

# Perioperative pain management in fast-track knee arthroplasty

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**Summary.** Fast track surgery for knee arthroplasty is characterized by a perfect perioperative management from patient education to multimodal control of bleeding and excellent pain control. Pain protocols need to be a combination of multimodal pharmacological therapy and Local Infiltration Analgesia with no locoregional analgesia techniques. In Istituto Fiorentino di Cura e Assistenza (IFCA) clinical records 92% of patient have been mobilized the day of surgery achieving a complete autonomy in going to bath-room and in walking with the aid of two crutches by 87% on day one and 100% on the second postoperative day; all patients were also able to climb and walk down the. At discharge all patientes presented at least 90° of knee flexion. Only 9% incidence of nausea occurred and only 3% needed to delay physical therapy. ([www.actabiomedica.it](http://www.actabiomedica.it))

**Key words:** perioperative pain, knee, arthroplasty

## Introduction

Knee arthroplasty presents a high risk of severe postoperative pain with relevant consequences for patient recovery and postoperative rehabilitation (1).

Fast-track surgery in orthopedics involves an early mobilization of the patient after surgery, an early oral hydration and nutrition, thereby abolishing any kind of invasive procedure such as urinary catheterization or needle-tube beyond 48 hours. This new approach is characterized by an extremely precise management of the whole perioperative period of candidate to total knee arthroplasty; patient education through informative material and meeting with medical staff is therefore crucial. Patient plays an active role starting from pre-operative phase thanks to his knowledge of his own recovery steps. During the entire perioperative period, short acting anesthesia and excellent pain management assuring an early mobilization represent the real challenges.

In fast-track surgery pain management must be advanced since it must treat pain not only during rest

but above all during early activities as walking, knee flexion and extension, climbing the stairs.

Simultaneously, it is important to have a multimodal control of bleeding in order to avoid anemia and to limit hemarthrosis. A swollen joint raises difficulties also from an antalgic point of view.

Spinal anesthesia proved to be the best approach since it allows an excellent and quick recovery at the end of surgery and it presents a low risk of morbidity.

## Pain genesis

Pain at surgical incision is characterized by a nociceptive component due to peripheral nociceptors activation, an inflammatory component due to pro-inflammatory mediators release, which in turn reduces activation threshold of nociceptors (1) and, lastly, by a neuropathic component evoked by nerve damage at joint level (2).

As a consequence peripheral and central sensitization and hyperalgesia mechanisms are triggered.

Peripheral sensitization is caused by both local and systemic inflammatory response, whereas central sensitization is triggered 3-6 hours after surgery by a nociceptive input from surgical field towards spinal cord resulting in excitatory neurotransmitters release (3).

Pain duration and intensity before surgery, affects postoperative pain. This is related to aberration of somatosensory perception and an imbalance between excitatory and inhibitory endogenous pain processes (4).

### Perioperative pain management protocol

In order to achieve fast-track surgery goals it is necessary to adopt a multimodal pain therapy (5), combining pharmacological therapy with local infiltration analgesia (LIA) (6).

The antalgic protocol adopted in our institute considers the preoperative administration of oral acetaminophen 15 mg/kg, oral etoricoxib 90 mg, which selectively inhibits COX-2, does not affect platelet aggregation, causes no intestinal side effects (7) and proved to be an effective drug for pre-emptive analgesia (8). Beyond its known anti-inflammatory effect, etoricoxib produces analgesia by inhibiting PGE<sub>2</sub> synthesis, which reduces the activation threshold of peripheral neurons.

In our pre-emptive analgesia protocol we administer also oral oxycodone/naloxone 10/5 mg, a prolonged release combination of opioid agonist/antagonist with demonstrated analgesic efficacy during arthroplasty (9). Naloxone limits gastrointestinal side effects induced by oxycodone, such as constipation, nausea and vomit.

At the moment of anesthesia, also dexamethasone 0,1-0,2 mg/kg is administered in order to prevent nausea and vomit and to reduce joint edema (10-11).

In postoperative period (day 0 and day 1) patient receives intravenous acetaminophen 15 mg/kg every 8 hours, Ketorolac 30 mg every 12 hours and oral oxycodone/naloxone 10/5 mg every 12 h.

Starting from day 2 until discharge (usually on day 3) oral therapy combines acetaminophen, oxycodone/naloxone and diclofenac 150 mg once daily.

The aim of multimodal analgesia is to administer several drugs at submaximal dosage, minimizing side effects of each drug and maximizing efficacy thanks to a synergistic effect (12).

The adoption of analgesics alternative to morphine produced a strong reduction of many side effects, such as cognitive side effects, respiratory depression, postoperative nausea and vomit and urinary retention. In order to early identify patients possibly prone to develop side effects after oxycodone/naloxone, this combination is administered to patients few days before surgery and, in case of poor tolerability, it is substituted with a weak opioid (tramadol 1 mg/kg intravenously, twice a day).

This multimodal analgesia protocol is summarized in table 1.

### Local infiltration analgesia

Local infiltration analgesia (LIA) represents the keystone in multimodal pain management during arthroplasty.

