 1984; Rashidi et al., 2005). This was aimed at ensuring that all patients were started on the same scale: 0 (no pain).

The standard (bard) incision was made to raise a three-sided mucoperiosteal flap for all cases. This design relieves anteriorly just mesial to the interdental papillae between the second and third molars. Posteriorly, an ascending buccal relief on the external oblique ridge is employed. A stopwatch was used to time the intervals for measurements.



The guttering technique was employed for bone removal. A rose-head surgical bur on a high speed straight hand piece was employed for bone removal. This was copiously irrigated continuously with normal saline at room temperature. The saline was removed from the mouth with high pressure suction.

All cases requiring tooth division for facilitated delivery had the teeth divided to ease delivery, using a fissure bur on same hand-piece and the teeth delivered in pieces. The teeth were divided at the furcation to enable delivery of the crowns and the roots separately, when indicated.

The wound was debrided of bone smear and tooth fragments. Sockets were copiously irrigated with normal saline. The overhanging bones nibbled, with Roguer's bone nibbler.

All wounds were closed, using 3/0 black silk suture material, attached to cutting needle. The first incision stabilized the papilla and the second closed the distal relieving incision. On cutting the last suture, surgery time was stopped on the stop watch and the duration noted. All cases exceeding 30 min were excluded from the study.

To ensure uniformity in surgery, all consenting 210 patients meeting the inclusion criteria and from whom the data for this study were obtained had their surgery done by the same surgeon and all surgeries took place in the fore noon. The use of ice packs was not allowed. Patients remained in the clinical research area for a 6 hour observation after surgery.

Immediately after cutting the last stitch, patient had a mouth rinse with warm saline and was given 1000 mg of paracetamol (Emzor®) or 400 mg of ibuprofen (Ranbaxy®) or 200 mg of ascorbic acid (Emzor®), depending on the cohort the patient was assigned earlier. This was timed zero (0), the reference point for all recorded scores on the VAS. Patients scored the intensity of pain having been briefed that the scale represented the degree of pain sensation.

After drug administration, patients were allowed drinking water ad libitum but food was withheld throughout the study period. The use of ice packs was not allowed. These were ensured by keeping the patients in the recovery room, throughout the period they participated in the study.

Alarms were set to remind patients to score pain intensity at time points 0.5, 1, 1.5, 2, 2.5, 3, 4, 5 and 6 hrs, post-dosing¹⁵. A measure of the difference between the pain scores at the various time interval and that at the basal level (time 0) is the pain intensity difference. It is the degree of pain felt by the participants in the study at the end of various time intervals. Analgesic effectiveness was assessed by the patients at the end of the study (sixth hour) on a categorical scale with the following categories: 1-Poor, 2-Fair, 3-Good and 4-Excellent.

The patients were monitored in the departmental clinical research area within the waiting room and within sight of a trained attendant nurse, for the 6-hr period to ensure compliance with the protocols and also to observe for possible adverse effects.

The results obtained are presented in descriptive statistics as mean \pm standard error of mean (SEM), frequency (percentages) tables, graphs, pie and bar charts. Data obtained were analysed, using the SPSS version 16.0. (Chicago, IL, USA). Results are presented in simple frequency tables and cross tabulations.

Inferential statistics used include Chi squared (X²) test and a two-way analysis of variance (ANOVA). P<0.05 was considered significant.

The approval for this study was obtained from the Ethics Committee of the University of Benin Teaching Hospital (REFERENCE: ADM/E.22 A/VOL. VII/125).

Result

Two hundred and ten of the patients seen met inclusion criteria, consented and were recruited for the study; they were fully compliant. Therefore these two hundred and ten patients were matched on basis of age and sex and constituted the population used for this study.

Figure 2 shows the age distribution of the study population in the study. The age ranged from 18-35 years. The peak age group is 24-26 years, constituting 25.2% of the study population. The least proportion (9.5%) is contributed by the 18-20 years age group. While the oldest patients (33-35 years age group) were twenty-four, 11.4% of the study population.

