SEDATION & ANALGESIA IN INTENSIVE CARE UNIT

ESSAY

SUBMITTED IN PARTIAL FULFILMENT FOR THE DEGREE OF M. Sc. ANAESTHESIOLOGY

BY

AMGAD KAMAL IBRAHIM
M.B., B. Ch
(AIN SHAMS UNIVERSITY)

UNDER SUPERVISION

OF

PROF. DR. FAROUK AHMED SADEK
PROFESSOR OF ANAESTHESIOLOGY & INTENSIVE CARE
AIN SHAMS UNIVERSITY

PROF. DR. NEHAL GAMAL EL-DIN NOOH
ASSISTANT PROF. OF ANAESTHESIOLOGY & INTENSIVE CARE
AIN SHAMS UNIVERSITY

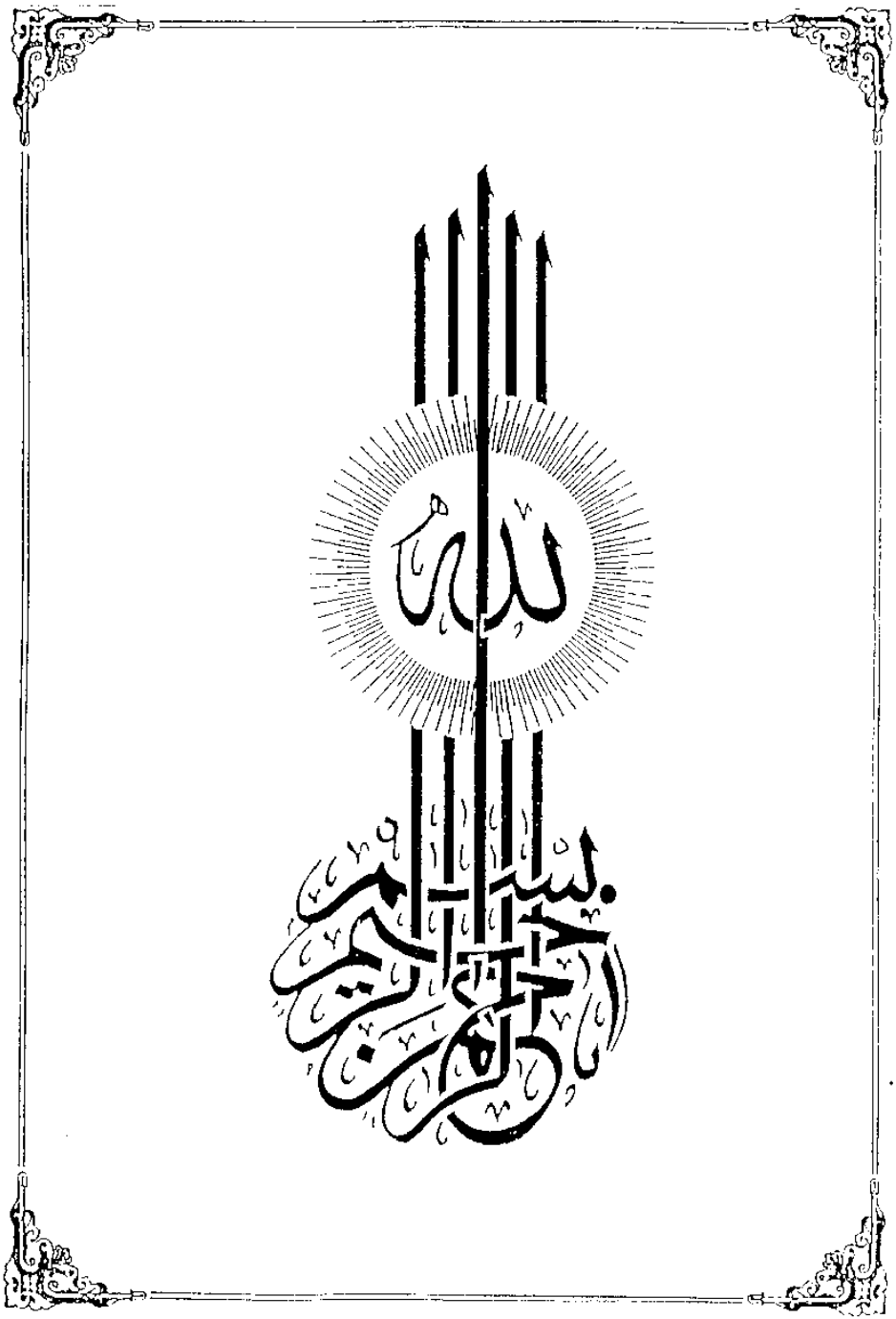
FACULTY OF MEDICINE
AIN SHAMS UNIVERSITY

1990

ACKNOWLEDGMENT

I would like to express my sincere gratitude and heartful thanks to professor **Dr. Farouk Ahmed Sadek,** Professor of Anaesthesiology, Ain Shams University, for his valuable advice and kind encouragement.

