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An Investigation of the Comparative Effectiveness of Ibuprofen and Paracetamol in the Management of Orthodontic Discomfort

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Keywords

Paracetamol, orthodontic, ibuprofen

Abstract

Aim: An investigation of the comparative effectiveness of ibuprofen and paracetamol in the management of orthodontic discomfort was carried out in a randomised clinical study. Material and methods: One hundred patients who were about to get therapy with a fixed appliance volunteered to take part in the trial. The experiment's subjects were randomly divided into two groups. Paracetamol (1 gramme, split into two caplets of 500 milligrammes each) was administered orally to participants in Group A, once an hour before the customary separator installation and again 6 hours after the first dose. Those in Group B were given 400 milligrammes of ibuprofen split between two caplets (for a total of 800 milligrammes) to be taken orally twice: first an hour before the standard separator installation, and again six hours following the initial dosing. Results: On day 7, 82% (82) of individuals had pain levels below or equal to 10 mm on the VAS, necessitating a separate analysis of these data. This meant that there was an upward bias in the data. On day 7, respondents' VAS pain levels were categorised as either 0-10 mm (not significantly different from no pain) or 10+ mm (considerably different from no difference). If the patient's score was more than 10 millimetres, it meant that discomfort was still present. Pain scores higher than 10 mm on the VAS persisted in 24% (intention-to-treat analysis) and 26% (per-protocol analysis) of the paracetamol group, but in only 18% and 14% (intention-to-treat, P = 0.61; per protocol, P = 0.22) of the ibuprofen group. Conclusions: Compared to taking one gramme of paracetamol two hours prior to bedtime on the day of treatment and again after the placement of orthodontic separators, we found that taking 400 milligrammes of ibuprofen an hour before the placement of separators and again six hours after the initial dose was more effective. On the first and subsequent days of the trial, those in the ibuprofen group reported significantly less pain than those in the paracetamol group at most time intervals. The orthodontic pain that was felt the day after the separator was installed could not be alleviated by the two doses of ibuprofen used the day before.

1. Introduction

Almost every patient who undergoes orthodontic treatment complains of some kind of pain or discomfort, albeit how each person experiences it may vary greatly. There's also the possibility that some people may avoid getting orthodontic treatment completely because of the pain they anticipate feeling. There is currently no consensus guideline on the use of analgesics in orthodontics;

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nonetheless, paracetamol (also known as acetaminophen) and ibuprofen are widely advised for the alleviation of orthodontic discomfort. Yet, both of these drugs may assist reduce discomfort associated with orthodontic treatment. Ibuprofen has been shown to be more effective than aspirin or a placebo when given soon after the insertion of a separator or arch wire. Patients who were given 400 milligrammes of ibuprofen an hour before the installation of a separator reported much less pain than those who had received either postoperative ibuprofen or a placebo. Over the course of a week, patients who were given preemptive ibuprofen reported much less pain compared to individuals who did not receive preemptive analgesia [3,4]. Moreover, fewer of these patients looked to need extra rescue medicine. The patients who did not get pain medication before they felt pain It also seems that two doses of ibuprofen, one taken an hour before surgery and the other six hours after surgery, are more beneficial than the preoperative dose alone. Recent research randomised 150 individuals to receive either paracetamol, ibuprofen, a placebo, or one of six different therapy options. Patients who had arch wires placed to straighten their teeth were surveyed about the level of discomfort they experienced afterwards. [5] Comparisons of analgesic effectiveness were done, despite the study's lack of statistical power, and it was shown that both paracetamol and ibuprofen were more successful than the placebo in lowering pain levels in the first 24 hours following arch wire installation. In spite of the placebo's status as the gold standard, this was the result.

It is theorised that the analgesic action of NSAIDs like ibuprofen is due to the drugs' ability to reduce the production of prostaglandins at the site of tissue injury. It is thought that this occurs because COX-1 and COX-2 cyclooxygenase enzymes are being blocked. [6] There is some evidence that paracetamol's actions are not primarily at either enzyme. [7] Bone resorption is facilitated by prostaglandins, which play an essential role in orthodontic tooth movement. It has been hypothesised that suppressing prostaglandins would slow down the movement of teeth during orthodontic treatment. So, those who are getting orthodontic treatment should generally avoid NSAIDs, since doing so might extend the duration of the procedure. [8] Unfortunately, the therapeutic effects of NSAIDs on orthodontic tooth mobility are yet unclear. This is particularly true when analgesics are used for a short time before to the start of treatment. As paracetamol has a somewhat weak inhibitory effect on peripheral prostaglandin production, it was assumed that it would be an ideal pain reliever for orthodontic patients since it would have little impacts on tooth movement. Paracetamol is thought to reduce central rather than peripheral pain by inhibiting cyclooxygenase-3 (COX-3) in the central nervous system, as stated in [9].

