The Role of Non-opioid Analgesics for the Management of Postoperative Pain

Michael A. Ashburn, MD, MPH, and Carla R. Rubingh, PharmD

Introduction

Since the introduction of acute pain services into clinical practice by Ready and associates, interest in the management of postoperative pain has been increasing. Effective pain control may improve clinical outcomes and is clearly an important consideration about therapy for the patient.

Pain following surgery is a significant concern of patients prior to surgery. Warfield and Kahn recently reported that pain following surgery was the leading concern in 57% of patients prior to surgery. In addition, it appears that these individuals had reason for concern, as the same survey reported that 80% of them reported moderate to severe pain following surgery.

Pain following surgery occurs not only after major surgery, but also after relatively minor surgery. As the health care environment changes, there is increasing pressure to complete operations in the ambulatory setting that would traditionally be completed in the hospital. As a result, physicians are challenged to provide effective pain control in new settings. Unfortunately, current efforts have not been entirely effective. For example, a recent survey that included patients who underwent surgery reported that 77% of adults experienced pain after surgery, with 80% of those experiencing moderate to extreme pain.

This article reviews the general principles concerning the management of postoperative pain. The roles of nonsteroidal anti-inflammatory drugs (NSAIDs) in the management of postoperative pain are reviewed, and the potential benefits and problems associated with the use of this class of medications in this setting are described.

The Management of Postoperative Pain

The Agency for Health Care Policy and Research (AHCPR) has published clinical practice guidelines for the management of postoperative pain. These guidelines clearly state that the management of pain following surgery should be integrated into the overall care plan of each patient. In addition, the guidelines emphasize the need for integration of pain assessment into the ongoing evaluation of the patient. The presence of adverse side effects of pain therapy should be monitored, and care provided to minimize these effects should be instituted. Pain therapy should be individualized, constantly monitored, and changed as necessary to ensure that each individual’s pain is effectively treated.

Opioids remain the mainstay for the management of postoperative pain. NSAIDs can be effective in the treatment of mild to moderate pain, but opioids are the first-line drugs for the treatment of moderate to severe pain.

Opioids must be administered with care. The effective dose required varies from individual to individual. As a result, the dose used must be titrated to avoid dose-related adverse side effects as well as inadequate analgesia. As with all analgesics, the effects of treatment must be constantly monitored, and changes in therapy should be made as indicated.

Unfortunately, opioid-induced adverse side effects are common and can be serious. Common side effects of opioids include nausea, vomiting, sedation, and pruritus. Less common but more serious side effects include respiratory depression and sometimes cardiac arrest. Clearly, patient care includes appropriate monitoring and therapy for these events.

In an effort to improve pain control and decrease the incidence and severity of drug-induced adverse side effects, many clinicians have introduced the use of NSAIDs into the management of postoperative pain. In fact, the AHCPR guidelines suggest that NSAIDs be the first-line drugs for the treatment of mild to moderate pain and be used in combination with opioids if not contraindicated for more severe pain. Some investigators have reported that the combination of NSAIDs with opioids in this setting is more effective than either class of drug alone, and the use of NSAIDs with opioids will decrease the necessary dose of the opioid and therefore decrease the incidence and severity of opioid-induced adverse side effects.

Mode of Action of NSAIDs

The ability of NSAIDs to reduce pain is attributed to their influence on the central nervous system (CNS). This action is achieved through the partial inactivation of both cyclooxygenase B1 (COX-1) and cyclooxygenase-2 (COX-2) that in turn inhibit prostaglandin biosynthesis (Figs 1-2). The inactivation of these enzymes blocks sensitization and activation of peripheral nerve fibers and decreases the number of pain impulses delivered to the CNS.
COX-1 is present in a wide variety of cell types and influences the "housekeeping" functions of prostaglandins. This activity is particularly important in the gastrointestinal (GI) tract, the kidneys, and the circulatory system. In the GI tract, prostaglandin F2 and prostacyclin maintain mucosal integrity by inhibiting acid secretion and stimulating bicarbonate and mucus secretion. The suppression of these cytoprotective functions by currently available NSAIDs explains the GI complications associated with the use of these drugs. In the kidney, prostaglandins increase renal blood flow that in turn elevates glomerular filtration and helps regulate both tubular salt and water resorption. Again, the suppression of these functions by NSAIDs explains the adverse effects on renal function that occurs with this class of drugs. In the circulatory system, prostaglandins participate in maintaining vascular tone and are involved in control of platelet function. Administration of NSAIDs can adversely affect platelet function, resulting in clinically important bleeding disorders.

Fig. 2. - Differing roles of COX-1 and COX-2 enzymes.

