شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

شبكة المعلومـــات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

﴿ قـسـم ﴾

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
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في درجة حرارة من 15 – 20 مئوية ورطوبة نسبية من 20-40 %

To be kept away from dust in dry cool place of
15 – 25c and relative humidity 20-40 %

بعض الوثائق الأصلية تالفة

بالرسالة صفحات

لم ترد بالأصـــل

Efficacy of Preemptive Single Dose Intravenous Ketamine Hydrochloride on Postoperative Analgesia after Lower Abdominal Surgery

Thesis

Submitted to the Faculty of Medicine,
Alexandria University,
In partial fulfillment of the requirements of the degree
of

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By

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INTRODUCTION

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Many millions of patients worldwide undergo surgery each year and benefit from knowledge, skills, and sophisticated technology that characterize most aspects of modern surgical treatment. Although effective pain control is essential for optimal care of surgical patients, and despite advances in knowledge of pathophysiology, pharmacology of analgesics, and the development of more effective techniques for perioperative analgesia, many patients continue to experience distressing pain. [1, 2]

A successful method of analgesia must be suitable for use on a general surgical ward and require only simple routine nurse monitoring. [3]

The International Association for the Study of Pain has defined pain as an *unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage.* [4] Postoperative pain is an acute pain, which starts with the surgical trauma and usually ends with tissue healing. Autonomic disturbances, shallow breathing and reduced body movements accompany this pain. There is also a pain component, which is not dependent solely on the trauma, but on the way of the patient perception of pain which is influenced by social, cultural and psychological factors. [5]

Anatomical aspects:

Pain is conducted along three-neuron pathways that transmit noxious stimuli from the periphery to the cerebral cortex. (Fig 1) [6] Primary afferent neurons are located in the dorsal root ganglia, which lie in the vertebral

foramina at each spinal cord level. Each neuron has a single axon, which bifurcates, sending one end to the peripheral tissues it innervates and the other to the dorsal horn of the spinal cord. In the dorsal horn, the primary afferent neurons synapse with a second order neuron; its axons cross the midline and ascend in the contralateral spinothalamic tract to reach the thalamus. Second order neurons synapse in thalamic nuclei with third order neurons, which in turn send projections through the internal capsule and corona radiata to the post-central gyrus of the cerebral cortex. [7]

