

## CHAPTER I

### INTRODUCTION



#### Rational and background

Pain after surgery is one of people's concerns when they are going to have an operation. National surveys in North America in 1995, 2001 and 2003 revealed that 47-59% of the respondents were concerned about postoperative pain (1-3). Meanwhile Cohen J et al. reported as high as 89% of patients expected to have moderate and severe pain after surgery and only 36% of them believed that postoperative pain can be effectively controlled by medication (4). Although modern health care is becoming more aware of postoperative pain management, we are passing the time when postoperative pain was of no concern to both surgeons and anesthesiologists. However postoperative pain is still undermanaged (3).

Besides patients' unhappiness, postoperative pain also induces many physiological changes to the patient such as increased sympathetic activity: tachycardia, hypertension, and increased systemic vascular resistance. The other adverse outcomes include hypoxia, urinary retention, increased metabolism, fatigue and even immunological impairments (5). Acute postoperative pain not only distresses patients during the immediate postoperative period, but also causes chronic pain thereafter in approximately 20% of patients (4,6). Accordingly effectively alleviating postoperative pain can prevent patients from unnecessary discomfort and also reduce postoperative morbidity and mortality (7-9). Consequently postoperative pain should be treated early and aggressively. Otherwise these may become a burden to both patients and society.

Pain after transurethral resection of the prostate (TURP) is no exception either. It is frequently neglected (10) and poorly controlled (11). The physicians usually focus on treating the underlying disease and assign the pain or discomfort to the patient

as low priority even though there are analgesics within their reach. Since most of the patients having TURP done are elderly patients who are vulnerable to serious postoperative complications that may result from pain as mentioned above, pain after TURP should be promptly treated.

Pain after TURP consists of 2 components. The first one is induced from the injury of tissues in the urethra which has a high number of nociceptors (12). The second is from the urinary catheter which is retained in the patient's urethra as long as 48-72 hours postoperatively. The urinary catheter increases the smooth muscle tone in the urethra and urinary bladder. Therefore it may lead to spastic pain (12). So multimodality pain therapy may improve the efficacy of pain relief after TURP (13).

Normally acute postoperative pain therapy can be managed in many ways. The common and popular one is the pharmacological treatment that has come a long way including both opioid and non-opioid drugs. For opioid drugs, morphine and its derivatives have been effectively used to treat moderate and severe postoperative pain. But the usages of these drugs are limited by their side effects such as respiratory depression, drowsiness, hypotension, nausea, vomiting, constipation, and dependency. Apart from those side effects, the intramuscular injection of narcotics as requested does not efficaciously treat postoperative pain in more than 50% of the patients (14). This route of medication is painful to the patient as well.

For non-opioid drugs, non-specific nonsteroidal anti-inflammatory drugs (NSAIDs) provide an excellent pain relief for moderate to severe pain (15-17). They are widely used due to them having no serious side effects such as respiratory depression, drowsiness and addiction. However the conventional NSAIDs still cause other adverse effects including gastrointestinal hemorrhage, renal toxicity and bleeding complications when used during the postoperative period. Nevertheless NSAIDs has been shown to be safe for use in early postoperative analgesia in adult patients with normal preoperative renal function (18).

Due to a better understanding of the mechanism of pain we know that only cyclooxygenase (COX)-2 iso-enzymes are involved in the sensitization of

prostaglandin that induces a pain response (19). This has led to the development of cyclooxygenase (COX)-2-selective inhibitors which are known as coxibs (20). These drugs inhibit the COX-2 iso-enzyme; an inducible enzyme which will rise in the peripheral and central nervous system including monocyte following injury or inflammation (21). Selective COX-2 inhibitors (coxibs) have fewer side effects than the traditional NSAIDs including the gastrointestinal tract (22) and platelet dysfunction (23). Studies in rheumatoid arthritis patients receiving valdecoxib, nonselective NSAIDs and a placebo, found no difference in the incidence of thrombotic events between patients who received treatment and a placebo (24,25). Two systematic reviews have shown that the analgesic effect of coxibs in acute postoperative pain is more effective than opioid-containing analgesics (26,27). Meanwhile compared to the traditional NSAIDs, the coxibs also have an equipotent analgesic efficacy (26,27).

Besides the pharmacological choice of treatment efficacy, the timing of the drug administration also has an effect on the efficacy of the treatment as well. In 1983 Woolf had introduced the concept of preemptive analgesia to reduce the magnitude and duration of postoperative pain (28). He showed evidence for a central component of postinjury pain hypersensitivity in experimental studies. So administering analgesia before the start of injury will contribute to better pain relief in the postoperative period.

As mentioned earlier, pain after TURP can also be due to retaining a urinary catheter that might cause bladder spasms. This pain can be treated with antispasmodic agents such as oxybutynin, flavoxate, hyoscine sulphate, or tolterodine (29).

Therefore, combined selective COX-2 inhibitors with a urinary antispasmodic should be studied for their analgesic efficacy in treating patients undergoing TURP. Moreover they can be given preoperatively.