Recent Updates In Postoperative Pain Management After Total Knee Arthroplasty

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1. ACLS ... Advanced Cardiac Life Support
2. ASIS ... Anterior Superior Iliac Spine
3. ASRA ... American Society of Regional Anesthesia
4. CEI ... Continuous Epidural Infusion
5. CFNB ... Continuous Femoral Nerve Block
6. cGMP ... Cyclic Guanisine Mono Phosphate
7. CGRP ... Calcitonin Gene Related Peptide
8. CNS ... Central Nervous System
9. COX ... Cyclooxygenase
10. CSNB ... Continuous Sciatic Nerve Block
11. DOP ... Delta Opioid Receptor
12. EREM ... Extended Release Epidural Morphine
13. FNB ... Femoral Nerve Block
14. GABA ... Gamma Amino Butyric Acid
15. GPCSs ... G Protein Coupled Receptors
16. IASP ... International Assossiation for the Study of Pain
17. IM ... Intramuscular
18. INR ... International Normalized Ratio
19. IV ... Intravenous
20. KOP ... Kappa Opioid Receptor
21. LA ... Local Anaesthetic
22. LAST ... Local Anaesthetic Systemic Toxicity
23. LFCN ... Lateral Femoral Cutaneous Nerve
24. LMWH ... Low Molecular Weight Heparin
25. LPB ... Lumbar Plexus Block
26. M3G ... Morphine 3 Glucuronide
27. M6G ... Morphine 6 Glucuronide
28. MAM ... Monoacetylmorphine

29. MEAC ... Minimum Effective Analgesic Concentration
30. MOP ... Mu Opioid Receptor
31. NMDA ... N-Methyl D-Aspartate Receptor
32. NO ... Nitric Oxide
33. NOS ... Nitric Oxide Synthase
34. NRM ... Nucleus Raphe Magnus
35. NSAIDs ... Non Steroidal Anti Inflammatory Drugs
36. OTFC ... Oral Transmucosal Fentanyl Citrate
37. PACU ... Post Anaesthesia Care Unit
38. PCA ... Patient Controlled Analgesia
39. PCEA ... Patient Controlled Epidural Analgesia
40. PCIA ... Patient Controlled Intravenus Analgesia
41. PCRA ... Patient Controlled Regional Analgesia
42. PCTS ... Patient Controlled Transdermal System
43. PGE_2 ... Prostaglandin E_2
44. PTT ... Partial Thromboplastin Time
45. SFNB ... Single Femoral Nerve Block
46. sP ... Substance P
47. TKA ... Total Knee Arthroplasty
48. VAS ... Visual Analogue Scale
49. VGSC ... Voltage Gated Sodium Channel
50. VIP ... Vasoactive Intestinal Polypeptide
51. VR-1 ... Vanilloid Receptor 1
52. WDR ... Wide Dynamic Range Neurons

Introduction

Total knee arthroplasty, also known as total knee replacement, is one of the most commonly performed orthopedic procedures. As of 2010, over 600,000 total knee replacements were being performed annually in the United States and were increasingly common. By 2030, the incidence of TKR in the United States is expected to increase by more than 6-fold. ***(Gregory M. Martin. 2014).*** Whereas, more than 70,000 knee replacements are carried out in England and Wales each year, and the number is rising. Most people who have a total knee replacement are over 65 years old.

The rising prevalence of total knee arthroplasty is necessarily associated with a rise in the concern of performing an adequate postoperative pain management following this procedure. Not only ethical and humanitarian aspects are against inadequate management of severe postoperative pain, it may also lead to many consequences such as compromised immunity, increased oxygen demand, higher strain on cardiovascular system, prolonged hospital stay and hospital readmission. ***(Aditya V. Maheshwari, et al. 2009).*** Moreover, effective treatment of postoperative pain continues to be a challenge because it influences the surgical outcome and for prosthetic joints pain management is a must for early mobilization and functionality of the new joints. ***(Denisa Madalina Anastase, et al. 2014).***

A variety of pathologic conditions affecting the knee can be treated with total knee arthroplasty, leading to pain relief, restoration of function, and free painless mobility. Osteoarthritis of the knee accounts for more than 90% of total knee replacements. ***(L. Stefan LOHMANDER. 2013).*** Osteoarthritis is commonly a bilateral pathology which requires a bilateral intervention. This is sometimes associated with the patient's refusal to perform a total knee replacement for the second leg if he/she experienced inadequate or prolonged postoperative pain.

