# GUIDELINES ON PAIN MANAGEMENT IN UROLOGY

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## Introduction

Pain is defined as "an unpleasant sensory and emotional experience associated with either actual or potential tissue damage, or described in terms of such damage". Two different kinds of pain exist. The first is termed nociceptive because of its direct link with noxious stimuli: it is a key component of the body's defence mechanisms and is associated with tissue damage or inflammation, so it is also called inflammatory pain. The second is defined as neuropathic pain and results from a lesion to the peripheral or central nervous systems. Pain can also be divided into acute and chronic. Acute pain arises after trauma, surgery, or nerve damage. Chronic pain persists beyond 3 months: it inhibits feelings and emotions, thought and reactions, and may restrict social interactions and work.

## Nociception and Innervation

The sensation of pain starts at the site of tissue injury. The peripheral neural apparatus alerts the organism of potential injury sending messages to the central nervous system regarding the location and intensity of noxious stimuli.

It operates through highly specialized sensory fibres and a specific set of primary sensory neurones called "nociceptors", subclassified as unmyelinated (C-fibre) versus myelinated (A-fibre) parent nerve fibres.

Unlike cutaneous pain, deep pain is diffuse and poorly localized. It may be associated with strong autonomic responses such as sweating and changes in heart rate, blood pressure and respiration. In addition, deep pain may be produced by non-tissue-damaging stimuli, e.g. distension of bowel and bladder.

## Postoperative Pain Management

Postoperative pain (POP) is expected by 77% of adults and represents the primary fear for nearly 60% of them before surgery. The common practice of giving "as required" intramuscular opioids does not relieve pain in over 50% of patients. Unrelieved pain can lead to many adverse effects, both cardiovascular and respiratory. It is considered good clinical practice to treat postoperative pain early and aggressively by means of regular assessment, easy access to strong opioid drugs, teaching and education.

Tables 1 and 2 report on the most commonly used approaches to POP, while Table 3 outlines a recommended postoperative approach to the most common urological procedures.

## Table 1: Analgesic drugs

| Class | Drug | Dosage | Route |
|---|---|---|---|
| NSAIDs | Diclofenac | 50 mg 3X per day | orally |
| | | 100 mg every 16 hours | rectally |
| | Ibuprofen | 200-400 mg 3X | orally |
| | Ketorolac | 10-30 mg 6-4X | orally or IV |
| | Rofecoxib | 20 mg 1X | orally |
| COX inhibitors | Paracetamol | 1 g 4X | orally or rectally |
| | Co-codamol (*) | 2 tab. 4X | orally |
| | Co-proxamol (§) | 2 tab. 4X | orally |
| Opioids | Tramadol | 50-100 mg 4X or continuously | orally or IV |
| | | Loading dose 100 mg + (maintenance) | 0.2 mg/kg/hr |
| | Morphine | 5-10 mg 8-6X | orally |
| | | Up to 10 mg per hour | IV/SC infusions |
| | | 10 mg 8X | IM/SC injections |
| | Oxycodone | 10 mg 6X | orally |
| Metamizole | | 500 mg 1X | orally |

(*) Codeine + paracetamol 500 mg

(§) Dextropropoxyphene 32.5 mg + paracetamol 325 mg

## Table 2: Analgesic techniques

| Technique | Drug(s) | Schedule |
|---|---|---|
| PCA* | Morphine 1-2 mg<br>Pethidine 10 mg<br>Fentanyl 20 mcg | Loading dose: 0.05-0.2 mg/kg<br>Incremental dose: M-P-F<br>Lock-out period: 5-8 minutes<br>Background infusions<br>(close monitoring)<br>1 hour infusion limit |
| Epidurals | Bupivacaine 0.125% | + Fentanyl 2 mcg/mL (or sufentanyl 0.05-0.1 mcg/mL), run at 5-15 mL/hr |
| | Ropivacaine 0.1-0.2% | |
| Nerve blockade | Bupivacaine 0.25-0.5% | Wound or iliohypogastric / ilioinguinal nerve infiltration (10-20 mL) |
| | 0.25% | Intercostal nerve infiltration (5-10 mL) |
| | 0.1% | Intrapleural catheters, continuous infusion (10 mL/hr) |

*Patient controlled analgesia

**Table 3: Analgesic drug options after urological procedures**

| Procedure | Drug | | Route | Schedule |
|---|---|---|---|---|
| ESWL | Diclofenac | 50 mg | orally | 8 hrs |
| Transurethral | | 100 mg | rectally | 16 hrs |
| surgery | Paracetamol 1 g | | orally | 6 hrs |
| Percutaneous | Co-proxamol; | 2 tab. | | 6 hrs |
| surgery | Co-dydramol | | | |
| | Tramadol | 50 -100 mg | orally | 6 hrs |
| Minor operations Inguinal approach Transvaginal surgery | Morphine 10 mg | | IM | 3 hrs |
| Laparoscopic surgery | - as above plus: | | | |
| | PCA morphine 1 mg | | bolus | 5 min lock out |
| Perineal open surgery | - as laparoscopic surgery plus: | | | |
| | Bupivacaine 0.25% + fentanyl 2 mcg/mL | | epidural infusion | 5-15 mL/hr |
| Laparoto-mies (all) Flank incisions | Morphine | | IV infus. | 1-10 mg/hr |
| | (+ bolus doses 1-2 mg as required) | | | |

## Treatment of Cancer Pain

In cancer patients pain may be caused by the cancer itself, may be due to secondary muscular spasm or to cancer treatments (e.g. radiation induced brachial plexopathy) or may have no relation to the cancer, e.g. arthritis.