The purpose of this randomised clinical trial (RCT) was to evaluate the relative efficacy of ibuprofen and paracetamol in reducing discomfort associated with separator installation. Since ibuprofen may affect tooth mobility, a noninferiority design was used for as the study's major end measure. This was done so that if the two therapies were equally effective at relieving pain, paracetamol might be used instead.

2. Material and Methods

One hundred patients who were about to get therapy with a fixed appliance volunteered to take part in the trial.

INCLUSION CRITERIA

- Age ranging from 13 to 17 years old
- Absence of a family history of peptic ulcer disease, renal impairment, hepatic impairment, or cardiac impairment
- There is no history of asthma that required the use of steroid inhalers, nor has there been any unstable asthma in the last year
- Ibuprofen and paracetamol have never been known to cause any harmful effects in the past
- No analgesics nor antibiotics are being taken at the moment

The experiment's subjects were randomly divided into two groups. Paracetamol (1 gramme, split into two caplets of 500 milligrammes each) was administered orally to participants in Group A, once an hour before the customary separator installation and again 6 hours after the first dose. Those in Group B were given 400 milligrammes of

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ibuprofen split between two caplets (for a total of 800 milligrammes) to be taken orally twice: first an hour before the standard separator installation, and again six hours following the initial dosing. Constrained randomization was utilised to ensure that similar numbers of patients were placed in each of the three treatment arms. The drug was dispersed in sets of eight, which served this purpose. Researchers, clinicians, and statisticians were all kept in the dark about which treatment groups their patients were assigned to. The capsules of the analgesics all looked the same, and they were all stored in numbered, hermetically sealed canisters. An envelope, with the secret order of the random allocation, was put in the room's centre.

Over the next week after the separator was placed, patients were asked to report their level of discomfort using a standardised pain questionnaire. Seven 10-centimeter-long visual analogue scales (VAS) were included in a numbered booklet and delivered to each patient. There was a cheerful face and a sad face, one at either end of the line, with the adverbs "no pain" and "worst agony imaginable," respectively. Patients were instructed to keep track of how much discomfort they felt when biting and chewing immediately after the placement of the separator, two hours later, six hours later, before going to bed on the day of the appointment, the following morning, two days later, three days later, and seven days later.

Patients were told they would not need any further analgesics, but may take whatever they deemed necessary for pain relief for up to 8 hours following their last dose of the study drug. In the case of a bad incident, they were instructed to contact both their doctors and the orthodontics office as soon as possible. Further analgesics and their administration times should be noted in the pain diary.

Each VAS measurement was taken by the same examiner, using the same stainless steel ruler, immediately after completion of the pain questionnaires. To the closest millimetre, every dimension was measured. To ensure the examiner's consistency, 20 questionnaires were randomly selected and measured again in the two weeks after the first measurements. At no time did the examiner have access to the unaltered baseline data. All rescores were found to be within 0.5 mm of the original values, suggesting that examiner reliability was rather high.

Average pain ratings were taken two hours, six hours, and again just before bedtime after the separator was inserted to determine how well the procedure went. It was hypothesised that the synergistic effects of the two drugs would be greatest at this time.

Secondary outcomes were the average pain ratings on days 1, 3, and 7 after separator installation, as well as the need for additional analgesics.

The sample size for this research was established by the primary endpoint that was to be analysed in a noninferiority trial. So, the total number of people who took part in the study was used as the sample size. Based on previous pain studies10, it was hypothesised that paracetamol may be considered not inferior to ibuprofen if it resulted in pain ratings no more than 10 mm worse than ibuprofen on the VAS. This was done using the Visual Analog Scale to see how the two drugs stacked up against one another (margin of noninferiority). Assuming a standard deviation of 20 mm, a one-sided significance level of 5%, and a power of 95%, it was calculated that 100 patients (50 in each group) would be needed to detect a difference in pain ratings of 10 mm.

3. Results

In all, there were a total of 64 female participants (64%) and 36 male participants (36%). This was deemed to be typical of the patient population that seeks orthodontic treatment. There was neither a statistically significant difference in the ages of people in each group nor the genders of those people. In the group that took paracetamol, 36% of the participants were male, while in the group that took ibuprofen, 36% of the participants were male (the chi-square test for association yielded a P value of 2.36), and the mean ages were 14.2±2.11 years and 14.5±2.33 years, respectively (the independent-samples t test yielded a P value of 0.41).

