Reports of Investigation

Audit of ketoprofen prescribing after orthopedic and general surgery

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Purpose: In 1994, we developed a practice guideline which stated that ketoprofen should be used in every adult patient after surgical procedures for which at least moderate pain was anticipated. The dose recommended was 50 mg every six hours *iv* in the operating room followed by oral administration as soon as possible for three days. The purpose of this study was to evaluate the success of the guideline implementation.

Methods: In 1995, an audit performed by a research pharmacist assistant under the supervision of the authors analysed prospectively the files of patients scheduled for orthopedic or general surgery during a one-month period. The compliance of the nurses was also recorded.

Results: Of 185 patients operated upon during the period, seven were transferred to the ICU and were not evaluated. Ketoprofen was not prescribed to 112 (63%) of the 177 remaining patients, either because minor pain was expected ($n = 55$) or because one or several contra-indications to its use were detected. In cases where ketoprofen was used although theoretically contraindicated (11%), review of the medical records and interviews of anesthesiologists showed that prescription was guided by a risk/benefit analysis. In 18% of cases, nurses did not administer at least one dose of ketoprofen although medical prescription requested regular administration.

Conclusion: Although the use of NSAIDs is still controversial, implementation by anesthesiologists of a practice guideline introducing ketoprofen for postoperative analgesia was successful and the nursing non-compliance rate to follow written orders was modest.

Objectif : En 1994, nous avons instauré des recommandations de pratique clinique (RPC) concernant la douleur post-opératoire qui incluaient des directives sur le kétoprofène: l'administration de kétoprofène (50 mg/6 heures) devait être systématique pour tout opéré chez lequel une douleur au moins modérée était prévue. L'administration intraveineuse devait être relayée par la voie orale dès que possible pour une durée totale de 3 jours. Le but de cette étude était de savoir si cet antalgique était bien prescrit (audit des pratiques médicales) et bien administré (audit des pratiques infirmières).

Méthode : En 1995, un audit réalisé par un pharmacien assistant de recherche supervisé par les auteurs a étudié prospectivement tous les dossiers des patients opérés de chirurgie abdominale ou orthopédique pendant un mois.

Résultats : Parmi les 185 patients, 7 n'ont pas été étudiés car ils ont été transférés en réanimation avec ventilation post-opératoire. Le kétoprofène n'a pas été prescrit chez 112 patients (63 %) soit parce qu'une douleur mineure était attendue ($n = 55$) soit parce qu'une contre-indication avait été détectée. Dans 11 % des cas, le kétoprofène avait été utilisé bien que théoriquement contre-indiqué. Dans tous ces cas, l'analyse du dossier avec le praticien suggérait un rapport risque/bénéfice acceptable. L'adhésion des infirmières était bonne avec la non-administration d'au moins une dose chez 18 % des patients.

Conclusion : La mise en oeuvre de ces RPC a été un succès et bien que l'emploi des AINS soit controversé, ces produits sont bien prescrits et l'adhésion des infirmières est satisfaisante.

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Accepted for publication October 21, 1998

ALTHOUGH opioids remain the cornerstone of postoperative analgesia, poor compliance to their use by both physicians and nurses is still observed.¹ Many educational attempts and quality assurance programmes as well as the development of acute pain services are tentative responses to this problem and have improved postoperative analgesia.²⁻⁵ Other strategies have also been developed to decrease the use of opioids. For example, non steroidal anti-inflammatory drugs (NSAIDs) used after surgery have opioid sparing properties⁶ and are increasingly used in this situation.⁷ However, the large number of absolute/relative contra-indications and their low therapeutic index explain why their use remains controversial.⁷ We instituted a protocol for postoperative analgesia which included considerable NSAID use and their use in patients after orthopedic or general surgery was evaluated with regard to 1) incidence of contra-indications to the use of NSAIDs, 2) compliance of physicians to the protocol and, 3) compliance of nurses to medical prescriptions.

