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#### **REVIEW ARTICLE**

### Role of buprenorphine in acute postoperative pain



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#### **KEYWORDS**

Buprenorphine; Acute postoperative pain; Opioid analgesics

Abstract Nowadays acute postoperative pain persists as a high prevalence symptom. The incidence, intensity and duration of postoperative pain vary considerably from one patient to another, from one surgery to another, from one hospital to another, and even from one country to another. It is important to learn about recent developments in central sensitisation, as it plays an important role in postoperative pain. Postoperative pain is mainly nociceptive somatic, in response to surgical damage. The surgical trauma and pain cause an endocrine response that increases the secretion of cortisol, catecholamines, and other stress hormones. Tachycardia, hypertension, decreased regional blood flow, impaired immune response, hyperglycaemia, lipolysis, and negative nitrogen balance also occur. All this plays an important role in morbidity and mortality in the postoperative period. Buprenorphine is a semi-synthetic opioid derived from thebaine. It has a binding affinity for the mu, kappa and delta receptors, and has a slow dissociation from these receptors. Because of its action on the mu and kappa receptors it can be used as an analgesic, as well as for maintenance therapy in patients with a history of drug abuse. This article will describe the characteristics of acute postoperative pain, the pharmacology of buprenorphine, and its interference in the management of postoperative pain. © 2016 Sociedad Médica del Hospital General de México. Published by Masson Doyma México S.A. This is an open access article under the CC BY-NC-ND license (http://creativecommons. org/licenses/by-nc-nd/4.0/).

#### PALABRAS CLAVE

Buprenorfina; Dolor agudo postoperatorio; Analgésicos opioides

#### Utilidad de la buprenorfina en el dolor agudo postoperatorio

**Resumen** En la actualidad el dolor agudo postoperatorio persiste como un síntoma de elevada prevalencia. La incidencia, intensidad y duración del dolor postoperatorio varían considerablemente de uno a otro paciente, de una a otra intervención quirúrgica, de uno otro hospital e incluso de un país a otro. Es importante conocer acerca de los recientes avances en la sensibilización central, ya que juega un papel importante en el dolor postquirúrgico. El dolor

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postoperatorio es principalmente nociceptivo somático, respuesta a la agresión quirúrgica. El trauma quirúrgico y el dolor causan una respuesta endocrina que incrementa la secreción de cortisol, catecolaminas y otras hormonas del estrés. También se produce taquicardia, hipertensión, disminución del flujo sanguíneo regional, alteraciones de la respuesta inmune, hiperglicemia, lipólisis y balance nitrogenado negativo. Todo esto juega un importante papel en la morbimortalidad en el periodo postoperatorio. La buprenorfina es un opioide semisintético derivado de la tebaina. Se vincula con afinidad hacia los receptores mu, kappa y delta, y tiene una lenta disociación sobre esos receptores por su acción en los receptores mu y kappa se puede usar como analgésico, asi como el mantenimiento y terapia de pacientes con historia de abuso de drogas. Este articulo describirá las características del dolor agudo postoperatorio, la farmacología de la buprenorfina y la injerencia de ésta en el manejo algológico de dolor postquirúrgico.

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#### Definition of pain

The most complete definition of pain is the one backed by the IASP (International Association for the Study of Pain), which says: "An unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (Merksey & Bogduk, 1994)."

Specifically, postoperative pain is that caused after surgery; characterised by diverse unpleasant sensory, emotional, and mental experiences associated with autonomic, endocrine-metabolic, physiological, and behavioural responses.<sup>2,3</sup>

According to the American Society of Anesthesiologists (ASA), acute surgery-related pain is pain that is present in the surgical patient after a procedure.<sup>4</sup>

#### Epidemiology of postoperative pain

Nowadays acute postoperative pain persists with a high prevalence. Despite advances in regional techniques, drugs, and studies conducted by specialised groups to decrease the incidence of pain in the postoperative period, in both developed and developing countries postoperative pain is reported at rates exceeding 70%, although they vary considerably from one patient to another, from one surgery to another, from one hospital to another, and even from one

**Table 1** Prevalence of acute postoperative pain. Modified from: Zaragoza F et al. Dolor posoperatorio. Madrid 2005.

Author	Year	Country	Patients with pain (%)
Cohen et al	1980	USA	75
Donovan et al	1983	USA	21.5
Oates et al	1994	United Kingdom	33
Poisson-Saloman et al	1996	France	46
Sed et al	2003	Spain	68
Apfelbaum et al	2003	USA	59

country to another. Cadavid and Chaustre<sup>4</sup> indicate that the incidence of moderate to severe pain in the postoperative period is between 8.4% and 47.0%. Some studies that demonstrate the prevalence of pain are mentioned in Table 1.

It has been described that during the postoperative period after intrathoracic, upper abdominal, and to a lesser extent, kidney surgery, movements that put pressure on the incision (deep breathing, cough, and body movement) aggravate the intensity of the pain.<sup>5</sup>

The type of incision also has a large influence, and it has been demonstrated that a transverse abdominal incision damages the nerves less, which causes less pain.

#### Pathophysiology of postoperative pain

It is important to learn about central sensitisation as it plays an important role in postoperative pain, which is primarily nociceptive somatic as the result of surgical damage.<sup>6</sup>

After the damage caused to the nociceptive receptors during the surgery, a hyperalgesic state occurs. This is divided into primary hyperalgesia, resulting from the sensitisation of the peripheral nociceptors, and secondary hyperalgesia, which is associated with sensitisation of the spinal cord and the central nervous system.<sup>7,8</sup>

After nociceptive stimuli, primary mediators such as prostaglandins, leukotrienes, serotonin, and bradykinins are released. These primary mediators stimulate the release of peptides such as calcitonin gene-related peptide (CGRP) and substance P at the site of injury. Vasodilation is induced by histamine, the release of nerve growth factor, and the sympathetic effect reflex release of norepinephrine, known as ''inflammatory soup''.8

The peripheral nociceptor impulses travel through delta and C synapse fibres in laminae II and V in the spinal cord. The C fibres also make synapses in spinal cord lamina I, known as second order neurons.<sup>8</sup>

There are two types of second order neurons in the spinal cord: the first, in lamina I, respond to impulses in the C fibres; the second, located in lamina V, respond to both harmful stimuli, mainly from Ad fibres, and non-harmful stimuli. Neurotransmitters such as glutamate and aspartate present in lamina V cause fast synaptic transmission. This happens by binding to and activating kainate

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