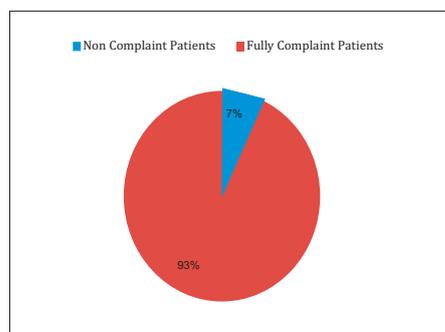


Figure 2. Degree of compliance among patients recruited for the study.

The age distribution of the patients among the different cohorts is seen in (Figure 3). There is no significant difference in the age distribution of the patients among the cohorts. This shows that the study population was matched for age

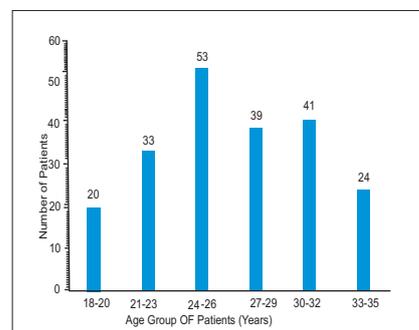


Figure 3. Age distribution of patients.

Range is 18-35 years, peak age range is 24-26 years and mean \pm SEM is 26.7 \pm 0.1 years.

Table 1 shows the gender distribution of the patients among the cohorts. There were a total of 105 males in the study, made up of 35, 36 and 34 in the ibuprofen, paracetamol and placebo treated cohorts respectively, While there were 36, 35 and 34 females

in the ibuprofen, paracetamol and placebo treated cohorts respectively; these make a total of 105 females in the study population.

Table 1. Distribution of patients, by Gender among the Cohorts

Test Group	Males n(%)	Females n (%)
Ibuprofen Treated Cohort	35 (33.3)	36 (34.3)
Paracetamol Treated Cohort	36 (34.3)	35 (33.3)
Control Group	34 (32.4)	34 (32.4)
Total	105 (100.0)	105 (100.0)

No significant difference in gender distribution among the cohorts (n = 210, p>0.05)

Most patients (81.9%) that participated in the study were educated to the tertiary level. This is made up of; fifty-eight in the ibuprofen treated cohort, representing 27.7%; fifty-nine in the paracetamol treated cohort, representing 28.0% and fifty-five representing 26.2% of the total study population. Eight of the patients were educated only to the primary level, made up of 3 (1.4%), 2 (1.0%) and 3 (1.4%) for the ibuprofen, paracetamol and placebo treated cohorts. There was no statistical significant difference in the distributions amongst the cohorts within the educational levels (**Figure 4**).

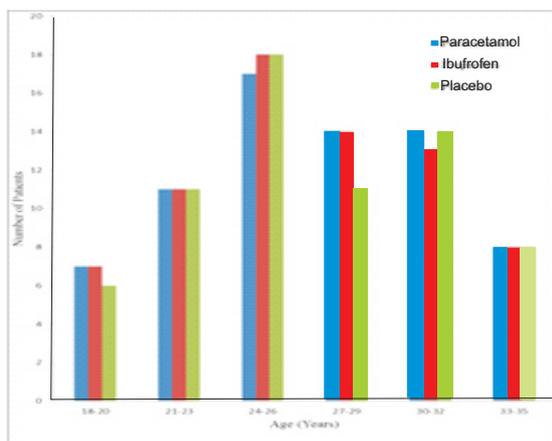


Figure 4: Distribution of patient among the cohorts. (Most patients were in the 24-26 age group, n = 210 and p>0.05)

The social habits of the patients recruited for the study is shown on **Table 2**. There were 14 occasional drinkers representing 6.7% of the study population. The contribution of the occasional drinkers to the number of the study population was not statistically significant (p>0.05).

Table 2: Social habits of patients in the study

Occasional use of Alcohol	ibuprofen Treated Group N(%)	Paracetamol Treated Group n(%)	Placebo Treated Group n(%)	Total
Yes	5(7.1)	4(5.6)	5(7.4)	14(6.7)
No	66(92.9)	67(94.4)	63 (92.6)	196(93.3)
Total	71(100.0)	71(100.0)	68(100.0)	210(100.0)

*Smokers were excluded from the study. 14 (6.7%) of the patients are occasional users of alcohol. This proportion is not statistically significant.

Figure 5 shows the indications for disimpaction of mandibular third molars in the study. The most common indication for disimpaction was caries, seen in 105 patients, representing 50% of the study population. Prophylaxis and orthodontic reasons contributed the least, 2 (1.0%) of the study population.