COX-2, on the other hand, is found in only a few cell types, especially macrophages and other leukocytes, fibroblasts, and endothelial cells, including those of the vascular system. COX-2 is involved in those aspects of the inflammatory process that are mediated by prostaglandins. Specifically, large volumes of prostaglandins are produced as an inflammatory response begins to build following a tissue injury such as a surgical incision. These prostaglandins potentiate other inflammatory mediators including leukotrienes, histamine, and bradykinin, the last of which is the most powerful normal vasodilator in human physiology. By potentiating vasodilatation and hyperalgesia, prostaglandins contribute to vascular permeability and thus to edema. By inhibiting the production of prostaglandins, NSAIDs temper this chain of pain-inducing events. This effect explains their influence on the frequency of pain impulses to the CNS. The analgesic effect of NSAIDs has a ceiling effect in that increasing doses may not lead to increasing analgesia. As a result, NSAIDs may be effective alone for the management of mild to moderate pain but not effective for more severe pain. However, as stated earlier, NSAIDs do appear to be opioid sparing and may improve the quality of analgesia when used in combination with opioids.

Potential Adverse Side Effects of NSAIDs

NSAIDs do not cause the respiratory depression seen with opioids. In addition, NSAIDs do not interfere with bowel or bladder function. However, that does not mean that they are void of potential adverse effects. These adverse effects are attributed to the suppression of the prostaglandin-mediated "housekeeping" functions of COX-1.

The most common adverse side effects of NSAIDs are gastritis, peptic ulceration, and bleeding. In general, the incidence of these effects rises with increased daily doses of NSAIDs and increased duration of NSAID therapy. Individuals with a prior history of peptic ulcer disease appear to be at increased risk for these complications.

In the postoperative setting, considerable attention has been paid to the potential for NSAIDs to increase the likelihood of bleeding. NSAIDs lead to reversible inhibition of the platelet function. Postoperative administration of NSAIDs has been reported to lead to an increased incidence of bleeding. However, this is usually associated with very select patient populations or in individuals who have received other anticoagulants in combination with the NSAIDs.

A rare but potentially serious complication is NSAID-induced depression of renal function. Individuals who suffer from chronic renal insufficiency, who are receiving concurrent diuretic therapy, or who are experiencing intravascular volume depletion are at increased risk for this adverse event. This complication is usually reversible with discontinuation of the NSAID, but long-term impairment of renal function has been reported.

The risk for adverse events associated with NSAID therapy increases when some drugs are used in combination with NSAIDs. Concurrent diuretic therapy increases the risk of renal complications. In addition, concurrent use of corticosteroids dramatically increases the risk of life-threatening GI bleeding. Finally, the use of any other drug that impairs coagulation, such as warfarin or heparin, will increase the likelihood of a clinically significant bleeding disorder.

Caution should be exercised when using NSAIDs during pregnancy. Analgesic therapy during pregnancy has been recently described in detail elsewhere.

Selected patients may also be at increased risk for NSAID-induced adverse events. Individuals with congestive heart failure, hepatic cirrhosis with ascites, systemic lupus erythematosus, and multiple myeloma are at increased risk for an adverse event. Also, elderly persons with significant atherosclerotic disease are at elevated risk for such side effects. Care should be taken in these patient populations. Dosing may need to be adjusted in order to decrease the potential for adverse events, and appropriate monitoring should be instituted when indicated.

Conclusions

The management of postoperative pain is an important part of the care of the surgical patient. Pain management should be individualized and integrated into the overall care plan of the patient. The patient should be monitored for both adequacy of pain control and the incidence and severity of treatment-induced adverse effects. This monitoring should allow the clinician to intervene when necessary; thus improving pain control and minimizing adverse side effects.

While opioids are the main drugs used in the management of postoperative pain, they are associated with frequent side effects. Rarely, these effects can be life threatening. NSAIDs are effective analgesics for the management of postoperative pain. For individuals experiencing mild to moderate pain, NSAIDs alone may be effective. For individuals experiencing more pain, NSAIDs can be used in combination with opioids. A combination of agents may be more effective than either agent alone and usually will allow a decrease in opioid use and a reduction in the incidence and severity of opioid-induced adverse side effects. However, NSAIDs can lead to their own drug-induced adverse side effects, some of which are serious. Appropriate patient selection and monitoring will decrease the risk for these events.

References


Dr Ashburn is Professor and Interim Chairman of the Department of Anesthesiology, University of Utah, Salt Lake City, Utah.

No significant relationship exists between the authors and the companies whose products may be referenced in this article or with Wyeth-Ayerst who provided an educational grant to support this supplement.