I am also extremely grateful to professor **Dr. Nehal Gamal El-din Nooh,** Assistant Professor of anaesthesiology for her efficient supervision and great assistance to complete this work.



CONTENTS

INTRODUCTION

INTRODUCTION

Patients admitted to an intensive care unit often require analgesia and sedation.

Although there is no substitute for caring and sympathetic nurses and doctors to ensure patient comfort on the intensive care unit (ICU), pharmacological intervention is often required for humanitarian and medical reasons.

Increased awareness of the potential dangers of sedative drugs and of the importance of optimizing their use has heightened interest in sedative regimens for the critically ill. The major concern in critically ill patients is to avoid excessive sedation and its complications. The regular monitoring of the depth of sedation is therefore an important clinical consideration.

The aim of this thesis is to review the pharmacological principles of some sedatives and analgesics and to discuss the indication of sedation and analgesia in ICU, methods of assessing sedation and different techniques of sedation and analgesia in ICU.

PHARMACOLOGICAL PRINCIPLES OF SOME SEDATIVES AND ANALGESICS

PHARMACOLOGICAl PRINCIPLES OF SOME SEDATIVES AND ANALGESICS

Analgesics are still the cornerstone of the management of pain. No other present therapy Can match drugs for offering cheap quick pain relief with minimal technical demands, Plus a high expectation of substantial analgesia with usually rapid reversibility of serious side effects on cessation.

Sedation in many ICUs is chiefly produced by use of analgesic drugs or intravenous or inhalational anaesthetic agents in concentrations lower than those required to induce anaesthesia. The ideal sedative drug should have a short half - life, inactive metabolites, be excreted independently of normal hepatic or renal function, should have no adverse effect on the cardiovascular or central nervous system, nor any interaction with other drugs and have no toxic effects on other organs. It might also be inexpensive, readily stored and easy to use. However, no currently available analgesic fulfils the requirements of every therapeutic situation and each has drawbacks, so that, new drugs and new formulations continue to be introduced.

The drugs that are available for sedation are divided into various classes:

1- Opioids or narcotic analgesic.

2- benzodiazepines.

3- Intravenous anaesthetic agents.

4- Inhalational agents.

5- major tranquilizers.

Opioids

An opioid is a compound having morphine-like activity and whose directly acting effects are stereospecifically antagonized by naloxone. This is in contrast to an "opiate" which is a compound specifically produced from the juice of the opium poppy (Papaver somniferum), e.g. morphine, codeine.

The opioids may be classified according to their clinical efficacy:-

1- low efficacy - codeine, dextropropoxyphene.

2- high efficacy- morphine, phenazocine, buprenorphine.

Alternatively they may be classified by their receptor activity (Thompson, 1986):-

1- Mu agonists- morphine, Codeine, pethidine.

2- Mu partial agonists- buprenorphine, propiram, profadol.

Approximate distribution and elimination half- lives of opioid agents in normal Patients.

Agent	Distribution half life (min)	Elimination half life (h)
Morphine	25	1.5–4
- glucuronides		3–6
Fentanyl	3	2–5
Alfentanil	3	1.5 - 3.5
phenoperidine	3	1.5 - 4
Pethidine	7	3 - 6.5
Nalbuphine	2	3.5 - 4

Classification of opioids according to latency (Time to peak effect after I.V. dose).

Ultrashort (1 min)	Short (4 – 10 min)	long (> 15 min)
Alfentanil	fentanyl	Morphine
	Sufentanil	Buprenorphine.
	pethidine	
	Methadone	

Classification of opioids according to duration of action.

Long	intermediate	short
Morphine	Fentanyl	Alfentanil
Methadone	Sufentanil	
lofentanil	pethidine	
Buprenorphine	Butorphanol	
	Nalbuphine	

3- Mixed agonist - antagonists- Pentazocine, nalbuphine.

4- Antagonists - naloxone, naltrexone, nalmefene.

