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Codafen continus® analgesia for dental day surgery (comparison of codafen continus vs. diclofenac)

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Satisfactory postoperative analgesia for intermediate day surgical procedures is a challenge for anaesthetists. This prospective, randomized, double-blind study examined the efficacy of a new combined analgesic tablet for dental day cases. Codafen continus® is an analgesic preparation containing ibuprofen controlled release 300 mg and codeine phosphate normal release 20 mg. This combination was compared with diclofenac 75 mg for pain relief following day case extraction of third molar teeth. There were no differences between the two preparations with respect to the amount of analgesia provided as measured by categorical pain scores and the use of escape analgesia. The study confirmed that analgesia provided by codafen continus was as effective as diclofenac 75 mg and no serious side-effects were noted.

Key words: Day surgery, dental, postoperative analgesia, non-steroidal anti-inflammatory drugs

Introduction

With the expansion of day surgery there is a need to develop and test safe analgesics for day cases. Codafen continus® tablet (ibuprofen controlled release 300 mg/codeine phosphate normal release 20 mg tablet) is a novel combination of controlled release ibuprofen and normal release codeine phosphate in a bilayer tablet which may be used to improve postoperative analgesia and reduce inflammation. After preliminary clinical use it was thought that this new formulation could represent an improvement on previous oral analgesics and might be suitable for postoperative pain relief following day surgery. Ibuprofen has already been shown to have analgesic properties in the treatment of pain following dental surgery[1]. Furthermore, a greater analgesic effect had been reported with the combination of ibuprofen and codeine than either agent alone[2]. Removal of third molars under general anaesthesia may result in severe pain and local oedema. Audit of postoperative pain following this procedure within the Addenbrooke's Day Surgery Unit (DSU) has revealed a need for improved analgesic medication for a period of up to 5 days after surgery.

The aims of this study were to compare the effectiveness and tolerability of oral codafen continus with diclofenac, a drug commonly used for the relief of postoperative pain in this group of patients.

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Methods

The study was approved by the Local Research Ethics Committee and each patient gave informed consent. One hundred and six patients of physical status ASA I or II, scheduled to undergo day surgical removal of three or four third molar teeth under general anaesthesia were recruited. The study was performed in a double-blind, placebo-controlled manner and all operations were performed in the DSU.

Patients were stratified by surgeon and gender and were then randomized to receive either diclofenac or codafen continus. The first dose of study medication (either 75 mg diclofenac or two codafen continus tablets) was given 2 h preoperatively with 50 ml of clear fluid and further identical doses were given at 12, 24 and 36 h after the first dose. Breakthrough medication for pain consisted of paracetamol 0.5–1 g 4 hourly as required to a maximum of eight tablets in 24 h.

All patients were anaesthetized using a standard anaesthetic technique which included induction and maintenance of anaesthesia with propofol and alfentanil. Patients breathed 30% oxygen in nitrous oxide spontaneously via a laryngeal mask airway and monitoring included non-invasive blood pressure, heart rate, ECG, inspired oxygen and end-tidal carbon dioxide concentration and pulse oximetry. Surgeons were asked,

Table 1. Patient demography: age, height and weight, mean (SD)

	Codafen continus			*Diclofenac*			*All patients*
	Female n = *36*	*Male* n = *17*	*All* n = *53*	*Female* n = *34*	*Male* n = *19*	*All* n = *53*	n = *106*
Age (years)	23.0 (4.89)	23.2 (3.29)	23.1 (4.41)	23.4 (3.67)	24.2 (4.01)	23.7 (3.77)	23.4 (4.10)
Height (cm)	164.9 (6.58)	179.5 (6.37)	169.6 (9.43)	166.1 (6.43)	179.4 (6.13)	170.7 (8.96)	170.1 (9.17)
Weight (kg)	59.5 (8.92)	79.2 (10.23)	65.8 (13.13)	61.7 (8.86)	76.1 (9.97)	66.8 (11.51)	66.3 (12.3)

at the end of the procedure, to assess the degree of trauma caused by surgery. This parameter was measured using a 7 point categorical scale ranging from 1 (no trauma) to 7 (severe trauma).

