INTRODUCTION

Pain management is 'core–business' for the anaesthetist. Anaesthesia has been developed from the human desire to control pain during surgical operations. Involvement of anaesthetists in the management of acute post-operative and post-traumatic pain, labour pain, chronic and cancer pain soon followed **(Loeser & Treede., 2008).**

Acute postoperative pain, for many years, has been shown to be inadequately treated. 54% of post-operative patients had "moderate to severe pain" at hospital discharge after inpatient surgery and 46% of patients still had "moderate to severe pain" two weeks later **(Buvanendran et al., 2015).**

Acute pain in the post-surgical period is complicated by delayed ambulation, respiratory problems, and delayed transition in to lower levels of medical care. The advantages of good analgesia after surgeries are:

patient comfort and subsequently satisfaction, early mobilization after surgery, lower risk of cardiac and respiratory complications, a diminished risk of the development of deep venous thrombosis, faster recovery with lower incidence of neuropathic pain, and lower costs of medical care **(Nussenzveig, 1999).**

After hundreds of years of advances, opioids are still the mainstay of postoperative analgesia. Although opioids are very effective analgesics, they also have many undesirable side actions. Most common adverse effects of opioids are respiratory depression. nausea and vomiting, sedation, bradycardia and hypotension. pruritus, and reduction in gastrointestinal function. The management of complications such as pruritus and nausea may include the antihistamines administration. Antihistamines have an additional effect on respiratory depression and sedation **(Ashburn et al., 1994).**

Pregabalin is a drug that has been widely used in pain management. It has an analgesic effect as it is a structural analogue of gamma-aminobutyric acid which

acts as a potent ligand for alpha 2 - delta subunits, of the voltage - gated calcium channels in the nervous system. This action results in a reduction in the depolarization-induced calcium influx and therefore, a reduction in excitatory neurotransmitters release including noradrenaline, glutamate, dopamine and serotonin **(BenMenachem, 2004).**

AIM OF THE WORK

The aim of the work is to assess the postoperative analgesic effect of paracetamol and pregabalin combination in comparison with paracetamol alone in open hip surgeries.

PAIN

Pain is an unpleasant emotional and sensory feelings. It accompanies occurred or impending damage of a tissue. Pain is the most prevalent experience reported by the patients. It is a sensual and perceptual phenomenon, that causes suffering and emotional state of risks connected to anxiety **(Domzał, 2007)**.

Before we become aware of that something is hurting, there are physiological series of actions in human body. Painful stimuli have to pass "in milli-seconds". So, if there is an acute pain, it warns and alerts about relative or impending danger, increasing the chance for recovery. However, chronic pain causes a miserable part in the body, such as disability or unusable limb. A single, sharp pain stimulus can disappear, probably without leaving a trail. Repeated stimulation causes adaptation in the central nervous system and also activation of other systems, both inhibiting or supporting the pain. In the brain and spinal cord, synthesis and activation of

various receptor systems and also, synthesis of different compounds can occur, leading to modification of pain sensation. It is also known that the glial cells play an important role in this process. It is a very sophisticated process that can lead to the pain preservation, even after disappearance of impulse of pain **(Zylicz & Krajnik, 2003).**

Pathway of pain:

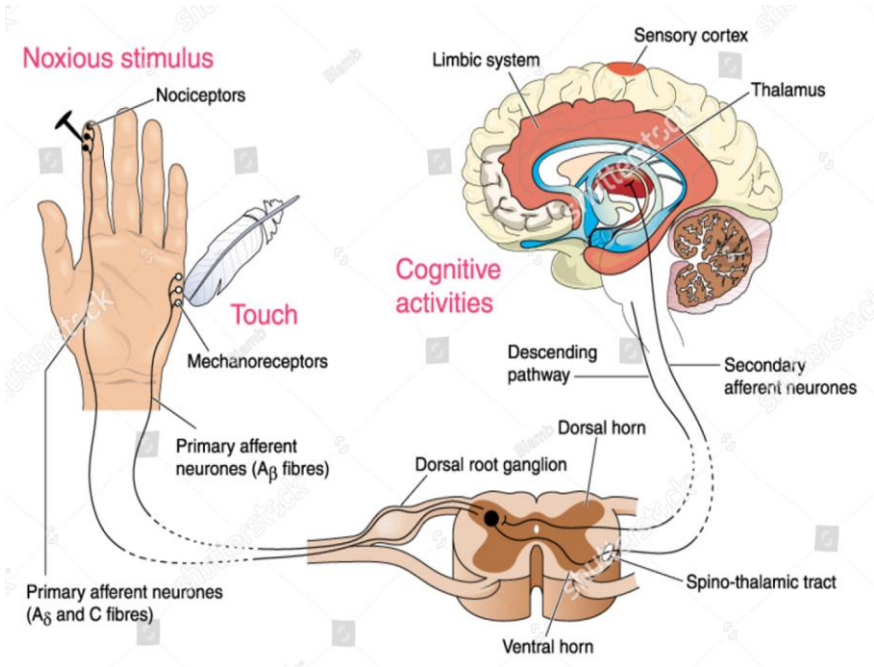

Figure (1) pathway of pain (**Helms &Barone, 2008**)

Pain is caused by stimulation of pain receptors (the nociceptors), which are nerve endings that can make response to painful stimulation. They are located in skin, organ of motion (muscles, ligaments, periosteum, and joint capsule), dental pulp and the cornea. Inside the body, nociceptors are also numerous in the pleural membrane, peritoneum, meninges, and walls of organ. They are stimulated by electrical, biological, mechanical, thermal, and chemical stimuli. **(Helms & Barone, 2008).**

These stimuli are transmitted into the spinal cord then to the brain centres where perception of the pain occurs. Impulses run in the dorsal horn neurons of the spinal cord, which synapse with dorsal horn neurons in substantia gelatinosa, then enter to the brain. The fundamental sensation of pain occurs in the thalamus. It continues to the limbic system (emotional center) and the cerebral cortex, as perception and interpretation of pain occurs. **(Helms & Barone, 2008).**

Pain could be also generated without receptors, from the peripheral and central nervous systems. This is a pathological pain that arises in response to nervous system damage. This type of pain has a different nature and clinical presentation from the physiological type of pain. It is important to differentiate receptor (nociceptive) pain, physiological pain from (non-receptor) pathological pain, central and peripheral **(Konturek, 2007).**

In transmission of pain, two types of fibers are involved: Aδ and C. The large fibers (A-delta), produce well-defined and sharp pain, which is stimulated by a physical blow, cut, an electrical stimulation. These fibers are myelinated and could allow propagation of an action potential at a rate of 20 meters per second. Through these fibers, transmission is very fast and the body responds faster than the stimulus of pain. This results in withdrawal of the affected part of the body before perceiving the pain. This allows a quick response: "escape" or preparation for "fight" **(Apkarian et al., 2005).**

C fibers are very thin and susceptible to be damaged. These fibers are not myelinated, thus the painful stimuli conduction is very slow (about 0.5 - 2 meters/ second). Multiple C fibers are combined in a "net"; thus, the area which is covered by C-fibers is broad. So, the patient can be able to detect the pain location "only approximately". C fibers react to thermal mechanical, and chemical stimuli. They lead pain stimuli and also pruritic stimuli (which is a part of the fibers, especially sensitive to histamine). Patients describe pain conducted by C fibers as rapid, hitching, pulsing. **(Schmelz et al.,1997).**

Regulators of Pain:

When damage of tissue happens, chemical substances which are involved in the pain transmission are released into the extracellular tissue. Pain receptors are activated by irritation of the nerve endings. Chemical mediators which are responsible for activation of pain include prostaglandins, bradykinin, histamine, leukotrienes, substance P and acetylcholine. At the site of injury, mediators can produce other reactions, like vasodilatation, vasoconstriction, or alteration of capillary permeability. Prostaglandins stimulates inflammation and other

inflammatory mediators. Aspirin blocks (cyclo- oxygenase 2), the enzyme which is needed for synthesis of prostaglandin, thus reducing sensation of pain. These drugs are often prescribed for painful conditions due to inflammation **(Besson, 1999)** .