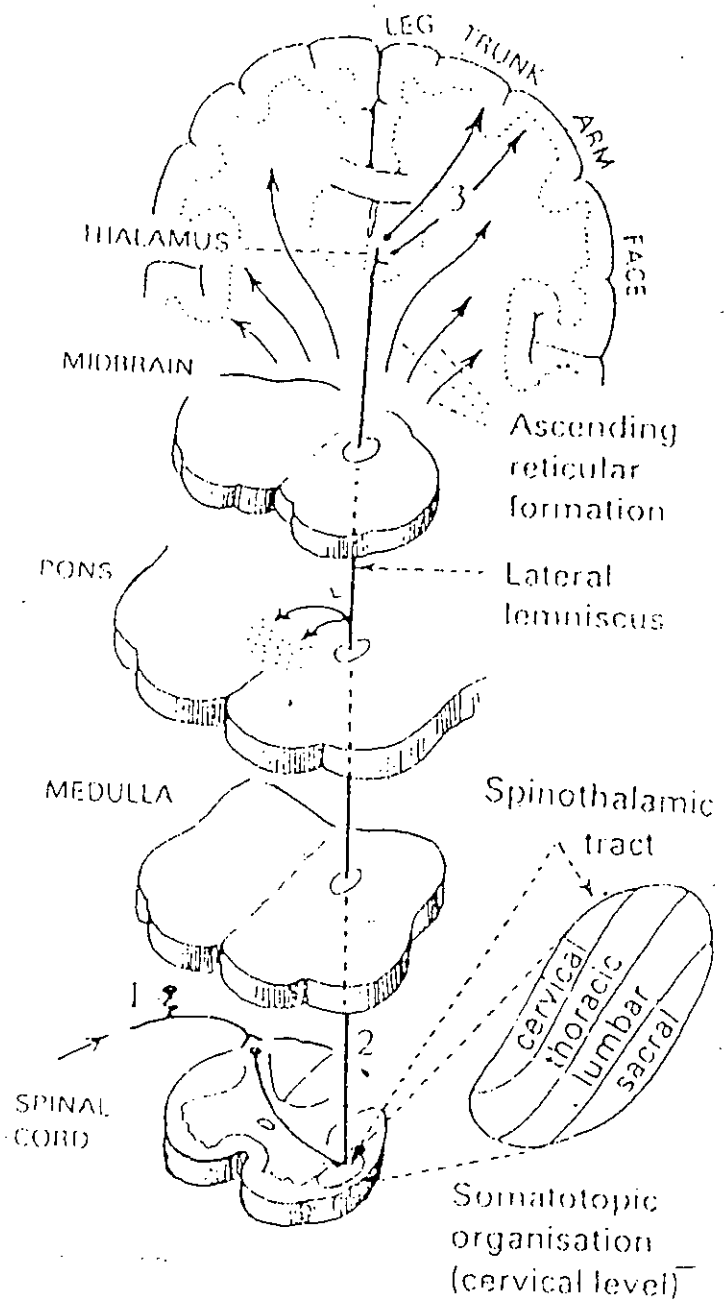

Figure 1: Pain Pathway [6]

Neurobiology of Pain

Enormous progress is currently being made by the exploitation of modern neurobiologic techniques in the elucidation of mechanisms that may contribute to the pathogenesis of pain. [8] These indicate that pain can be generated in multiple ways at a number of different sites that may coexist between and across diverse disease states. [9] Molecular biologic techniques are contributing to the analysis of pain mechanisms and are leading to the discovery of new targets, which are being used in high throughput screens by the pharmaceutical industry for the discovery of highly specific small molecules as potential novel analgesics. The discovery of targets specific to particular pain mechanisms will soon enable therapy to be targeted specifically at those mechanisms. [10]

Tissue injury produces sensory changes that can be readily measured clinically. Responses to stimuli applied both at and adjacent to the site of injury are typically enhanced and involve both peripheral and central mechanisms. [11]

Peripheral sensitization

Most structures of the body contain nerve endings that are responsive to a variety of mechanical, thermal, and chemical stimuli named ***primary afferent nociceptors.*** [12] These receptors associated with the transmission of noxious information can be grouped into two main categories: A delta fibers mechano- thermal and C fibers polymodal nociceptors. [13]

Nociceptive stimulation results in a neurogenic inflammatory response with the release of substance P, neurokinin A and calcitonin gene-related peptide from the peripheral terminals of nociceptive afferent fibers. [14] Release of these peptides results in change excitability of sensory and sympathetic nerve fibers, vasodilatation, extravasation of plasma proteins as well as release of chemical mediators from inflammatory cells. These interactions result in the release of a 'soup' of inflammatory mediators such as potassium, serotonin, bradykinin, substance P, histamine, cytokines, nitric oxide (NO), and products from the cyclo-oxygenase and lipo-oxygenase pathways of arachidonic acid metabolism. (Fig 2) [15] These chemicals then act to sensitize high-threshold nociceptors and following tissue injury the threshold for eliciting pain decreases both within the area of the injury, ***primary hyperalgesia*** and in the surrounding uninjured tissue, ***secondary hyperalgesia.*** [16]

Central sensitization:

The nervous system does not modulate sensory stimuli in a fixed and unchanged manner. Animal experiments have shown that in response to intense or repeated stimulation, the nociceptive pathways of the dorsal horn develop a persistent reflex hyperexcitability that represents a central sensetization. Persistent C afferent fiber excitation with the facilitation of the discharge of dorsal horn wide-dynamic-rang neurons (WDR) is referred to as wind-up. [17]

Wind-up is dependant on activation of the ***N-methyl D-aspartate receptor (NMDA)*** and therefore, has the potential to be modified by agents acting at this site. This wind-up may make these neurons more sensitive to other input and is a component of central sensitization.