Reviewer's report

**Title:** Variation in postoperative analgesic use after colorectal surgery: a prospective database study

**Version:** 1

**Date:** 20 October 2013

**Reviewer:** Dan Benhamou

**Reviewer's report:**

This is an interesting audit of practice in Denmark which certainly reflects the general inconsistency in NSAID prescribing.

The manuscript however needs several changes before being considered for publication. First, the use of NSAIDS is controversial in many respects. Many physicians fear this class of drugs in general due to the well-known risks of side effects and this certainly leads to a reduced use of NSAIDs in general. Moreover due to their numerous side effects, NSAIDs should not be prescribed in many patients, especially the elderly ones, because of the important interactions with the cardiovascular system and with drugs acting on the cardiovascular system. In an audit performed 15 years ago, Benhamou et al (Can J Anaesth 1999) showed that NSAIDs could be used in about 40% of general surgery patients only, when the many contraindications were taken into account. Due to the recent information gathered on the risks of non-specific NSAIDs on the cardiovascular system (not only Cox-2 inhibitors), it is suggested that a similar audit performed today would show an even greater incidence of patients with contraindications. Unfortunately, we are not told if the overall prescription rate was in agreement with the rate of pre-existing contra-indications and if the case mix cannot explain the difference (this is an unlikely explanation but which should be formally eliminated). The authors also do not report on patients who were users of NSAIDs preoperatively and if this rate was similar in all Departments.

In colorectal surgical patients who generally are patients in their sixties-seventies, the above-mentioned general contra-indications to their use will be found and this should be associated to a basic rate of contra-indications of at least 50%. It is however likely that the inconsistency seen in the present work is even greater in colorectal surgery due to the different opinion that anesthesiologists and surgeons may have on this class of drugs. On one hand, anesthesiologists are generally willing to prescribe this class of drugs to improve multimodal analgesia and obtain a morphine sparing effect. This efficacy has been confirmed in small randomized trials in colorectal surgery (see for example Chen JY et al, 2009) which cannot evaluate the rate of side effects, especially those with a low incidence. On the other hand, surgeons generally emphasize the risk of anastomotic leakage and are prone to avoid using NSAIDs. This discrepancy and the general picture are not well described in the Introduction section in which the reader cannot really understand why such an audit would be useful.
The avoidance of Cox-2 inhibitors, well described in the Discussion section, would be a nice solution which should allow to find a reasonable medium position if confirmed because it is still possible that non-selective NSAIDs may also be associated with anastomotic leakage (Gorissen KJ et al, Br J Surg 2012). This should be mentioned in the text.

Another significant problem is the statement that doses are insufficient or not. There is not a single reference to support the statement that ibuprofen daily dosage should be 800 mg or more. As well, there is no mention of what should be the minimal daily dose for diclofenac. This is not an easy task as the reviewer is not aware of well performed dose-response studies in postoperative patients with these two drugs. A plateau effect should be seen with NSAIDS after acute administration as shown for with ketorolac for example. Unfortunately, very few drugs have been studied similarly. This also suggests that the question that should be asked is not necessarily if the drug has been used in “sufficient” dosage but rather if the drug has been used at the minimum dose. Storm et al for example have shown that if ketorolac is used at low doses (i.e. corresponding at the plateau effect), gastrointestinal hemorrhage or renal failure does not occur. The authors should modify their manuscript by showing what are the doses that produce the plateau with either ibuprofen or diclofenac and using these doses as threshold for good or poor practice. For example, with the new formulation of intravenous diclofenac (Dyloject®), the clinical efficacy was similar with 37.5 and 75 mg and possibly also similar with 18.75 mg. With intravenous ibuprofen, 800 mg every 6 hours produces a significant morphine effect which is not observed with 400 mg every 6 hours (Southworth S et al et al, 2009).

Moreover, these doses may not be similar whether or not the drugs are used orally or parenterally. This should be explained.

The authors do not describe the duration of NSAIDs use. This is unfortunate as the duration may be important for both the occurrence of gastrointestinal and renal side effects (Strom L et al, 1996 & 1997) and the risk of anastomotic leakage (Gorissen KJ et al, Br J Surg 2012).

The authors state that their review will permit to evaluate the doses prescribed and those received. In fact, if the reviewer is right, only prescribed doses can be analyzed here. The manuscript should be modified accordingly.

An additional problem is the fact that they studied only 6 departments whereas their database could have led to a national audit. Why limiting the study to a portion of Danish practice?

Finally, because of apparent technical problems, the list of references is largely incomplete. As well, Figures cannot be read as legends are lacking. It is thus impossible for the reviewer to address any question associated with these Figures.

In conclusion, although this is a much interesting audit which has the potential to highlight an important clinical problem, the manuscript needs significant revision and should address many important queries.
**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

I declare that I have no competing interests