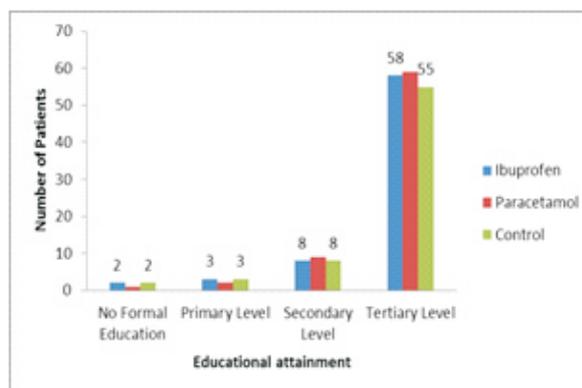


Figure 5. Educational attainments of the patients. Eighty-one per cent of the patients were educated to tertiary level, made up of 58, 59 and 55 for the ibuprofen, paracetamol and placebo treated cohorts. The difference in distribution within the cohorts is not statistically significant.

Figure 6 shows that 157 patients, representing 74.8% of the study population had mesio-angular impaction and 4 representing 1.9% of the studied population had disto-angular impaction. There was no statistical significance in the proportion contributed by disto-angular impaction to the study (p>0.05).

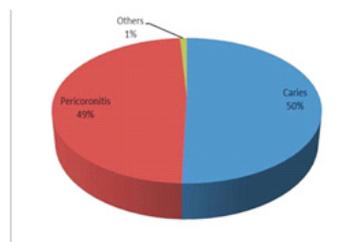


Figure 6. Indications for disimpaction of the molars used in the study. Caries is the commonest indication for disimpaction, contributing 50% of the indications (n = 210).

The difficulty index of the disimpacted molars is shown in Figure 7. Most (206 representing 98.1%) of the disimpacted molars were of mildly to moderately difficulty categories, while 4 (1.9%) were of severe difficulty. The proportion contributed by molars of severe difficulty category is not statistically significant ($p > 0.05$).

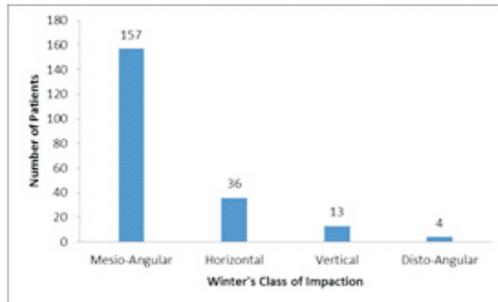


Figure 7. Winter's classification of the impacted molars used in the study. 156 showed mesio-angular impaction, 36 displayed horizontal impaction and 13 vertical impaction while 4 showed disto-angular impaction (There is no significant contribution to the total number by disto-angular impaction, $n = 210$).

Figure 8 displays the duration of surgical stimulation per cohorts. Maximum surgery time was 30 minutes and 9 of the molars were disimpacted in 21-30 minutes. Most of the molars (183, 87.1%) made up of 60 (28.6%), 62 (29.5%) and 61 (29.1%) for the ibuprofen, paracetamol and placebo treated cohorts, were disimpacted in 11-20 minutes and 18 (8.6%) were disimpacted within 10 minutes. The differences in the distribution per cohort were of no statistical significance ($p > 0.05$).

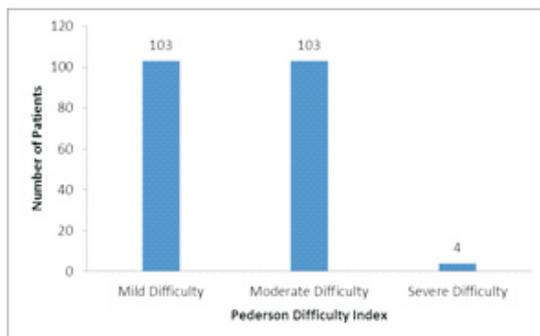


Figure 8. Duration of Surgical Stimulation per Cohort (Most of the molars were disimpacted in 11-20 minutes. The difference in duration of surgical stimulation among the cohorts is of no statistical significance, $n = 210$).