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Table 1: Mean pain scores (in millimeters) from 2 hours to bedtime

	Group A, paracetamol	**Group B, ibuprofen**
Combined mean pain score (2 hours to bedtime)	32.25±4.58	24.25±2.69
Mean difference in pain scores (A-B) 90% CI of the difference	9.6(4.1-14.25)	9.8(3.9-12.55
p value	0.22	

Table 2: Mean pain scores (in millimeters) at days 1 to 3

	Group A, Paracetamol	**Group B, ibuprofen**
Combined mean pain score (days 1-3)	25.52±8.85	23.58±6.98
Mean difference in pain scores (A-B) 95% CI of the difference	2.85(-1.58-10.85)	5.22(-1.55-10.74)
P value	0.27	

Table 3: Mean pain scores from 2 hours to day 7 following separator placement for intention to treat analysis

Pain scores	**Group A, Paracetamol**	**Group B, ibuprofen**
2 hrs	26	20
6hrs	35	25
bed	33	27
day 1	32	32
day 2	22	18
day 3	16	13
day 7	7	7

A non inferiority analysis was utilised to test the null hypothesis for the main outcome measures at 2 hours, 6 hours, and bedtime. From two hours before night, paracetamol-induced pain ratings are at least 10 mm (the margin of equivalency) greater than ibuprofen-induced scores. It was shown that the issue of multiple significance tests might be mitigated by averaging the pain ratings collected at 2-, 6-, and before-bedtime. Each group's average pain rating was determined over this time period.

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When comparing the means of pain ratings between groups, the non inferiority analyses' null hypothesis necessitated using a one-sided, 5% level, t test (with a test value of 10 rather than 0). In Tables 1 and 2, you'll see the outcomes. The right-hand whiskers of the 95% confidence intervals fall beyond the +10 mm line (margin of equivalence), indicating that paracetamol's impact is not the same as or better than ibuprofen's. Perprotocol and intention-to-treat analyses provide confidence intervals that are all above the 0 line, indicating that they are statistically equivalent. This implies that, on day one, between the hours of 2pm and night, ibuprofen was much superior versus paracetamol. A 2-sided 5% significance test of the null hypothesis that mean pain scores in both groups were identical using an independent-sample t test yielded a P value of 0.003 (in the intention-to-treat analysis), supporting the finding of a significant difference between the 2 analgesics when a superiority (rather than noninferiority) perspective was adopted.

Using a noninferiority strategy was inappropriate for the secondary outcome measure of pain at 1–3 days. Two-sided tests were performed at the 5% level of significance, with the null hypothesis being that there was no difference between the two treatments (Table 2). The ratings with paracetamol and ibuprofen were statistically the same from day 1 to day 3. The chi-square test for association was used to examine the percentages of patients in each group who still had pain ratings more than 10 mm on day 7, despite the fact that most patients reported no discomfort by that point. Neither the intention-to-treat analysis nor the protocol-based analysis revealed any statistically significant changes. There were 10% of patients in the paracetamol group (5 patients) and 12% of patients in the ibuprofen group (6 patients) who need supplemental analgesia (P =.41 for a chi-square test of association).

Patients in the ibuprofen group reported increased discomfort beginning 2 hours after separator implantation and continuing until the morning of the following day, as shown by the mean pain ratings and 95% CI of the mean in table 3. Following that, most patients saw a decline in levels until day 7. Paracetamol-treated patients also reported greater discomfort beginning 2 hours after separator implantation, with the pain reaching its climax 6 hours later on the same day. Nevertheless, the paracetamol group reported considerably greater pain ratings over this time period. In both groups, pain ratings decreased gradually over the course of seven days.

Each patient's pain score for the subsequent time period is the average of their values from days 1, 2, and 3. Table 2 displays the results of a two-tailed, paired t test comparing the means of pain ratings at the 5% significance level. No statistically significant difference in mean pain ratings between ibuprofen and paracetamol was seen between the two treatment groups either in the intention-to-treat (P = 0.41) or the per-protocol analysis (P = 0.06).