Methods

Practice Guideline Development

In 1994, after improved analgesia was initiated in our post anesthesia care unit,⁸⁻¹⁰ it was believed that better analgesia was also required in the surgical wards. Analysis of the literature suggested that a combination of NSAIDs and opioids improved postoperative analgesia. As ketoprofen is the only drug available in France for both intravenous and oral administration, a specific literature search for this agent was made using the Medline® database. A Practice Guideline was then written and presented to the Department staff to obtain consensus. A schematic representation describing the steps of the protocol was placed in the protocol booklet of each operating room to facilitate physician prescription of postoperative analgesia. The portion of the Practice Guideline describing the use of

ketoprofen can be summarized: ketoprofen should be used in every adult patient (> 15 yr old) after each surgical procedure for which at least moderate pain was anticipated. The dose recommended was 50 mg *iv* which may be changed to oral administration of the same dose every six hours for a maximum of three days. The first dose was administered 60 min before the anticipated end of the surgical procedure whenever possible (or as close as possible from this interval in shorter procedures) to provide analgesia from this drug at the time of recovery from general anesthesia. This dose was chosen although it was less than that recommended by the manufacturer because a ceiling effect has been observed in post-Caesarean patients.¹¹ Because of its almost complete bioavailability, the dose was not modified when given orally. The drug should be prescribed and given on a regular basis (every six hours) and not on demand. On the pre-printed document used for the preanesthetic visit, the absence of contra-indication (absolute or relative) was checked by the consulting anesthesiologist. A list of absolute and relative contra-indications was also provided in the protocol booklet for confirmation (Table I).

Audit method

In November 1995, case files from all inpatients undergoing orthopedic or general surgery were prospectively followed by a research assistant (from the Laboratory of Pharmacy and Toxicology) to determine: 1) the incidence of contra-indications to ketoprofen administration and its real use, 2) the compliance of doctors to the NSAID practice guideline, 3) the compliance of nurses to medical prescriptions. The audit was blind: anesthesiologists and ward nurses were not aware that a study was performed.

The medical record was also reviewed to search for any medical history which would represent a contra-indication to the use of ketoprofen. The number (one or more factors) as well as the severity of the risks (rel-

TABLE I Contra-indications to ketoprofen in the Practice Guideline

<i>Absolute</i>	<i>Relative</i>
History of gastrointestinal ulcer	Age ≥ 75 yr
Renal failure (creatinine concentration > 150 µmol·l ⁻¹ or creatinine clearance < 70 ml·min ⁻¹)	Age < 15 yr
Asthma	Cardiac failure
Nasal polyposis	Hypovolemia
Hypersensitivity to aspirin or allergy to non steroidal antiinflammatory drugs	Drug interferences
Thrombocytopenia <150.000-mm ³ or other known coagulation abnormality	- Lithium
Preoperative treatment with unfractionated heparin	- Aspirin or other non steroidal
Administration of converting enzyme inhibitors within 48 hr	- Diuretics
Renal or liver transplantation	- Methotrexate
Uncompensated liver failure	- Coumadin or related drugs

ative or absolute contra-indication) were recorded. This was compared for each patient with the prescription written by the attending anesthesiologist in the latest part of the surgical procedure. Thus, it was possible to classify patients as to whether or not they had contra-indications and whether or not they had received the drug. The dose of ketoprofen prescribed and the duration of treatment were also compared with the Practice Guideline. The number of patients in whom at least one dose of ketoprofen was omitted was recorded from the nursing files.

Results

One hundred and eighty five patients were operated upon during the month of the audit for orthopedic or abdominal surgery. Eight patients were not included because the severity of their illness required immediate transfer to the surgical ICU with mechanical ventilation of the lungs and postoperative sedation. Thus, 177 patients were available for analysis in the audit. Their mean age was 51 ± 20 yr (mean $\pm$ sd) ranging from 12 to 100 yr. Surgery was elective in 108 patients (61%) and emergency in 69 patients (39%). Patients were scheduled for orthopedic surgery (60%) or for general surgery (40%). Overall, 69 of the patients (39%) had at least one contra-indication to ketoprofen (Table II). Less than half of these patients ($n = 29$) had only one relative contra-indication while 28 had one absolute contra-indication and six had both an absolute and a relative contra-indication.

TABLE II Contraindications recorded in the audit period.

<i>Absolute (n = 40)</i>	<i>Relative (n = 41)</i>
History of gastrointestinal ulcer: $n = 14$	Age < 15 yr: $n = 20$
Renal failure: $n = 3$	Age > 75 yr: $n = 14$
Asthma: $n = 11$	Diuretics: $n = 7$
Nasal polyposis: $n = 1$	
Hypersensitivity to aspirin or allergy to NSAIDs: $n = 5$	
Coagulation abnormality: $n = 3$	
Converting enzyme inhibitors: $n = 3$	

TABLE III Cross-tabulation of the incidence of contraindications with administration of ketoprofen.