Figure 9 shows a graphic presentation of the mean pain intensity difference (MPID) of the patients studied within the cohorts. Ibuprofen showed a statistically significant superiority over paracetamol and placebo from the 2nd through the 6th hour of the study ($p < 0.05$). Between 1.5 and

2.5 hours, the placebo tends to exhibit superiority over paracetamol.

The first evidence of paracetamol over placebo was noted in the 3rd hour and continues through the sixth hour. These differences between paracetamol and placebo are however of no statistical significance.

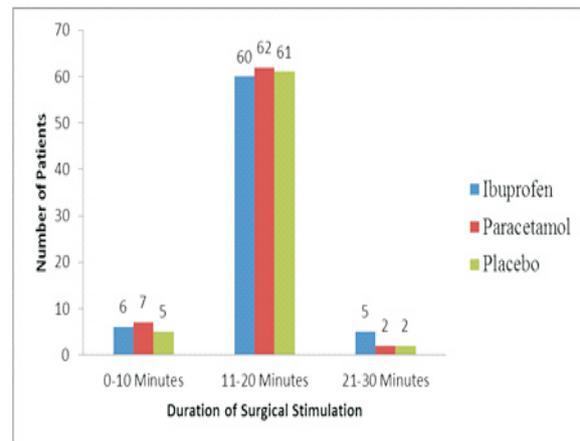


Figure 9. Duration of Surgical Stimulation per Cohort (Most of the molars were disimpacted in 11-20 minutes. The difference in duration of surgical stimulation among the cohorts is of no statistical significance, $n = 210$).

Seven percent of the total population recruited for the study had cause to withdraw from the study, while two hundred and ten, representing ninety-three percent of all recruited patients were fully compliant and represent the study population ($n = 210$). [The level of compliance (93%) is therefore statistically significant ($p < 0.05$)].

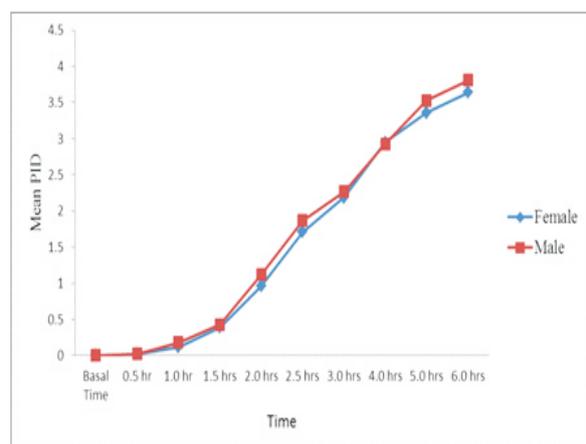


Figure 10. Comparison of MPID by gender over a 6-hr period for all cohorts combined. $n = 210$.

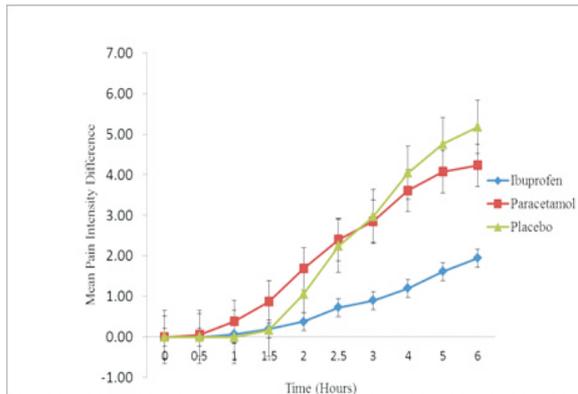


Figure 11. Graphical representation of the MPID, over a six-hour period. (The ibuprofen exhibited a statistically significant superiority over paracetamol, from the 2nd hour through the 6th hour of study ($p < 0.05$). Before the 3rd hour placebo exhibited superiority over paracetamol. The trend was reversed after the 3rd hour ($n = 210$).

Discussion

Alleviating pain is of utmost importance when treating dental patients as it is prevalent and has far reaching effects for both the patient and the clinician alike^(16,17). The age range of the participants in this study was 18-35 years, mean \pm SEM is 26.7 ± 0.1 years.

