Adjuvant Drugs In Spinal And Epidural Analgesia

An Essay

Submitted for the partial fulfillment of

Master degree in anaesthesia

Presented By

Ahmed Fawzy Fawzy Arafa

M.B.B.CH

Faculty of Medecine – Cairo university

Supervised by

Prof. Dr. Ahmed Abd Al-kader Sheesh

Professor of anaesthesiology and Intensive care

Faculty of Medecine – Ain Shams university

Prof. Dr. Ashraf Mahmoud Hazem

professor of anaesthesiology and Intensive care

Faculty of Medecine – Ain Shams university

Dr. Mohamed Saleh Ahmed

Lecturer of anaesthesiology and Intensive care

Faculty of Medecine – Ain Shams university

2017

العقاقير المساعدة في السد الشوكي و ما فوق الأم الجافية

رسالة تمهيدية

توطئة للحصول علي درجة الماجستير في التخدير

مقدمة من

الطبيب / أحمد فوزي فوزي عرفة

بكالوريوس الطب و الجراحة

كلية الطب - جامعة القاهرة

تحت اشراف

ا.د أحمد عبد القادر شيش

استاذ التخدير و الرعاية المركزة

كلية الطب – جامعة عين شمس

ا.د أشرف محمود حازو

استاذ التخدير و الرعاية المركزة

كلية الطب – جامعة عين شمس

د. محمد صالح أحمد

مدرس التخدير و الرعاية المركزة

كلية الطب – جامعة عين شمس

Table of Contents

List of Figure

List of Tables

List of Abbreviations

Abbrev	
AAG	Alpha-1-acidic glycoprotein
ASA	American Society of Anesthesiologists
CNS	Central nervous system
COMT	Catechol-O-methyltransferase
COX	Cyclooxygenase
CSF	Cerebrospinal fluid
LA	Local anesthetics
MAO	Monoamine oxidase
MRI	Magnetic resonance imaging
NMDA	N-methyl-d-aspartate
NMDA	N-methyl D-Aspartate
NRM	Nucleus raphe magnus
NRPG	Nucleus reticularisparagigantocellularis
PAG	Periaqueductal grey
PCEA	Patient controlled epidural analgesic
VGSCs	Voltage-gated sodium channels

Introduction

Central Neuraxial Block occupies an important part in anaesthesia and pain management. Local anaesthetic agents block the generation and propagation of action potential in all excitable tissues primarily by impairing the function on sodium channels in the axonal membrane, the complex neurophysiology of dorsal horn involves many neurotransmitters, these substances include substance P, Serotonin, Acetylcholine, Adenosine and Glutamate are related in the dorsal horn and modulate peripheral nociceptive input ***(Borgeat and Aguirre, 2010)***.

A wide variety of adjuvant agents are used along with local anaesthetic mixtures to enhance and prolong the reaction, reduce unwanted motor weakness and autonomic dysfunction and reduce central nervous system and cardiovascular toxicity, the adjuvant drugs interacts with one or more of these neurotransmitters exerting an anti-nociceptive effect ***(Elvir-Lazo and White, 2010)***.

Adjuvant drugs are pharmacological agents possessing little pharmacological effect by themselves, but enhance or potentiate the action of other drugs when given at the same time.

Neuraxial drug administration describes the technique of delivering analgesics and other drugs in close proximity to the spinal cord i.e. intrathecally into cerebrospinal fluid (CSF) or epidurally into the epidural space ***(Hindle, 2008)***.

Drugs deposited into CSF or epidural space traverses different meningeal layers to gain access to receptors located in the spinal cord gray matter. Drugs absorbed by the systemic circulation also reach the central nervous system (CNS) to produce its effects ***(Stein and Lang, 2009)***.

The most widely used drugs are opioids agonist like morphine, Fentanyl, alpha 2 adrenergic agonist like clonidine, epinephrine, anti-cholinergic agents like neostigmine, NMDA receptor antagonist like ketamine and magnesium sulphate ***(Förster and Rosenberg, 2003)***.

Knowledge and use of adjuvant drug therapy has rendered neuraxial analgesia more effective in the management of both acute and chronic pain conditions, whatever the agent used, it should be preservative free, non-toxic to neurons and should not contain any inhibitory neurotransmittors ***(Gunter, 2002)***.

Aim of the Assay

In the current study, we will mainly discuss the adjuvant drugs used in spinal and epidural anaesthesia and their importance in central neuraxial techniques.

Central NeuraxialAnaesthesia

Local anesthetics (LA) are indispensable in contemporary regional anesthesia and pain management. Introduced in Western medicine in the late 19th century, the prototype substance cocaine had been widely used by South American cultures for thousands of years. However, these tribes were used to chewing coca leaves, which dried out during shipping to Europe, such that the real breakthrough of cocaine was made possible only by the isolation of cocaine in 1859***(Goerig et al., 2012)***.

Cocaine was used in oral form for various psychiatric diseases and fatigue by, among others, Sigmund Freud. However, it was his colleague, Carl Koller, who is widely credited for the first experimental topical application of cocaine***(Markel, 2011)***. Koller was ophthalmologist at the Vienna General Hospital, and had been looking for ways to alleviate the pain of cataract surgery***(Goerig et al., 2012)***.