On day 7, 82% (82) of individuals had pain levels below or equal to 10 mm on the VAS, necessitating a separate analysis of these data. This meant that there was an upward bias in the data. On day 7, respondents' VAS pain levels were categorised as either 0-10 mm (not significantly different from no pain) or 10+ mm (considerably different from no difference). If the patient's score was more than 10 millimetres, it meant that discomfort was still present. Pain scores higher than 10 mm on the VAS persisted in 24% (intention-to-treat analysis) and 26% (per-protocol analysis) of the paracetamol group, but in only 18% and 14% (intention-to-treat, P = 0.61; per protocol, P = 0.22) of the ibuprofen group.

4. Discussion

Maximizing analgesia helps alleviate the pain that comes with moving and adjusting orthodontic appliances, which is a big deal. Ibuprofen considerably outperformed paracetamol in delaying the start of peak pain after separator installation, according to the findings of a randomised controlled experiment. Paracetamol may not be effective enough, according to the findings, even when administered at the maximum dosage. The alternative hypothesis, which holds that ibuprofen is more efficacious than paracetamol, was shown to lack evidence via a noninferiority research with a margin of equivalency of 10 mm of discomfort. The use of a standard superiority analysis demonstrated this. There is evidence from this study that ibuprofen, taken both before and after a

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separator is implanted, is more beneficial than paracetamol for managing pain in the immediate postoperative period. The fact that the trial took place provides this evidence.

Overall, ibuprofen users reported less discomfort than paracetamol users from day 1 to day 3. This held true despite the fact that both groups received the same quantity of painkillers. The long-term effects of ibuprofen in the treatment of orthodontic pain may be more favourable than those of paracetamol, even when blood levels of the medicine are undetectable or below the therapeutic window of efficacy. As the half-life of ibuprofen is longer than that of paracetamol, it is more effective. In an earlier trial, ibuprofen's advantages were shown to stay much longer than those of a placebo. [4,9,10] Those who took both ibuprofen before and after surgery had lower pain levels than those who took a placebo or postoperative ibuprofen alone commencing on day 2. The pain ratings of patients who had taken ibuprofen both before and after surgery were significantly lower than those of patients who had only taken ibuprofen after surgery. Yet, neither the intention-to-treat nor the per-protocol analysis in our study found a statistically significant difference in the mean pain ratings across this 1- to 3-day interval. This was true regardless of the methodology used to examine the data. Around 14% of participants in the paracetamol group had pain levels more than 10 mm on day 7. The ibuprofen group had a rise of between 14% and 18%. Given that just two doses of each analgesic were delivered at the start of the test, roughly six days earlier, it is not surprising that the difference did not reach the criterion for statistical significance. Despite the fact that most patients' pain ratings were minor at this time, there was still a general trend for those who had ibuprofen to experience less pain than those who were in the group that received paracetamol.[11]

In this study, 12 percent of patients needed additional analgesics, most often given the night before or the day after the separator was implanted. Intuitively, it seems to reason that those who had the most intense initial pain would gain the most from taking further analgesics. Nevertheless, only 6 of the 20 patients who reported pain levels of 70 mm or greater on the VAS really needed emergency treatment. Although the study design required participants to use just the trial drugs if at all possible, this is probably the case. If that's the case, it might explain it. The results imply that a more continuous regimen of regular analgesic may be necessary besides only two split doses of either painkiller, one hour before and six hours after the installation of the separator. To figure this out, we split the dosages of each analgesic in half.

A randomised controlled trial (RCT) involving many physicians is complex to organise and carry out, and the researchers in this study faced various obstacles. After the unintentional enrollment of 20 patients who did not match the inclusion criteria, it is obvious that there is a need for improved communication between the various research divisions. This study also emphasises the need of planning for the handling of unwanted side effects in randomised controlled trials (RCTs). One participant in this study had what may have been an adverse reaction to paracetamol. It is crucial to have a complete medical history and thorough records of the incident, in addition to swiftly notifying the monitoring organisations. It is crucial to do thorough follow-up. The pain questionnaire in this particular RCT lacked a provision for documenting adverse events, which is something that should be standard in future studies of this kind. The adverse reaction, triggered by paracetamol in this case, has been documented before. [12]

5. Conclusions

Compared to taking one gramme of paracetamol two hours prior to bedtime on the day of treatment and again after the placement of orthodontic separators, we found that taking 400 milligrammes of ibuprofen an hour before the placement of separators and again six hours after the initial dose was more effective. On the first and subsequent days of the trial, those in the ibuprofen group reported significantly less pain than those in the paracetamol group at most time intervals. The orthodontic pain that was felt the day after the separator was installed could not be alleviated by the two doses of ibuprofen used the day before.

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