LIA induces an intra-articular sensory block which allows a gradual arrive of nociceptive input and the onset of multimodal pharmacological therapy at the same time.

During LIA high volumes of long acting local anesthetic are infiltrated in the joint and into the surgical site at the time of wound closure (12), in order to allow an early patient mobilization, a rapid recovery, a reduction in opioids administration (morphine can be abandoned) and a shorter hospitalization (13).

Ropivacaine (associated with lower cardiotoxicity than bupivacaine) 2% in a volume up to 200 ml can be used, in combination with adjuvants as ketorolac, adrenaline or morphine (14-15).

This high dosage proved to be safe and with no side effects because medium serum concentration is extremely low (1.30-2.5 ig/mL) and therefore well tolerated (16).

LIA is a simple and safe procedure and produces an excellent analgesia in the first 6-12 hours (17).

Adjuvants as ketorolac (15), magnesium (18) and adrenaline could be added to improve analgesia quality and duration. Unfortunately these drugs are not available in sterile packaging, therefore they must be administered very carefully in surgical field and with concomitant use of a 0.2 micron antibacterial filter.

Since at the moment there is no evidence of superiority of a mixture (cocktail) of drugs versus sin-

**Table 1.** Perioperative pain management

Drug	Dosage	Administration	Posology
<b>Analgesic treatment at home (starting 5 days before surgery)</b>			
oxycodone/naloxone	5/2.5 mg	oral	every 12 h
<b>Pre-emptive analgesia</b>			
oxycodone/naloxone	10/5 mg	oral	
acetaminophen	15 mg/kg	oral	
etoricoxib	90 mg	oral	
<b>Postoperative analgesic treatment (day 0 and 1)</b>			
dexamethasone	0.1-0.2 mg/kg	intravenous	in OR and after 48 h
acetaminophen	15 mg/kg	intravenous	every 8 h
ketorolac <sup>1</sup>	30 mg	intravenous	every 12 h
oxycodone/naloxone	10/5 mg	oral	every 12 h
tramadol + metoclopramide	0.5 mg/kg + 10 mg in 100 ml SF 0.9%	intravenous	rescue (if VNS > 3)
ondasentron <sup>2</sup>	4 mg	intravenous	in case of PONV
<b>Postoperative analgesic treatment (day 2)</b>			
oxycodone/naloxone	10/5 mg	oral	every 12 h
acetaminophen	15 mg/kg	intravenous	every 8 h
diclofenac	150 mg	oral	once daily
esomeprazole	20 mg	oral	once daily
<b>Post-discharge analgesic treatment (day 3-10)</b>			
oxycodone/naloxone	5/2.5 mg	oral	every 12 h
diclofenac	150 mg	oral	once daily (in the morning)
esomeprazole	20 mg	oral	once daily
<b>Post-discharge analgesic treatment (day 11-21)</b>			
oxycodone/naloxone	5/2.5 mg	oral	every 12 h
celecoxib <sup>3</sup>	200 mg	oral	twice daily
esomeprazole	20 mg	oral	once daily
<b>Post-discharge analgesic treatment (day 3-21)<sup>4</sup></b>			
acetaminophen	1000 mg	oral	rescue (up to 3/die)

<sup>1</sup> To be replaced by tramadol 1 mg/kg in case of moderate-severe renal failure, coagulation disorders, hepatic cirrhosis or allergy to active ingredient

<sup>2</sup> To be replaced by metoclopramide 10 mg in case of congenital long QT syndrome or prolongation of the QT interval on electrocardiograms (ECGs)

<sup>3</sup> To be replaced by naproxen 500 mg 2 tablets/die in patients with coronaropathy.

<sup>4</sup> Rescue therapy in case of non-controlled pain with around-the-clock (ATC) analgesics

gle anesthetic during LIA, we prefer not to add other drugs to anesthetic, which is available in sterile blisters suitable for surgery.

During LIA procedure 20 or 30 cc luer-lock syringes and 21-22 G spinal needles are used. 4-5 ml must be infiltrated in multiple peri-articular sites and especially into the surgical site at the time of wound closure, which is rich in nociceptors.

In particular drug must be infiltrated in medial tibial periosteum, medial meniscocapsular junction, patellar tendon and preserved intrapatellar tissue. In femoral region, drug must be infiltrated along bone resection, suprapatellar synovial cavity, posterior capsule next to its medial and lateral femoral insertion, quadriceps tendon and cut medial subcutaneous tissue (since lateral side is denervated by the incision).

During subcutaneous infiltration adrenalin must not be used, in order to avoid a risk of oxygen perfusion decrease in the wound, due to vasoconstriction.

In USA liposomal L-bupivacaine is used (Exparel, Pacira, Parsippany, NJ) to prolong LIA duration up to 48-72 hours. This drug is currently not available outside USA and recent prospective head-to-head trials showed that there is only a little benefit or no advantage versus standard LIA.

Recently some authors described the possibility to potentiate LIA effect with an intra-articular block of saphenous nerve, which can be performed by the surgeon during LIA procedure. A long epidural needle could be used to reach saphenous nerve in the adductor canal. Safety and efficacy profile of this procedure is still under investigation.

