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# PAIN MANAGEMENT IN HEPATIC PATIENTS IN THE INTENSIVE CARE UNIT

*An Essay*
Submitted for Partial Fulfillment of Master Degree in
General Intensive Care

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قسم التخدير والرعاية المركزة وعلاج الألم

# Pain Management In Hepatic Patients In The Intensive Care Unit

## علاج الألم في مرضى الكبد بوحدة العناية المركزة

An Essay

Submitted For Partial Fulfillment of Master Degree In Intensive Care

By

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رسالة مقدمة من الطبيب / تامر عبد المنعم عبد السلام الطنملى

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بسم الله الرحمن الرحيم


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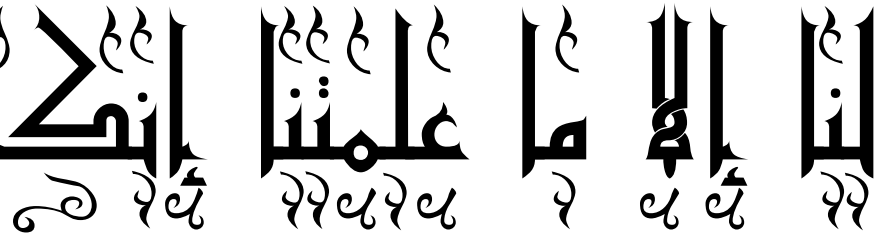
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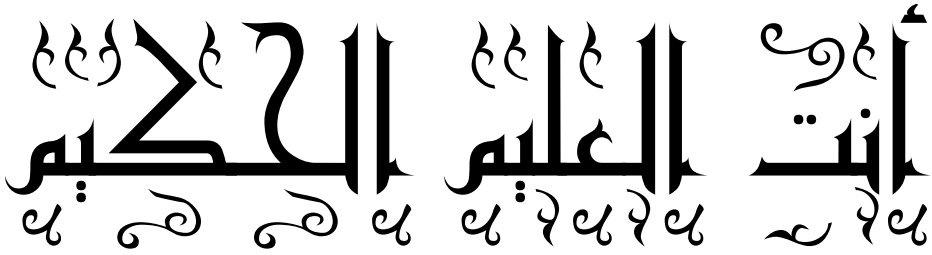
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# LIST OF ABBREVIATIONS

| | |
|---|---|
| ACC | Anterior cingulated cortex. |
| ACTH | Adreno-cortico-trophic hormone. |
| ADH | Anti-diuretic hormone. |
| AEDS | Anti-epileptic drugs. |
| ALF | Acute liver failure. |
| BPI | Brief pain inventory. |
| BP | Blood pressure. |
| cAMP | Cyclic adenosine monophpsphate. |
| CGB | Celiac ganglia block. |
| CGRP | Calcitonin gene related peptide. |
| CNCP | Chronic non cancer Pain. |
| CNS | Central nervous system. |
| COX | Cyclo-oxygenase. |
| COX-2 | Cyclo-oxygenase-2. |
| COX-3 | Cyclo-oxygenase-3. |
| CPP | Cerebral perfusion pressure. |
| CSF | Cerebro spinal fluid. |
| CT | Computerized tomography. |
| CVP | Central venous pressure. |
| CYP-450 | Cytochrome P-oxidase 450. |
| DVT | Deep venous thrombosis. |
| EA | Epidural analgesia. |
| FFP | Fresh frozen plasma. |
| FHF | Fulminant hepatic failure. |
| FRC | Functional residual capacity |
| GABA | Gamma-aminobutyric acid |
| GH | Growth hormone. |
| HE | Hepatic encephalopathy. |
| HRS | Hepato-renal syndrome. |
| IAH | Intra-abdominal hypertension. |
| IAP | Intra-abdominal pressure |
| ICH | Intra-cerebral hemorrhage. |
| ICP | Intra-cranial pressure. |
| ICU | Intensive care unit. |
| IM | Intra-muscular. |
| INR | International normalized ratio. |
| IV | Intra-venous |

| | |
|---|---|
| IVI | Intra-venous infusion |
| IV-PCA | Intra-venous patient-controlled analgesia. |
| LA | Local Anesthetics |
| LC | Locus coeruleus |
| LHA | Lateral hypothalamic area |
| MOF | Multi-Organ failure |
| MPQ | McGill pain questionnaire. |
| MRI | Magnetic resonance imaging |
| NAPQI | N-acetyl-p-benzo-quinone imine |
| NK-A | Neuro-kinin A |
| NK- B | Neuro-kinin-B |
| NMDA | N-methyl-D-aspartate. |
| NO | Nitric oxide |
| N/OFQ[ORL-1] | Nociceptin/orphanin FQ/ opioid-receptor-like |
| NOS | Nitric oxide synthetase |
| NSAIDS | Non-steroidal anti-inflammatory drugs |
| PAG | Peri-aqueductal grey matter |
| PCA | Patient-controlled analgesia |
| PEEP | Positive end expiratory pressure |
| PT | Prothrombin time |
| PVB | Para-vertebral block |
| PVN | Peri-ventricular hypothalamic nucleus |
| RBCs | Red blood cells |
| SAAG | Serum-to-ascites-ablumin gradient |
| SBP | Spontaneous bacterial peritonitis |
| SC | Sub-cutaneous |
| SHN | Sub-massive hepatic necrosis |
| SIRS | Systemic inflammatory response syndrome |
| TENS | Trans-cutanous electrical nerve stimulation |
| TCAS | Tricyclic antidepressants |
| TIPS | Transjugular intrahepatic portosystemic |
| TNF | Tumer necrosis factor |
| TPVS | Thoracic paravertebral space |
| 5HT3 | 5-hydroxytryptamine |

