

**Toxicity and/or insufficient analgesia by opioid therapy: risk factors and the impact of changing the opioid. A retrospective analysis of 273 patients observed at a single center.**

Kloke M, Rapp M, Bosse, Kloke O. Support Care Cancer 2000; 8:479-486.

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**Abstract:**

The charts of 273 cancer patients were retrospectively analyzed in order (1) to evaluate the frequency of opioid change (OCH) when adjuvants (antiemetics/laxatives) were administered on a regular basis and co-analgesic medication as indicated by the specific type of pain, (2) to define risk factors for the request of OCH, and (3) to reveal settings in which OCH may not be recommended as a first-line therapeutic intervention. Opioids used included morphine, fentanyl, 1-methadone, and buprenorphine. Out of 273 patients, 103 changed opioids at least once, with a success rate of 65%. The indications for the OCH were insufficient analgesia in 43%, intolerable side effects in 20%, both in 15%, and other reasons in 22% of patients. The frequency of OCH was not influenced by the routine use of adjuvants or co-analgesics except corticosteroids, which raises queries about the concept of an opioid-sparing effect of co-analgesics. The occurrence of intolerable side effects is thought not to be dose dependent so much as to reflect differences in the individual tolerability of a distinct opioid for whatever reason (genetically fixed or individually acquired pharmacodynamic or kinetic properties). Moreover, there was strong evidence for the existence of an unpredictable and incomplete cross-tolerance between opioids, which meant careful titration of the new opioid was required after COH. The overall frequency of OCH was similar to that observed in previous studies in spite of the documented addition of adjuvants and co-analgesics. This retrospective study supports the notion that opioid rotation must be retained as an essential therapeutic option even with optimized adjuvant and co-analgesic regimens.

**Comments:**

**Strengths/uniqueness:** A large study of 273 consecutive patients. Single external reviewer lessens the bias of the chart review process.

**Weaknesses:** The authors fail to describe the many weaknesses inherent in their retrospective study, that inevitably limit the value of their conclusions

**Relevance to Palliative Care:** This report is a valuable addition to the increasing literature on the controversy of sequential opioid trials. The conclusion raising the question of the true opioid sparing effect of adjuvant analgesics should encourage further research in this area.