Most opioids produce sedation, often with euphoria, as well as analgesia. side effects of opioids may be useful, as in the respiratory depression caused by morphine and to a greater extent by phenoperidine, when patients require controlled ventilation or unwanted, such as the hypotension that can occur with a single dose of morphine. Significant hypotension and cardiac dysrhythmia can occur after administration of virtually all narcotic analgesics.

Morphine is the principle alkaloid contained in opium, of which it forms 10% by weight. While the tertiary amine group confers on morphine the property of a weak base, the phenolic and alcoholic hydroxy groups have weakly acidic properties so, morphine is a poorly lipid - soluble drug and thus its rate of absorption from muscle will be slow and it will not rapidly cross the blood - brain barrier. Its onset of action will thus be slower than that of more lipid - soluble drugs. The hydrophylic nature of morphine also contributes to its duration of action as it is less readily removed from the receptor sites in the brain than more lipid - soluble drugs.

Morphine is metabolized in the liver into morphine – 6 – glucuronide which is also analgesic and is normally metabolized further into an inactive metabolite. Morphine reduces both venous and arterial tone in humans, induces bradycardia by vagal stimulation and release histamine although it causes little myocardial depression in healthy patients. Other disadvantages of morphine include meiosis, making assessment of pupillary signs more difficult, reduction of gastric emptying and impaired intestinal absorption, stimulation of the chemoreceptor trigger Zone and development of tolerance with long – term use. In patients with hypotension, the profound fall in liver blood flow markedly reduces morphine clearance (Macnab et al., 1986). However, other factors such as sepsis, age and inotropic therapy also affect morphine elimination. Hypercapnoea reduces the volume of distribution of morphine thereby potentiating its effect (Finck et al., 1977).

Papaveretum It is a preparation containing the water soluble alkaloids of opium. Standardized to contain 50 percent anhydrous morphine. The other 50 percent consists of the hydrochlorides of the remaining opium alkaloids (Mainly papaverine, codeine, narcotine, thebaine). It has similar advantages and disadvantages to morphine. (Bion & ledingham. 1987).

Pethidine is a synthetic opioid analgesic with a totally different structure to that of morphine. It is more plasma protein bound than morphine. About 70 percent of pethidine is bound to-alpha 1 acid glycoprotein. Pethidine binds only to a minor extent to plasma albumin. It is even less unionized (less than 10 percent) than morphine at physiologic PH but is significantly more lipid soluble. The volume of distribution of pethidine is quite similar to that of morphine (about 4 ± 1 l/kg), as is its clearance about 8 to 18mg/kg/min). Like morphine, a high hepatic extraction ratio results in biotransformation that is hepatic blood flow dependent. (Mather et al., 1975). It has morphine like action on pain (about 1/8 - 1/10) as potent as morphine. Its duration of action and other side effects are similar to those of morphine. It has however, also got atropine - like and quinidine - like actions. Pethidine has a potential advantage in that it produces less spasm of the sphincter of oddi than morphine and can be used in asthmatic patients. Prolonged use at high dosage results in accumulation of the metabolite norpethidine, which has convulsant properties.

Phenoperidine and fentanyl are potent lipid soluble synthetic analgesic drugs chemically related to pethidine. Phenoperidine is relatively long acting and produce profound

respiratory depression. Cardiovascular collapse has been reported (Green, 1981). Some reduction of cortisol level occurs after prolonged use but of greatest concern is the increase in intracranial pressure, which has been reported and seems to be related to its vasodilator effect (Grummitt & Goat, 1984).

Fentanyl is highly fat- soluble and significantly bound (about 80%) to plasma proteins, and less than 10% is unionized at physiologic PH. Clearance of fentanyl is predominantly dependent on hepatic metabolism, although other sites of metabolism do exist (e.g. lung) (Hug, et al., 1981).

Its main advantages include absence of histamine release, reversal of its action by a narcotic antagonist and minimal effects on the cardiovascular system. Disadvantages include bradycardia, bronchoconstriction, miosis and muscle rigidity after large doses or during prolonged infusion which may interferes with ventilation of the patient (Scamman, 1983).

Alfentanil is a new fentanyl derivative. It is approximately 1/3 to 1/5 as potent as fentanyl, but has a faster onset and shorter duration of action than that of fentanyl. Alfentanil is less lipophilic than fentanyl and has a smaller volume of distribution at steady state (0.5 to 1.0 l/kg).