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# INTRODUCTION

# INTRODUCTION

Pain management is an essential component of medical care for the critically ill patient. The intensive care unit (ICU) is a unique care setting where critically ill patients receive expeditious and aggressive life-sustaining interventions and where suffering is common. Thus, high-quality pain management and optimal palliative therapy are part of the therapeutic targets for every patient. Pain assessment and management fall within the comprehensive scope of palliative care that should be provided concurrently with curative interventions and supportive care in the ICU. Appropriate pain management begins with recognizing, evaluating, and monitoring pain. Achieving excellent pain management requires knowledge and skill in pharmacologic, behavioral, social, and communication strategies ***(Mularski et al., 2009)***.

Patients with liver disease represent an important population in the ICU because these patients experience a particularly high morbidity and mortality among the critically ill ***(Volk and Marrero, 2006).***

A number of factors complicate the management of pain in the hepatic patients as the clinical utility of most analgesic drugs is altered in the presence of impaired hepatic function. This is not simply because of variations in clearance of the parent drug, but also due to potential production and accumulation of toxic or therapeutically active metabolites. Some analgesic agents may also aggravate pre-existing hepatic disease ***( Murphy, 2005).***

Fortunately, newer drugs and pain control modalities emerge to enhance our pain control armamentarium, such as acetaminophen**,** fentanyl, remifentanil, patient-controlled analgesia, epidural analgesia, paravertebral block, celiac ganglia block, acupuncture and transcutaneous electrical nerve stimulation ***(Mularski et al., 2009)***.

A proper understanding of pain patho-physiology together with Proper selection of analgesic drug or analgesic modality tailored to patient's specific condition will lead to best adequate and safe pain control ***(Erstad et al., 2009)***

# HEPATIC PATIENTS IN ICU

# HEPATIC PATIENTS
# IN INTENSIVE CARE UNIT

Hepatic patients are admitted to ICU due to acute liver failure ***(Stravitz et al, 2007)*** or advanced de-compensated, complicated chronic liver disease ***(Volk & Marrero, 2006).*** Also, they can be admitted for post-operative care (e.g. Post-liver transplant) ***(Humer et al, 2003)*** or for non hepatic causes (e.g. acute myocardial infarction and polytrauma). Moreover, non hepatic patients may suffer from liver dysfunction during their stay in ICU (e.g. shock liver and post- traumatic liver failure) ***(Strassburg, 2003 and Bechstein et al, 2002).***

## I-Acute Liver Failure:

Acute liver failure, defined as the onset of hepatic encephalopathy and coagulopathy within 26 weeks of jaundice in a patient without preexisting liver disease ***(Stravitz et al., 2007).***

Once a patient is diagnosed with ALF, the patient should be stabilized and transferred to a liver transplant centre, as liver transplantation offers the best long-term survival in patient likely to die of this condition. The patient should be cared for in the ICU and supportive measures initiated, including close neurologic evaluation and glucose monitoring ***(Han and Hyzy, 2006)***.

Although survival rates for patients with ALF improved since the availability of liver transplantation, ALF remains a very critical condition that can take a previously healthy individual to terminal illness in a matter of days. The most important indicator that ALF is progressive and may be life-threatening is the development of acute hepatic encephalopathy. This condition is the key element in the definition of the most serious forms of

ALF: fulminant hepatic failure (F.H.F) and sub-massive hepatic necrosis (S.H.N). Fulminant hepatic failure is defined as the development of acute hepatic encephalopathy within 8 weeks of the onset of symptomatic hepato-cellular disease in a previously healthy person. Sub-massive hepatic necrosis is defined as the development of acute hepatic encephalopathy within 9-24 weeks of the onset of symptomatic hepato-cellular disease in a previously healthy person ***(Michael, 2001).***

Many different nomenclatures have been used to describe F.H.F O'Grady's nomenclature is frequently used which divides patients into three groups: hyper-acute, acute and sub-acute (Table 1-1) ***(Laurence et al., 1997).***

**Table 1-1: O'Grady's nomenclature of F.H.F.**

| Group | Time from onset of jaundice to encephalopathy (in days) | Frequency of cerebral odema (in percent) | Frequency of ascites |
|---|---|---|---|
| Hyperacute | <8 days | Frequent (69%) | Rare |
| Acute | 8-28 days | Frequent (56%) | Rare |
| Subacute | >28 days | Rare (14%) | Frequent |

***Laurence et al., 1997***

***Ostapowicz and his colleages (2002)*** reported that the most common causes of ALF in the United States are acetaminophen (paracetamol) toxicity (39%), idiosyncratic drug reaction (13%), hepatitis A and B (12%) and at times no etiology can be determined (17%).

The hall mark features of F.H.F are Hepatic encephalopathy and co-agulopathy. Patients with F.H.F can rapidly progress from mild hepatic encephalopathy to deep coma (Table 1-2) ***(Marrero et al., 2003)***.