The main outcome measures of analgesic efficacy were time to first request for analgesia, categorical pain scores and the use of escape analgesia. On discharge patients were invited to take home and complete a diary. In this they recorded their categorical pain scores (a 9 point scale was used where 0 represented 'no pain' and 8 represented 'very severe pain'), consumption of escape analgesics and the presence and severity of side-effects at set times. These times were:

1. prior to receiving the first dose of test medication,
2. prior to induction of anaesthesia,
3. on recovery from anaesthesia,
4. on discharge from the DSU,
5. at 8 h post-first dose,
6. at the time of receiving the second dose of test medication,
7. on waking on the next two mornings,
8. prior to receiving the doses at 24 and 36 h post-first dose,
9. at 48 h post-first dose.

Drug tolerability was also recorded and the specific symptoms assessed were difficulty with breathing and concentration, constipation, drowsiness, dizziness, impaired energy, headache, nausea, insomnia, vomiting and weakness. All patients were requested to rate each of these symptoms on a five point severity scale (none, mild, moderate, severe or very severe).

The pain intensity scores at each time point were assessed by analysis of variance taking into account the stratification of randomization by surgeon and patient gender. The total number of analgesic doses required throughout the study was also analysed using this model. The interval between recovery and the first dose of analgesic taken was analysed using the Wilcoxon rank sum test, and the incidence and severity of side-effect symptoms using Fisher's exact test. Differences between the groups were judged to be significant if $P < 0.05$. The trauma inflicted in removing the teeth was included as a co-variate.

Results

Of one hundred and six patients recruited to the study, four failed to return their patient assessment diaries and one was withdrawn from the study because of severe postoperative pain requiring parenteral opioids and admission to the inpatient ward. Table 1 shows no differences in demographic details between the two groups of patients studied.

There were also no differences between the groups in duration of anaesthesia, time to immediate recovery as shown in Table 2, or surgical assessment of the degree of trauma as shown in Table 3.

Assessment of efficacy

No difference in analgesic efficacy was demonstrated; the time of first postoperative analgesic requirement and the total number of doses of escape analgesics required during the study period being comparable between the two groups studied (Table 4).

Again, as shown in Figure 1, there were no significant differences between the two treatment groups in pain intensity scores. Female patients had significantly higher pain scores than male patients throughout the study

Table 2. Details of anaesthesia: duration of anaesthesia and time to recovery, mean (SD)

	Codafen continus n = *53*	*Diclofenac* n = *53*
Duration of anaesthesia (min)	20.8 (10.4)	21.6 (9.41)
Time to recovery (min)	8.7 (5.3)	9.5 (5.4)

Table 3. Amount of trauma caused by dental surgery: trauma score, mean (SD)

	Codafen continus n = *53*	*Diclofenac* n = *53*
Amount of trauma	4.11 (1.5)	4.08 (1.45)

Table 4. Time to first escape analgesia and total number of doses of escape analgesia received during the study period

	Codafen continus n = *53*	*Diclofenac* n = *53*
Interval between recovery and escape analgesia in h, mean (25th and 75th centiles)	0.89 (0.58–2.69)	2.30 (0.79–4.5)
Number of doses of escape analgesia received per patient, mean (SD)	2.92 (2.15)	3.13 (2.17)

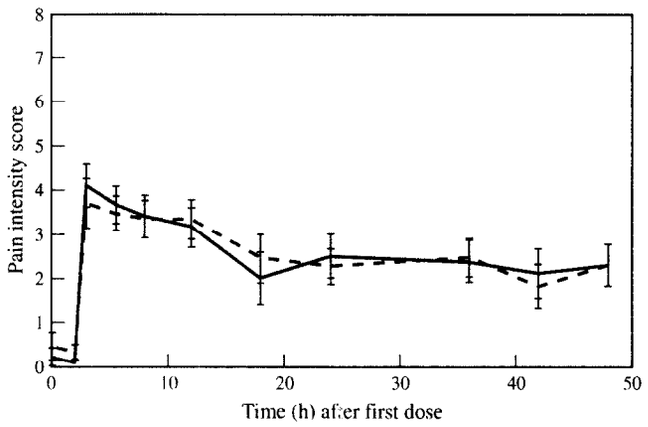

Figure 1. Pain intensity scores.

period. The amount of surgical trauma inflicted as assessed by the surgeon had some influence on the post-operative pain intensity scores at every measurement point from 8 h after the first dose of study medication (about 4 h postoperatively) to the end of the study period.