Cancer pain consists of two broad diagnostic types, nociceptive and neuropathic pain. Nociceptive pain includes bone pain and soft tissue pain; described as a dull, well localized and aching pain, it is largely sensitive to non-steroidal anti-inflammatory drugs and opioids. Neuropathic pain results from damage to the peripheral or central nervous system. Not particularly responsive to NSAIDs or opioids, it is usually described as a burning or sharp, shooting pain. Adjuvant analgesics such as anti-depressants and anti-convulsants should be used in the first instance. Pain caused by bony metastases is nociceptive pain, but can become associated in one-third of patients with neuropathic pain if the tumour invades or compresses a nerve, neural plexus or spinal cord. The efficacy of opioids may be diminished in neuropathic pain and hence additional co-analgesics are necessary.

General principles of management are listed below:

- Treatment individualization: in some cases surgical measures such as drainage and stenting can make analgesic medication redundant.
- Anti-cancer therapies should be used first (e.g. surgery, chemotherapy, radiotherapy).
- Use analgesic drugs according to the WHO ladder.
- Utilize both psychological counselling and physical therapy throughout.

Primary analgesic therapies include radiotherapy, chemotherapy, surgery and antibiotics but the mainstay of cancer pain management is represented by systemic analgesic pharmacotherapy. Analgesic drugs can be separated into three groups:

non-opioid analgesics, opioid analgesics and adjuvant analgesics (drugs with other primary indications that can be effective analgesics in specific circumstances).

The Cancer Unit of the World Health Organization (WHO) proposed a three-step approach to drug selection for cancer pain, which has become known as the '*analgesic ladder*' (Fig. 1).

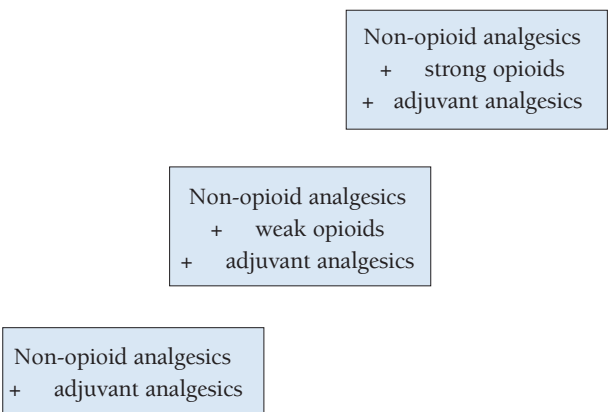


*Fig. 1. The 'analgesic ladder' according to WHO*

Step 1 Mild to moderate cancer-related pain: non-opioid analgesic + adjuvant analgesic (if required).

Step 2 Moderate to severe pain (or after a failed trial of a non-opioid analgesic): weak opioid. This treatment entails a combination of a non-opioid (e.g. aspirin or acetaminophen) and an opioid drug (such as codeine, oxycodone or propoxyphene).

Step 3 A strong opioid, such as morphine or hydromorphone (+/- combined with an adjuvant drug), should be administered for severe pain, or when adequate relief following appropriate administration of drugs on the second rung of the 'analgesic ladder' is not obtained.

1. Non-opioid analgesics include aspirin, acetaminophen and NSAIDs. They may be useful alone for mild to moderate pain (step 1 of the analgesic ladder), provide analgesia when combined with opioids and entail a ceiling effect of analgesic efficacy but no tolerance or physical dependence.
2. Opioid analgesics. Whilst patients with moderate pain are commonly treated with a combination drug containing acetaminophen or aspirin plus codeine, oxycodone or propoxyphene, severe cancer pain should generally be treated with a systemically administered 'strong' opioid from the start. It should be administered by the least invasive and safest route capable of providing adequate analgesia.
3. Adjuvant analgesics are defined as drugs with a primary indication other than pain but analgesic in some conditions. They may be combined with primary analgesics in any of the three steps of the 'analgesic ladder' to improve the outcome for patients who cannot otherwise attain an acceptable balance between relief and side-effects. They are classified in three groups:

**A. Multipurpose adjuvant analgesics**

- Corticosteroids: with antioedema and anti-inflammatory effect.
- Neuroleptics: to associate anxiolytic and antiemetic effects

- Benzodiazepines: to treat pain-associated anxiety and insomnia.

**B. Adjuvants for neuropathic pain**
- Tertiary and secondary amine tricyclic antidepressants.
- Anticonvulsants (mainly gabapentin).
- Clonidine: used transdermally in opioid-refractory patients.

**C. Adjuvants for bone pain**
- NSAIDs and corticosteroids.
- Bisphosphonates (mainly pamidronate).
- Radiopharmaceuticals (strontium[89], samarium[159], rhenium[186]).

Ten to 30% of patients with cancer pain do not achieve a satisfactory balance between relief and side-effects using systemic pharmacotherapy alone without unacceptable drug toxicity. Therefore, other options are worth considering:

1. Transcutaneous Electrical Nerve Stimulation (TENS).
2. Invasive techniques.
3. Physical/psychological therapy.

## Summary

The care of pain requires adequate knowledge of all the therapies to employ. Side-effects caused by the inappropriate use of anticancer treatments can be very distressing, and the disadvantages of a treatment must be balanced against the palliative benefit. Thus, the best approach to pain relief will be through interdisciplinary cooperation, in order to establish a comprehensive management.

*This short booklet text is based on the more comprehensive EAU guidelines (ISBN 90-70244-06-3), available to all members of the European Association of Urology at their website - http://www.uroweb.org.*