The discovery of the topical numbing properties of cocaine led to the development of regional anesthesia in its modern form, with the basic principle that injection of cocaine next to nerves produces a transient and reversible interruption of pain propagation, sensory and motor function. Over the following decades, many types of nerve block and neuraxial (epidural and spinal) anesthesia and analgesia were introduced. However, insufficient materials and medications with a narrow therapeutic

range hampered widespread acceptance. For example, the first published administration of continuous epidural anesthesia in 1949 was achieved by an urethral catheter introduced into the epidural space***(Mulroy, 2014)***.

Another anecdote is the first performance, in 1889, of spinal anesthesia by Bier, which was successful from a pharmacological point of view, but the large needle used led to days of severe postdural-puncture headache. The introduction of the first short-acting amide-type local anesthetic, lidocaine, in 1947, and the standard long-acting amide-type local anesthetic, bupivacaine, were pharmacological milestones in regional anesthesia. In parallel, improved needle and catheter equipment meant that regional anesthesia could be applied in a more reliable and safe manner. In the 1990s, ultrasound-guided regional anesthesia was coined by a group of physicians in the in the Vienna General Hospital, the very workplace where hundred years earlier Carl Koller had made his ground-breaking discovery. Stephan Kapral and Peter Marhofer described theguidance of the regional anesthesia needle by ultrasound, sparking renewed interestin regional anesthesia techniques***(Kapral et al., 1994)***.

Epidemiological studies suggest that after neuraxial (spinal, epidural) anesthesia, neurological complications such as transient radicular irritation (back pain with radiation down one or both buttocks or legs occurring within 24 h after surgery ***(Lirk et al.,***

2008)) may follow up to 30 % of spinal anesthetics, and devastating complications such as cauda equina syndrome (severe low back pain, lower extremity motor weakness and sensory loss, bladder dysfunction, bowel incontinence) affect roughly 1:8000 patients ***(Auroy et al., 2002)***. This is in accordance with a recent retrospective analysis of more than 100.000 neuraxial anesthetics, in which the incidence of presumed neurological complication was 1:1000, but when imaging techniques were used to validate these assumptions, the incidence was 0.07:1000 (with a 95% confidence interval of 0.02 – 0.13/1000) ***(Pumberger et al., 2013)***.

I. Anatomical Considerations

Recent investigations into the anatomy of the spinal canal have uncovered new insights into the anatomy pertinent to neuraxial anesthesia***(Hogan and Toth, 1999)***. The information garnered by new methods such as cryomicrotome sectioning, epiduroscopy and magnetic resonance imaging (MRI) reveals more about the mechanism of neuraxial blockade and enables the development of new techniques. With regard to the CSE techniques at thoracic level, it is relevant to consider the margins that are available to the clinician administering the spinal bolus. To this end, the anatomy of the spinal cord and surrounding tissues is revisited.

When performing a spinal anesthetic using the midline approach, the layers of anatomy that are traversed (from posterior

to anterior) are skin, subcutaneous fat, supraspinous ligament, interspinous ligament, ligamentum flavum, dura mater, subdural space, arachnoid mater, and finally the subarachnoid space. When the paramedian technique is applied, the spinal needle should traverse the skin, subcutaneous fat, ligamentum flavum, dura mater, subdural space, arachnoid mater, and then pass into the subarachnoid space.

The length of the spinal cord varies according to age. In the first trimester, the spinal cord extends to the end of the spinal column, but as the fetus ages, the vertebral column lengthens more than the spinal cord. At birth, the spinal cord ends at approximately L3 and in the adult, the cord ends at approximately L1 with 30% of people having a cord that ends at T12 and 10% at L3. The position of the conus medullaris, cauda equina, termination of the dural sac, and filum terminale are shown. A sacral spinal cord in an adult has been reported, though this is extremely rare***(Reiman and Anson, 1944)***. The length of the spinal cord must always be kept in mind when a neuraxial anesthetic is performed, as injection into the cord can cause great damage and result in paralysis***(Bromage, 1997)***.