This represents 'healthy' young subjects that are capable of complying with the study and in whom surgical removal of the mandibular third molars is indicated⁽⁶⁾. It has the advantage of recruiting young patients with pliable bones and less chances of systemic co-morbidity and/or concurrent use of medications that could constitute significant confounders in the study. Being healthy and young, the patients are able to comprehend and adapt to the protocols easily. This is a major strength of this present study. Also all patients presented with M3 that are indicated for elective disimpaction; this is of great ethical value.

The patients recruited for the study were matched for age, and gender. Furthermore, there exist no statistically significant variations ($p < 0.05$), with respect to educational attainment, social habits, difficulty index and duration of surgical stimulation.

These are all very important in ensuring that the cohorts were made of homogeneous patient populations and therefore a fair assessment of the agents used in the study.

This study recruited two hundred and ten patients. Most of the patient, which is 172 (81%), was educated to the tertiary level. This is most likely due to the proximity of the study location to the University of Benin campus. This proportion was distributed among the cohorts in such a manner that the differences with the cohorts were not statistically significant ($p < 0.05$). The level of education is advantageous to this study and must have contributed to the ease of understanding and compliance with the study protocol and lends strength to findings from the study. The availability of such a large number of consenting

students is possibly due to the fact that the study period coincided with a period in the history of the University of Benin when there are numerous part-time and/or diploma courses. The advantage of this to the researcher is that patients are easily available for study and to the patients; and to the study population timely treatment at reduced rates as rebates are usually provided when patients' treatment protocols involve any planned research work.

The advantage of this to the participants in this research is of great value and profound as participation here cares of a major reason (financial constraints) why patients fail to seek and/or demand dental treatment in our environment⁽¹⁸⁾, even in the face of utmost need for such treatments.

The major cause of disimpaction of M3 from this study was caries accounting for 50% of all the cases treated. This finding is in contrast to findings of Obiechina et al⁽¹⁹⁾. In 2001, Bataineh et al⁽²⁰⁾ in 2002 and Gbotolorun et al⁽²¹⁾ in 2007, where pericoronitis was the commonest indication for extraction, contributing 46.8% and 63.1% respectively. Though pericoronitis contributed the most indication for removal of mandibular third molars, in the finding of Bataineh and co-workers, the relative contribution of pericoronitis to the indications is pretty close to findings in this study. In their study, Obiechina et al⁽¹⁹⁾ found that the proportion of cases of pericoronitis was smaller (42.9%) than finding in this study, but it constituted the most common cause of extraction of the impacted mandibular molars. In this present study, pericoronitis accounted for 49% of the cases treated. The emergence of caries as a leading indication for disimpaction of M3 is probably due to social habits of the population studied, with an increased intake of cariogenic snacks, meals and an ineffective or reduced oral health care practices.

Radiographic evidence from the studied population, with reference to the long axis of the second mandibular molars, revealed that mesio-angular impaction was commonest (74.8%), this is similar to the finding of Unwerawattana in 2006, but the relative contribution of mesio-angular impaction in this study (74.8%), is higher than that in the findings of Unwerawattana (59.1%), but is in conformity with the findings from Pakistani⁽²³⁾, United States of America⁽²⁴⁾ in 2003, China⁽²⁵⁾ in 2003, Spain⁽²⁶⁾ in 2005, and earlier report from Nigeria⁽²¹⁾, where the common type of M3 impaction was mesio-angular impactions. This finding contrasts that of Bataineh and co-researchers⁽²⁰⁾, who found vertical impaction to be the commonest cause of impaction, contributing 61.4% of the studied cases. The high incidence of mesio-angular impaction of the M3 may be due to their late development and maturation of M3, their path of eruption and lack of adequate space in mandible.

There is a dearth of information in literature on work done on blacks and particularly amongst Nigeria to compare effectiveness of agents and influence of gender on pain perception. Finding in this study shows a difference that is not statistically significant ($P > 0.05$). This is unlike the finding of Vallerand and Polomano⁽²⁷⁾ which identified gender differences in the perception of pain intensity for both acute and chronic pain and with responses to analgesics, with females showing higher pain ratings, and a lower tolerance for pain. The finding in this present study may be attributed to generational changes with tendencies for gender equality in psychological, economic and social spheres of life.



