

Impact of pharmaceutical intervention in intravenous dexketoprofen use

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ABSTRACT

Objective: To evaluate whether or not a pharmaceutical intervention can improve prescribing by doctors of a new non-steroidal anti-inflammatory (NSAID) analgesic (dexketoprofen) introduced to our hospital in order to make it more adaptable to our analgesic guidelines.

Methods: A prospective and comparative two-month study was performed. Between the study periods (period I: pre-intervention period; period II: post-intervention period), a pharmacist gave an informative talk about the hospital analgesic guidelines to traumatologists. The results from period I were also presented, pointing out the major deviations from the established guidelines.

Results: Our study was based on 88 patients. In period I ($n = 41$), the mean age was 66.5 years [27-88] and 58.4% were women, while in period II ($n = 47$), the mean age was 60.77 years [20-87] and 57.45% were women. In period I, 78.05% of all dexketoprofen was prescribed to treat post-surgical pain compared with 85.1% in the second period ($P > 0.5$). The proportion of prescriptions as fixed doses was similar in both periods (75.61% versus 74.47%). The mean duration of treatment after the pharmacist intervention was reduced and better adapted to our analgesic guideline recommendations: 3.12 days in period I and 2.11 days in period II ($P > 0.05$). Dexketoprofen was mostly combined with paracetamol. A combination with diclofenac accounted for 12% and 17% of combinations in periods I and II respectively.

Conclusion: After pharmaceutical intervention, dexketoprofen use with reference to the indication and duration of therapy was better adapted to our analgesic guidelines. However, the proportion of prescriptions of IV dexketoprofen combined with another NSAID (diclofenac) between period I and period II was not reduced after pharmaceutical intervention.

KEYWORDS

Dexketoprofen, pharmaceutical intervention, analgesia, post-surgical pain

INTRODUCTION

Dexketoprofen (DKP) is a non-steroidal anti-inflammatory agent (NSAID) that inhibits the cyclooxygenase (COX) sub-unit of prostaglandin synthetase. DKP is a dual and balanced inhibitor of COX-1 and COX-2 isoenzymes. A central action can contribute to analgesic activity, although the mechanism of this effect remains unclear [1].

Intravenous (IV) DKP is indicated for the treatment of moderate to severe acute pain, when oral administration is not appropriate, such as post-operative pain, renal colic and lumbar pain. IV DKP indications are limited to short periods

and to the acute symptomatic phase. Some studies have demonstrated a marked reduction in post-operative opioid requirements when used as part of a balanced analgesic regimen, thereby diminishing the potential opioid-induced side effects [2]. These findings are confirmed by other authors, who additionally demonstrated an attenuation of the pro-inflammatory mediator IL-6 post-operatively [2, 3]. The recommended dose is 50 mg every eight to 12 hours. The maximum daily dose is 150 mg. In renal failure and/or moderate liver disease, the maximum daily dose should be reduced by up to 50 mg [4].

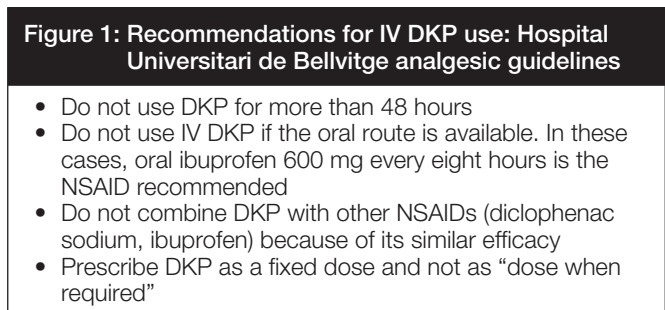
IV DKP was introduced during the first half of 2004, in our hospital, for treating post-operative pain. Our analgesic guideline recommendations regarding DKP use are shown in Figure 1.

As a consequence of the increased use of DKP, we designed a study to evaluate whether or not pharmaceutical intervention could improve its prescribing by doctors so that it was better adapted to our analgesic guidelines.

Pharmacist intervention outcomes include economy, health-related quality of life, patient satisfaction, medication

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appropriateness and fewer adverse drug events. Pharmacists can play an active role to induce positive and sustained changes in prescribing practices so that a drug therapy becomes better aligned with best available evidence [5]. In fact, the Institute of Medicine report, *Crossing the Quality Chasm*, proposes that clinical pharmacists have a significant role in addressing quality issues in hospitalised patients [6].