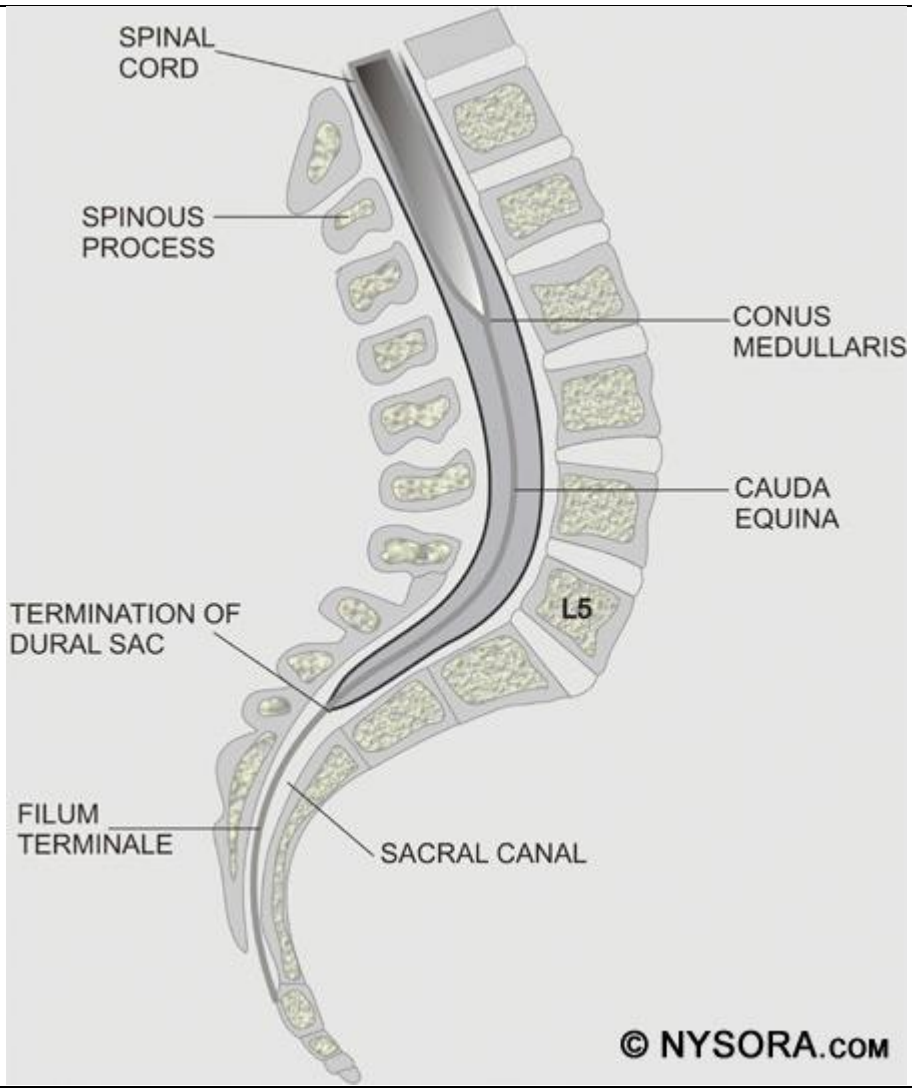

Figure 1: A cross section of the lumbar vertebrae and spinal cord.

Spinal nerves in thTe cervical region are named according to the upper cervical vertebral body from which they exit. However, the eighth cervical nerve exits from below the seventh cervical vertebral body, and this method of naming continues in the thoracic and lumbar regions. The spinal nerve roots and spinal cord serve as the target sites for spinal anesthesia.

A. Boundaries and contents of the epidural space:

The posterior longitudinal ligament binds the epidural space anteriorly. The ligamenta flava and the periosteum of the lamina encompass the space posteriorly, whilst the periosteum of the pedicles and the intervertebral foramina encompass it laterally***(Elizaga, 1998)***.

Figure 2: Medial sagittal preparation of a part of the human thoracic spinal canal, with dura held slightly away from the spinal cord

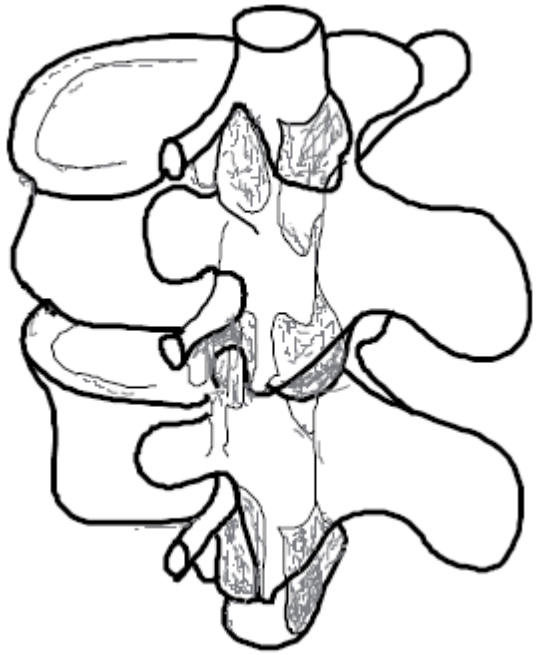

Figure 3: A drawing of the compartments of the lumbar epidural space (stippled).

B. Posterior epidural space:

The posterior epidural space is enclosed by two steeply arched ligamenta flava that may not completely merge at the midline. The ligaments extend laterally as far as the articular facets, and their thickness increases with distance down the column. Claims of a midline fibrous septum to the homogenous low viscosity fat of the posterior epidural space are not necessarily confirmed by cryomicrotome or histological examinations. In fact, the epidural fat is unique in the body in having no fibrous content***(Hogan, 1998)***.

Traditional techniques have shown that the anterior-posterior depth of the posterior epidural space varies with the vertebral level, ranging from 1–1.5 mm at C5, to 2.5–3 mm at T6, to its widest point of 5–6 mm at the L2 level***(Reina et al., 2006)***. When