To the best knowledge of the researchers no work has been published from this part of the world, on the subject matter. Available information is on work done elsewhere amongst the Caucasians and even at that, direct comparisons between paracetamol and non-steroidal anti-inflammatory drugs has not been extensively studied⁽²⁸⁾. Globally, ibuprofen showed a superior analgesic efficacy to both paracetamol and placebo ($p < 0.05$). This can be explained by the superior anti-inflammatory property of ibuprofen conferred on it by its ability to efficiently inhibit inducible cyclo-oxygenase-2, which is a major source of prostanoids in inflammation and cancer⁽²⁹⁾. This finding contrasts the findings of Angelopoulou et al⁽³⁰⁾, which revealed no statistically significant difference between the ibuprofen and paracetamol, but this finding is similar to that in an earlier study by Lala et al⁽³¹⁾, in 2000 where ibuprofen showed a statistically significant superiority to paracetamol in a study that employed 'sore throat' pain model. This notwithstanding, paracetamol remains a viable alternative to the NSAIDs in post-operative period and should be preferred in patients prone to side effects from the NSAIDs⁽²⁸⁾. The explanation to analgesic activity of the placebo with compared favourably with paracetamol is attributable to "placebo effect" a situation where the thought of having taken a drug produces some degree of desired effects among the patients.

No adverse effects were noted during the period of study in the patients. This is possibly because of the short period of observation (6 hours) and definitely a pointer to the degree of safety of the drugs. Though the price of paracetamol is less than that of ibuprofen per unit dose, the differences in prices of the agents are not strikingly different. Evidence available from this study will therefore be useful when deciding on pharmacologic management of a patient, post-third molar surgery.

Conclusion

This study concludes that ibuprofen is superior to paracetamol in the management of pain following a third molar surgery, secondly, there is no statistically significant difference between paracetamol and placebo in post-surgical dental pain and lastly, there are no statistically significant differences between the genders in pain perception following a third molar surgery.

Acknowledgement

This work is an abridged thesis. It was presented in the annual scientific conference of the School of Dentistry, University of Benin and the synopsis was accepted by the School of Postgraduate studies, University of Benin in 2012, in partial fulfillment of requirements for the award of Masters of Science, in Clinical Pharmacology and toxicology.

References

1. Kiwanuka SN, Lström AN. Self-reported dental pain and associated factors in Ugandan School children. *Norsk Epidemiologi* 2005; 15:175-182.

2. Peres MA, Barros AJ, Peres KG, Araújo CL, Menezes AM. Life course dental caries determinants and predictors in children aged 12 years: a population-based birth cohort. *Community Dent Oral Epidemiol* 2009; 37:123-133.
3. Grendell RN. Pain management. Available on www.delmarlearning.com accessed on June 5, 2012.
4. Hobdell M, Petersen PE, Clarkson J, Johnson N. Global goals for oral health 2020. *Int Dent J* 2003; 53:285-288.
5. Chang DJ, Desjardins PJ, King TR, Geba GP. The analgesic efficacy of etoricoxib compared with oxycodone/acetaminophen in an acute postoperative pain model: a randomized, double-blind clinical trial. *Anesth Analg* 2004; 99:807-815.
6. Sortino F, Ciccù M. Strategies used to inhibit postoperative swelling following removal of impacted lower third molar. *Dent Res J (Isfahan)* 2011; 8: 162-171.
7. Norholt SE, Sindet-Pedersen S, Bugge C, Branedjerg PE, Ersboll BK, Bastian HL. A randomized, double-blind, placebo-controlled, dose-response study of the analgesic effect of lornoxicam after surgical removal of mandibular third molars. *J Clin Pharmacol* 1995; 35:606-614.
8. Lynch M. Pain as the fifth vital sign. *J Intraven Nurs* 2001; 24:85-94.
9. Okeson JP. Bell's orofacial pains: the clinical management of orofacial pain. 6th ed, Quintessence, Chicago 2005. Pg 6.
10. Hargreaves K, Abbott PV. Drugs for pain management in dentistry. *Aust Dent J* 2005; 50:14-22.
11. Stephens J, Laskin B, Pashos C, Pena B, Wong J. The burden of acute postoperative pain and the potential role of the COX-2-specific inhibitors. *Rheumatology* 2003; 42:40-52.
12. Williams Frydman. Effective Post-Surgical Pain Management. *Oral H Journal* 2010. Available at: <http://www.oralhealthgroup.com>, assessed on 28th August 2013.
13. Ehigiator O, Odai CD, Obuekwe ON and Azodo CC. Evaluation of Drug Prescription in Oral Surgery. *Nig Hosp Pract* 2011; 7:77-81.
14. Perrott DA, Piira T, Goodenough B, Champion GD. Efficacy and Safety of Acetaminophen vs Ibuprofen for Treating Children's Pain or Fever A Meta-analysis. *Arch Pediatr Adolesc Med* 2004; 158:521-526.
15. Ziccardi VB. Single-dose vicoprofen compared with codeine and placebo in patients with acute post-operative pain after third molar extractions. *J Oral maxillofac Surg* 2000; 56:622-628.
16. Menhinick KA, Gutmann JL, Regan JD, Taylor SE, Buschang PH. The efficacy of pain control following nonsurgical root canal treatment using ibuprofen or a combination of ibuprofen and acetaminophen in a randomized, double-blind, placebo-controlled study. *Int Endod J* 2004; 37:531-541.