Assessment of tolerability

On recovery from anaesthesia, patients in the codafen continus group reported more weakness and difficulty concentrating than did patients in the diclofenac group (Fisher's exact test $P = 0.031$ and $P = 0.015$, respectively). Patients in the codafen continus group continued to report more weakness on assessment at discharge ($P = 0.028$), at 8 h post-first dose ($P = 0.042$), and prior to receiving the second dose of study medication ($P = 0.021$). Thereafter there were no differences between the groups in the reporting of this symptom. Also there were no other significant differences between the groups in the reporting of other symptoms at any assessment time in the study.

Discussion

The National Health Service Management Executive Task Force Report on Day Surgery, 1993, stated that day surgery could now be considered the best option for 50% of elective surgical cases[5]. At Addenbrooke's, the department of oral and maxillofacial surgery is currently performing over 60% of its workload on a day case basis. In 1994, audit within this day unit showed that while 70% of patients had little or no pain post-operatively, 14% had moderate or severe pain in the recovery area[6]. There is therefore a need for continued research to identify the best analgesic regimen.

Non-steroidal anti-inflammatory drugs (NSAIDs) have been shown to demonstrate an opioid sparing effect after many types of surgery, including day case procedures, and the reduced use of opioids has been associated with particular advantages for day case patients, including earlier patient discharge[7]. Combination therapy with opioids, NSAIDs and local anaesthetic agents where appropriate is the logical way to prevent and treat postoperative pain whilst reducing the unwanted side-effects of each individual drug group. Although it is recognized that NSAIDs may be useful as analgesics after day case surgery, patients should be carefully screened if the well known side-effects of these drugs are to be avoided, e.g. bronchospasm, renal impairment, gastric irritation and haemorrhage. Audit in the Addenbrooke's DSU in 1994 revealed that patients complained of more recovery room pain and that the use of NSAIDs was decreased as compared with the results from 1993[6]. The reasons for this may be that several recent publications have highlighted the potential adverse effects of NSAID therapy[4,8,9]. There is wide variation in the relative toxicity of these drugs, however, and ibuprofen (the NSAID present in codafen continus) has an excellent safety record when compared to other drugs in this class[4]. Indeed, ibuprofen is now available as a non-prescription medicine in the UK. In addition, combination therapy with normal release preparations of ibuprofen and codeine have already been shown to be of value following oral surgery[10–12]. Diclofenac has also been used effectively as an analgesic following dental surgery[3].

We have shown that codafen continus is as efficacious as diclofenac for pain relief after dental day surgery. The dose of codafen continus used in the study (two tablets 12 hourly) is the recommended starting dose and may be increased to three tablets 12 hourly. The dose of diclofenac used, however, is the recommended maximum daily dose (150 mg in 24 h). While this study was not designed to demonstrate pre-emptive analgesia, the preoperative use of oral analgesics is logical in order that they may be effective during the recovery period. This study did not demonstrate any adverse effects, in particular clinically significant bleeding, associated with the preoperative use of NSAIDs. Both drugs were well tolerated by fasting patients although the increased weakness postoperatively reported in those patients given codafen continus is difficult to explain.

Finally, this study showed that the degree of surgical trauma associated with the extraction of third molar teeth influenced the severity of postoperative pain. Consideration should be given to the development of a surgical scoring system to predict the probable degree of surgical trauma involved in such extractions. This would enable improved day surgery patient selection and the optimization of postoperative analgesic protocols.

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