METHODS

Selection of patients

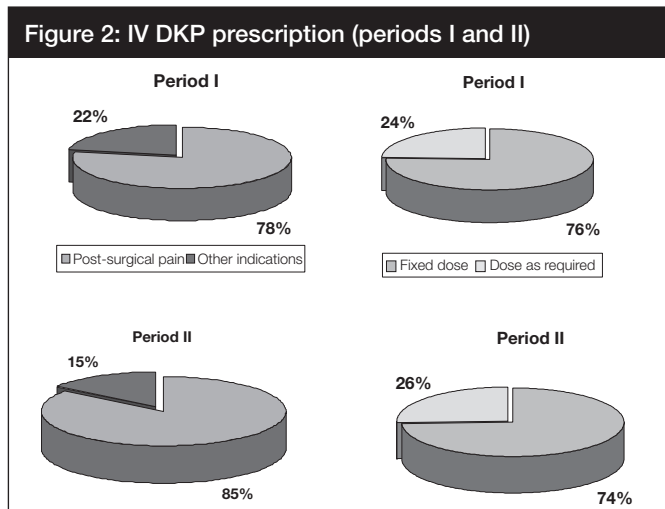
A prospective and comparative two-month study was performed in an orthopaedic surgery unit of the Hospital Universitari de Bellvitge. During November 2004 (period I) and April 2005 (period II), all patients admitted to this unit and treated with IV DKP were selected. The patients numbered 41 and 47, respectively.

Pharmaceutical intervention

Between the two study periods, a pharmaceutical intervention consisting of an informative talk on the subject of the hospital analgesic guidelines was given to the orthopaedic surgeons. The recommendations related to IV DKP are shown in Figure 1. Results from period I were also presented, pointing out the major deviations from the established guidelines and IV DKP use.

Prescribing variables

In order to analyse prescribing of IV DKP, data on demographic characteristics of patients, indication (post-operative



pain or other), treatment duration and kind of prescribing (i.e. as a fixed dose or when required) of DKP were collected. We also collected data on other analgesics prescribed in combination with DKP.

Statistical analysis

Statistical analyses included descriptive values (mean, confidence interval (CI) 95%). Because data were not normally distributed, a U-MannWhitney non-parametric test was used for the analysis of significant differences in both periods studied. The significance level was set at $P < 0.05$.

RESULTS

A total of 88 patients treated with IV DKP were included in our study: 41 during the first study period and 47 in the second period (after pharmaceutical intervention). Women accounted for 58.4% and 57.6% respectively. The mean age of patients included was 66.5 years [27-88] in period I and 60.8 years [20-87] in period II.

During the first study period, 78.2% of all IV DKP prescriptions were to treat post-operative pain; 9.8% were for pain related to bone fractures and 12.2% for treating lumbago episodes. After the pharmaceutical intervention, the post-operative pain indication for prescribing IV DKP rose to 85.1% and the remaining 14.9% was indicated for pain related to bone fractures.

Table 1: Comparison of the mean treatment duration between periods I and II

	Period I (pre-intervention)	Period II (post-intervention)	P
Treatment duration (days)	3.12 (1-13)	2.11 (1-11)	0.395

		Period I (pre-intervention)	Period II (post-intervention)	P
Post-surgical pain	Yes	2.53 (1-10)	2.08 (1-11)	0.981
	No	5.22 (1-13)	2.29 (1-6)	0.096
Dexketoprofen prescribed as	Fixed dose	2.45 (1-10)	1.71 (1-4)	0.470
	Dose when required	5.20 (1-13)	3.25 (1-11)	0.395

Neither the difference between periods in the indication nor the kind of IV DKP prescription reached statistical significance.

The mean treatment duration after the pharmacist intervention was reduced and better adapted to our analgesic guideline recommendations: 3.1 days in period I and 2.1 days in period II. However, this reduction was not significant (Table I).

The mean treatment duration was stratified by prescription indication (post-operative pain or another kind of pain) and by fixed dose or ‘when required’ prescriptions. We found that the duration of treatment was longer when IV DKP was used to treat non-post-surgical pain and when prescribed as ‘when required’ doses in both periods. But in both cases, after the pharmaceutical intervention, the days of treatment were reduced without reaching a statistical significance (Table 2).