<i>n (%)</i>	<i>(ACI/RCI)+</i>	<i>ACI/RCI -</i>	<i>Total</i>
Ketoprofen administered	19 (11%)	46 (26%) -	65 (37%)
Ketoprofen not administered	50 (28%)	62 (35%)	112 (63%)
Total	69 (39%)	198 (61%)	177 (100%)

Sixty five patients received ketoprofen (37%) although 19 of them had an absolute or relative contra-indication (Table III). Detailed review of their medical records and interviews of the senior attending anesthesiologists showed that in 10/19 cases, ketoprofen was not administered in the operating room but its use was delayed and decided upon in the PACU because pain remained considerable (visual analogue pain scale > 60 mm) although intravenous morphine had already been administered. In the other nine cases, although a contra-indication was known, ketoprofen was injected in the operating room because the senior anesthesiologist considered that the risk/benefit ratio was in favour of its use. None of the six patients who had both a relative and an absolute contra-indication received the drug.

Sixty-two patients (35%) did not receive ketoprofen although no contra-indication was present. Minor surgery with little pain anticipated was the reason in 55 cases although in 16/55 patients, other analgesics were prescribed (acetaminophen $\pm$ propoxyphen). In three other patients, hemorrhagic complications during surgery precluded the use of postoperative ketoprofen on the request of the surgeon. Thus, ketoprofen was omitted without clear reason in 4/62 patients (6%).

In every patient who had received ketoprofen, the duration of treatment was 3 days and the dose was 50 mg according to the guideline. In 18% of cases, at least one injection of ketoprofen was not administered because the nurse believed that pain was minor.

Discussion

This is the first audit evaluating the attitudes of physicians and nurses toward the use of non steroidal anti-inflammatory drugs (NSAIDs) after surgery. Recommendations were well followed and escapes from the protocol were almost always the consequence of satisfactory medical reasoning. The non-compliance rate on the part of nurses to follow written orders was 18%.

This audit is important because NSAIDs are drugs with a low therapeutic index and which use remains controversial.⁷ As a major cause of the undertreatment of postoperative pain is the reluctance of doctors and nurses to prescribe and administer morphine,^{1,12} it is very useful to evaluate the perception that physicians and nurses have about this class of analgesics and their practice patterns. The major finding of this audit is that practice guidelines are overall well followed by both nurses and doctors. When ketoprofen was administered in spite of a known contra-indication, case-by-case analysis revealed a favourable risk/benefit ratio. On the

other hand, when ketoprofen was not used in spite of the absence of contra-indication, valuable reasons were provided in 58/62 cases. In no case, was ketoprofen administered when a combination of several contra-indications were seen. Dose and duration of treatment were correct. In 18% of cases, nurses did not administer the NSAID although medical prescription ordered regular administration. This low percentage of inadequacy should be compared with the high rate of non-administration of morphine by nurses in a recent French survey¹ and in older studies.¹³ This relatively low rate of protocol escape is corroborated by the fact that informal discussions with ward nurses have shown that, contrary to their traditional fear of morphine, they are not afraid of using NSAIDs.

Another interesting finding was that 39% of adult patients scheduled for orthopedic or general surgery had at least one contra-indication to NSAIDs and thus could not, theoretically, benefit from their use. This high rate of contra-indications is not surprising as the population studied comprised a large number of old patients with significant medical history and who were receiving other drugs likely to interfere with NSAIDs (i.e. diuretics, anticoagulants, aspirin, converting enzyme inhibitors). This should be compared with the much lower rate of contra-indications seen in patients scheduled for thyroid surgery¹⁴ or for Caesarean delivery (Tecsny M, Mercier FJ, Bouaziz H, Benhamou D. Audit de l'utilisation du kétoprofène (AINS) après césarienne. La Presse Médicale-submitted).

Although not the goal of this study, no NSAID induced-postoperative complication was seen in our patients. The number of patients studied precludes any definitive conclusion of safety but several reasons support the optimism. Ketoprofen has a short half life ($t_{1/2}$ - two hours)¹⁵ and Connelly *et al.* have shown a direct relationship between this $t_{1/2}$ and the risk of postoperative complications.¹⁶ Moreover, our dosing schedule consisted of daily doses less than those proposed by the manufacturer (200 vs 300 mg·day⁻¹) and the Practice Guideline emphasized a short duration of treatment. As excessive doses and duration have been recognized to be major risk factors for gastrointestinal bleeding complications,¹⁷ our regimen which took these factors into account should carry a low risk.

In conclusion, this study was performed as an audit to evaluate the implementation of a Practice Guideline on the use of ketoprofen for postoperative analgesia. Recommendations were well followed and escapes from the protocol were almost always the consequence of satisfactory medical reasoning. When compared with recent data, the compliance of nurses to the postoperative use of NSAIDs was better than for

morphine. Finally, the incidence of patients in whom contra-indications to the use of NSAIDs after surgery was high in the population studied.

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