However, approximately half of total knee replacement patients present with extreme pain immediately after surgery. ***(Korean knee Society, 2012).*** Variable methods and interventions can be used individually or in combination with each other to achieve adequate levels of pain control that helps to reach the patient's satisfaction and relief. For instance, Patient controlled intravenous analgesia (PCIA) would be one of the major choices for patients receiving general anaesthesia especially when regional anaesthesia or peripheral nerve blocks is contraindicated. On the other side, patients who received regional anaesthesia would be strong candidates for neuroaxial analgesia such as epidural analgesia or continous peripheral nerve blocks such as continous femoral nerve block or three in one blocks. Even when no difference in pain scores is reported between the systemic and regional analgesia, patient satisfaction scores still favors continuous femoral nerve block compared with

intravenous patient controlled analgesia. ***(Alan J. R. Macfarlane, et al. 2009).***

During the last couple of decades and especially the last few years, major technological breakthroughs that have the potential to significantly advance the field of postoperative analgesia have occurred and are still progressing. The advances in this field included opioids with prolonged action and with easier administration formulas. For example, extended action epidural morphine and transdermal fentanyl are some of these new formulas. Others include the use of various non-analgesic substances as adjuvants, major examples are ketamine, some anticonvulsants such as gabapentin and alpha 2 agonists such as dexmeditomedine. In addition, Patient-controlled regional analgesia (PCRA) encompasses a variety of techniques that provide effective postoperative pain relief without systemic exposure to opioids. Using PCRA, patients control the application of pre-programmed doses of local anesthetics, most frequently ropivacaine or bupivacaine (individually or in combination with an opioid). ***(Nalini Vadivilu, et al. 2010).***

Chapter1
Physiology of Knee Pain

1.1. Definition of Pain

Pain is defined by the International Association for the Study of Pain (IASP) as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. ***(Bonica JJ. 1990)*** Thus pain has objective, physiologic sensory aspects as well as subjective emotional and psychological components. ***(Chaplan SR, Sorkin LS. 1997).***

The term **"nociception"** (Latin – noci = harm or injury) is used only to describe the neural response to traumatic or noxious stimuli. ***(Merskev HM. 1979).***

1.2. Peripheral Transmission:

Peripheral transmission of pain consists of production of electrical signals at the pain nerve endings (Transduction) followed by propagation of those signals through the peripheral nervous system (Transmission). ***(Behbehani MM. 1995)***

1.2.1. Transduction:

The primary sensory structure that accomplishes transduction is the nociceptor. Most nociceptors are free nerve endings that sense heat, mechanical and chemical tissue damage. Several types are described:

a) ***Mechanoreceptors***, respond to pinch and pinprick.
b) ***Silent nociceptors***, which respond only in the presence of inflammation.
c) ***polymodal mechanoheat nociceptors***, The last are most prevalent and respond to excessive pressure, extremes of temperatures (>42 ^{o}C and <18 ^{o}C), and algogens (pain producing substances).

Polymodal nociceptors are slow to adapt to strong pressure and display heat sensitization. ***(Raja SN, et al.1997) (Sosnowski M, et al.1992).***

Vanilloid receptor-1 (VR-1) was isolated from the sensory neurons. Vanillins are a group of compounds, including capsaicins that cause pain. The VR1 receptors not only respond to pain but also to protons and to temperatures >43 ^{o}C. Moreover receptor, VRL-1, which responds to temperatures above 50 ^{o}C but not to capsaicin, has been isolated from C fibers. (***Carl C Hug, Jr In. 2002) .***

Intact hyaline cartilage is completely free of nerve fibres. Therefore intact aneural cartilage cannot

be a source of pain. ***(Witoński D & Wagrowska-Danielewicz M. 1999).*** The patello femoral joint appears to be very sensitive to pain due to the high number of free nerve endings in different structures. The highest numbers are found in the quadriceps muscles, with significant numbers also in the retinacula, patellar tendon and synovium. ***(Biedert RM & Sanchis-Alfonso V. 2002).***

1.2.2. Transmission:

The knee joint is supplied by various peripheral nerves which include the femoral ($L_{2,3,4}$), obturator ($L_{2,3,4,5}$), and sciatic nerves ($L_{4,5}$,$S_{1,2,3}$). ***(Brian Catlin, et al. 2008).***

The innervation of the knee joint follows Hilton's law, meaning that all of the motor efferent nerves carry afferent branches from the knee capsule. ***(Horner G, Dellon AL. 1994).*** The innervation of the knee joint can be divided into two groups; a posterior and an anterior group. The posterior group is made up of branches of the tibial nerve and a terminal branch of the obturator nerve. If necessary, signals from the posterior capsule and cruciate ligaments are transmitted to the CNS. The anterior group consists of branches of the femoral, common peroneal and saphenous nerves. The femoral nerve divides into the vastus muscles and the anterior medial joint capsule. The saphenous nerve innervates the anterior medial capsule and some sensory branches to the patellar tendon. The medial side of the patella is innervated by the nerves of the vastus medialus muscle. The