Human body has a built-in chemical mechanism for management of pain. Fibers in the brain stem, dorsal horn of spinal cord, and peripheral tissues release endogenous opioids and neuromodulators, which inhibit the action of neurons transmitting the impulses of pain. Endorphins are (opioid-like) substances responsible for relief of pain. Endorphin levels vary between individuals. Therefore, different people experience pain differently. This endogenous opioid mechanism may be involved in the effect of placebo. A placebo is an inactive substance or treatment which is used in controlled studies for comparison with "real" drug, to cheat the recipient and to study the efficacy of the drug used in the study. **(Allan& Siegel , 2002).**

Clinical features of pain:

Clinical characters of pain include: intensity, duration, quality and location. The location of pain reflects the possible aetiology, and it does not always related to the site of injury or disease process. Deep organ pains are specially located poorly. Pain often occurs as a phenomenon reflected pain (projection). Phenomenon of projection is derived from the fact that there are no pain receptors in the internal organs, only the overlying peritoneum has a lot of pain receptors and sensory nerves. The pain intensity which is experienced by the patient is individual, and considered as the hardest feature to be assessed. We can deduce that the exponent of the pain intensity is its tolerance. Women have the highest pain tolerance, men and children the least **(Domzał , 2007)**.

The numeric pain scale is used for evaluation of the intensity of pain by a score: from 0= means no pain, to 10= means the strongest pain experienced in life **(Farrar et al., 2001).**

The pain duration is an important feature that divides pain to acute and chronic. In back pain, relapses may occur after acute phase, thus, acute pain becomes chronic pain. It is supposed that any pain for a duration more than three months is chronic pain. In headaches or neuralgia, pain can be continuous and paroxysmal. **(Matre et al., 2006).**

According to the duration of symptoms Pain can be divided into groups in:

• Acute pain: pain for a duration < or = 3 months. It acts as a warning defensive (traumatic, post-surgical pain, or pain associated with medical procedures).

• Chronic pain: pain for a duration > 3 months. It does not accomplish the role of warning and defensive, due to the nature and the symptoms of the disease is considered in itself, and also requires a multitherapeutic measures **(Domzał, 2007)**.

Types of pain killers:

• Non-Opioid analgesics: They are used in the management of moderately intensive pain. Drugs included in this group are paracetamol and nonsteroidal anti-inflammatory drugs "NSAIDs" (e.g.: diclofenac and ibuprofen). It is very difficult to portend which formula of this group is the most effective. Side effects must be taken into consideration, particularly, in the use of this drugs for long duration **(Schmelz et al., 1997).**

• Opioids: In the pain management, there are "weak" opioids and "strong" opioids. Weak opioids such as dihydrocodeine. tramadol and codeine show a trapping effect. This means that overriding the maximal dose will not increase the analgesic action of the drug. But, result in side effects. Strong opioids include: fentanyl, buprenorphine, morphine, oxycodone and methadone. They do not have a trapping effect **(Stein ,1995).**

. Opioids vary in efficacy, duration (short-acting, long-acting), metabolism. the bioavailability (absorption in the gut), possibility to combination with other drugs, or adverse effect (such as. dyspnea and constipation). They

affect the psychological and motor activity and using them interfere with driving or operating machines **(Cleeland et al., 1996)**.

Pain management in Hip Surgeries

Hip fractures are associated with increased morbidity and mortality rates. Incidence increases with age, rising for men and women respectively, from 22.5 and 23.9 per 100,000 population by age 50 to 63 and 1,289 per 100,000 population at age 80. Short-term mortality rates "in the first year after a hip fracture" are high and ranged from (25%) for women to (37%) for men. Furthermore, a large proportion of those patients who survive never return to their pre-fracture level of function, and approximately 25% to 50% of elderly patients with hip fractures have not returned home by 1year post-fracture **(Kannegaard et al., 2010).**

Pain after hip fracture is complicated by depression, delirium, sleep disorders, and decreased response to interventions for other disease states. So, it is important to adequately treat and manage pain complaints during acute treatment of hip fracture. Therefore, poor management of post-operative pain