17. Pozzi A, Gallelli L. Pain management for dentists: the role of ibuprofen. *Ann Stomatol (Roma)*. 2011; 2(3-4Suppl): 3-24.
18. Anyanechi C, Saheeb BDO. Reasons underlying failure to seek early dental treatment among patients presenting in a Nigeria Tertiary Hospital. *J Med Biomed Res* 2013; 12:37-45.
19. Obiechina AE, Arotiba JT, Fasola AO. Third molar impaction: evaluation of the symptoms and pattern of impaction of mandibular third molar teeth in Nigerians. *Odontostomatol Trop* 2001; 24:22-25.
20. Bataineh AB, Albashaireh ZS, Hazza'aAM. The surgical removal of mandibular third molars: a study in decision making. *Quintessence Int* 2002; 33:6 13-617.
21. Gbotolorun OM, Olojede AC, Arobita GT, Ladeinde AL, Akinwande JA, Bambose BO. Impacted mandibular third molars: presentation and postoperative complications at the Lagos University Teaching Hospital. *Nig Q J Hosp Med* 2007; 17: 26-29.
22. Unwerawattana W. Common symptoms and type of impacted molar tooth in King Chulalongkorn Memorial Hospital. *J Med Assoc Thai* 2006; 89:134-139.
23. Ishfaq M, Wahid A, Rahim AU, Munim A. Patterns and presentations of impacted mandibular third molars subjected to removal at Khyber College of Dentistry Peshawar. *Pak Oral Dent J* 2006; 26: 221-226.
24. Bui CH, Seldin EB, Dodson TB. Types, frequencies and risk factors for complications after third molar extraction. *J Oral Maxillofac Surg* 2003; 61:1379-1389.
25. Quek SL, Tay CK, Tay KH, Toh SL, Lim KC. Pattern of third molar impaction in a Singapore Chinese population; a retrospective radiographic survey. *Int J Oral Maxillofac Surg* 2003; 32: 548-552.
26. Chapparro-Avendano AV, Perez-Garcia S, Valmaseda-Castellon E, Berini-Ayets L, Gay-Escoda C. Morbidity of third molar extraction in patients between 12 and 18 years of age. *Med Oral Patol Oral Cir Bucal* 2005; 0:422-431.
27. Vallerand AH, Polomano RC. The relationship of gender to pain. *Pain Manag Nurs* 2000; 1:8-15.
28. Hyllested M, Jones S, Pedersen JL and Kehlet H. Comparative effect of paracetamol, NSAIDs or their combination in postoperative pain management: a qualitative review. *Br J Anaesth* 2002; 88:199-214.
29. Furst DE, Ulrich RW. Basic and clinical pharmacology. 10th ed. Kartzung BG editor. McGraw-Hill, Singapore 2007; 573-583.
30. Angelopoulou MV, Vlachou V, Halazonetis DJ. Pharmacological management of pain during orthodontic treatment: a meta-analysis. *Orthod Craniofac Res* 2012; 15:71-83.
31. Lala I, Leech P, Montgomery L, Bhagat K. Use of a simple pain model to evaluate analgesic activity of ibuprofen versus paracetamol. *East Afr Med J* 2000; 77:504-507.