IV DKP was mostly combined with oral or IV paracetamol in both periods (73.17% and 82.9%). In seven cases during the first period and in nine during the second period, IV DKP was used as rescue medication for a combined regimen based on paracetamol and metamizole (dipyrone), either oral or IV. The combination of IV DKP with diclofenac, which is not recommended by our guidelines because of their similar efficacy and adverse events profiles, accounted for the 12% and 17% in periods I and II respectively (Figure 3).

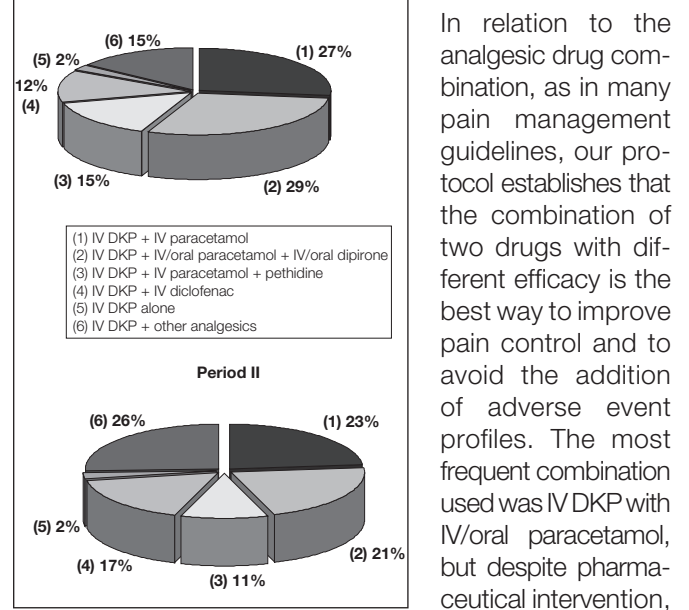
DISCUSSION AND CONCLUSION

When a new drug is introduced to a hospital formulary, it is usual for a follow-up of its use during the first months to be done. This allows the detection of deviations in the use of drugs and gives the necessary information to design an appropriate intervention.

In our hospital, IV DKP was introduced as a NSAID for treating post-operative pain under specific conditions. During the first period of the study, we detected a deviation from the indication for which IV DKP was prescribed. Although more than half the study group comprised post-surgical patients, approximately 25% of them were receiving IV DKP for non-surgical indications. The use of IV DKP for other indications was also reflected by duration of treatment. The rationale for this to happen is that post-surgical pain usually has a maximum intensity in the six hours after the effects of anaesthesia disappear, and tends to stabilise in 24 to 36 hours when the IV analgesics can be changed to the oral route [7]. When other kinds of pain were treated, it was more difficult to establish that only 48 hours of IV treatment would be required.

After pharmaceutical intervention, we observed an improvement in both indication of IV DKP and treatment duration. Non-post-surgical pain indications decreased to 15% with a mean of two days of treatment for all indications.

Another aspect of great importance in pain treatment, especially during the first 48 hours, is the need for fixed analgesic doses, avoiding the prescription to be written “as required”. Although this idea is reinforced during the pharmacist intervention, in 26% of cases, IV DKP was prescribed as a ‘when required’ dose.



the combination with intravenous diclofenac was not reduced.

Pharmacists can play an active role in prescribing practices so that drug use becomes more adapted to local protocols or guidelines and to best available evidence. Combining interventions to create a multifaceted approach appears to improve impact on prescribing practice. Grindrod et al. found that one of the most effective interventions for impact on prescribers is audit and feedback [8].

Young et al. demonstrated that effective communication has a direct positive influence on prescribing and is accomplished through dialogue that reflects the pharmacists' training in communication [9].

Our study was designed as audits, one before and one after a pharmaceutical intervention, which consisted of a talk where the deviations detected during the first period were pointed out. During the talk, the hospital protocol was explained, focusing on aspects that must be improved, such as treatment indication and duration. None of the differences found after the intervention has statistical significance, but we observed an improvement in some of the studied items. For this reason, we think that continuous pharmaceutical intervention can have a positive impact on physician education in order to ensure appropriate prescribing. In fact, the pharmacist is trained, qualified and accessible to filter out the noise of pharmaceutical industry marketing and encourage appropriate prescribing.

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