### Locoregional anesthesia

Femoral nerve block, both in single shot and in continuous infusion, is considered the gold standard for analgesia during arthroplasty. This is a simple procedure, which can be also performed bedside and produces an excellent analgesia with consequent reduction in opioid administration after surgery.

Unfortunately this technique is not suitable for fast-track surgery since it induces a 49% decrease in femoral quadriceps strength in case of local anesthetic at high concentration (19) or 15-23% in case of local anesthetic at low concentration, such as 0.1-0.2% ropivacaine (20). This contractility reduction is not compatible with an early patient mobilization.

As an alternative, ultrasound-guided adductor canal block can be performed; this is a very simple procedure with an high success rate, producing an excellent postoperative analgesia with a negligible reduction (8%) in femoral quadriceps contractility (19).

### Advanced cryotherapy

Cryotherapy involves the application of cold to the skin surrounding the injured soft tissues and plays a relevant role in postoperative period in fast-track surgery. It is a safe and non-invasive technique.

Advanced cryotherapy allows reducing swelling, pain and inflammation. Cold temperature produces, in addition to vasoconstriction, a reduction of neurotransmission with consequent anesthetic effect and a decrease of prostaglandin synthesis, which plays a role in pain genesis (22). Compression helps decreasing joint edema incidence by applying an external pressure and reducing liquid leakage in interstitial space (23).

### Rescue analgesic therapies

In case of insufficient analgesia (due to a badly performed LIA or patient allergies), many pharmacological and non-pharmacological rescue therapies are available.

Magnesium sulfate is a molecule with anesthetic, analgesic and muscle relaxant properties, which can be used as adjuvant to reduce postoperative opioid consumption (24). It is a NMDA receptor antagonist and controls calcium influx in cells. A 40-50 mg/kg bolus and a successive 10-15 mg/kg/h continuous infusion for the next 24 h are required to maximize efficacy; this approach reduces VNS and opioid consumption, even if it does not reduce side effects incidence (25).

Ketamine is another NMDA receptor antagonist blocking neurotransmission; low doses (0.15-0.3 mg/kg bolus and successive 0.1 mg/kg/h for 24 hours) allow reducing opioid consumption and nausea and vomit incidence; it shows an excellent hemodynamic stability with no side effects such as hallucinations and diplopia (26).

Acupuncture is a non-invasive and safe technique, which allows the treatment of multiple concomitant symptoms. Although evidence is quite scarce, some studies affirm it can reduce pain symptoms and opioid consumption; anyway few surgeons so far considered acupuncture for knee arthroplasty (27-28).

### Pain management and immediate functional results

We selected 334 candidates to unilateral fast-track total knee arthroplasty (TKA) in our institute (Istituto Fiorentino di Cura e Assistenza (IFCA, Florence) from September 2014 to September 2016. These

patients adhered to the multimodal protocol described before. In the years 2014 and 2015 the patients were recruited for fast-track protocol according to the following inclusion criteria: age under 76 years old, no major comorbidities, and not living alone at home. Since 2016 all the patient undergoing primary TKA at IFCA were considered eligible for the fast track protocol. Study population is made up of 118 males and 216 females, with an average age of  $67,2 \pm 10$  years, average BMI of  $28,3 \pm 4,6$  and an average of 2 preoperative comorbidities per patient.

An intra-articular drainage was applied in 9.3% patients for the first 24 hours. A urinary catheter was applied in 12.6% patients and removed the morning after surgery. Nine-two percent of the patients have been mobilized on the day of surgery for a short walk with crutches. A complete autonomy in going to bathroom and in walking with the aid of two crutches was achieved by 87% of the patients on day one and 100% on the second postoperative day. All patients were able to climb and walk down the stairs in the second postoperative day and 83% of them were able to do it on the first postoperative day. All TKA patients presented at least  $90^\circ$  of knee flexion at discharge. Nine percent patients had nausea in the day of surgery, at the moment of ward admission or after physical therapy; 4.2% had orthostatic hypotension after first walking; 14% patients showed surgical wound exudate requiring advanced dressing change, but only in 3% it determined a physical therapy delay. 6.6% patients showed a moderate hemarthrosis of the operated knee without the need for subsequent surgical treatment. There were no cases of urinary retention during the observation but ultrasound monitoring with bladder scanner after surgery was performed in all the patients and transient catheterization has been performed in 18% of the patients.

### Conclusion

Fast-track surgery in orthopedics involves an early mobilization of the patient after surgery, an early oral hydration and nutrition and a perioperative educational process which makes patient more informed and responsible during physical therapy.

It is therefore necessary to have an excellent analgesia with no side effects hindering patient early recovery. For this reason we developed a multimodal analge-

sic protocol with no peripheral nerve block thanks to the adoption of local infiltration analgesia. Many rescue therapy are available in case of insufficient analgesia.

Fast-track surgery involves a continuous teamwork between different specialists (orthopedic, anesthesiologist, physiatrist, physical therapist, internist) in order to have a perfect patient management during the entire perioperative period.

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