A PROSPECTIVE EVALUTION OF DIFFERENT KETOFOL CONCENTRATIONS FOR SEDATION AND ANALGESIA IN OPHTHALMIC PROCEDURES PERFORMED UNDER LOCAL ANESTHESIA

Thesis

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By

Sara Rezk Mahmoud Rezk

M.B.B.Ch, M.Sc. Anesthesiology

Supervised by

Prof. Dr. Mohamed Amr Mattar,M.D.

Professor of Anesthesiology

Cairo University

Prof. Dr. Maher Fawzy, M.D.

Professor of Anesthesiology

Cairo University

Assistant Prof .Dr.Mona Raafat Fahim, M.D.

Assistant Professor of Anesthesiology

Research Institute of ophthalmology (RIO)

Dr. Ahmed Zaghloul Fouad,M.D.

Lecturer of Anesthesiology

Cairo University

Faculty of medicine

Cairo University

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Abstract

This current study suggests that Ketofol (ketamine/Propofol) concentration at ratios 3:1 and 4:1 may provide effective and safe sedation for patients undergoing ophthalmic procedures under regional anesthesia. An intravenous infusion of a 4:1 ratio is a suitable alternative for delivering Ketofol; this provides more stability and consistency of sedation depth and less need for top-up doses that may lead to overshoot of sedation and a delayed recovery The ratio for the infusion regimen, however, seems best at 4:1 because the overall dose of both drugs required to achieve the same clinical end points is less with a constant infusion, so the ketamine component, which is responsible for the much longer recovery time, can be reduced and a consistent depth of sedation is achieved.

Keywords(Ketofo ,SADATION, OPHTHALMIC PROCDURES, ANALGESIA)

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Abbreviations

- **ASA**: American society of anesthesiology.
- **BIS**: Bispectral index.
- **CNS:** Central nervous system.
- **$CMRO_2$**: Cerebral metabolic rate of oxygen.
- **CPP**: Cerebral perfusion pressure.
- **CRPS:** Complex Regional Pain Syndrome.
- **EEG**: Electro-encephalogram.
- **FDA**: Food and drug administration.
- **GANA**: General anesthesia no airway.
- **GABA**: ɤ-amino butyric acid.
- **HR**: Heart rate.
- **ICU**: Intensive care unit.
- **ICP**: Intra cranial pressure**.**
- **IOP:** Intra-ocular pressure**.**
- **IL :** Interleukin.
- **LOC:** Loss of consciousness.
- **MAC:** Monitored anesthesia care**.**
- **MAP:** Mean arterial pressure**.**
- **MOAA/S:** Modified Observer's Assessment of Alertness/Sedation scale.
- **NMDA:** N-methyle d- aspartate**.**

- **NF-kB :** Nuclear factor-kB
- **OCR:** Oculo-cardiac reflex.
- **PACU:** Postanesthesia care unit.
- **PONV**: post operative nusea and vomiting**.**
- **RR:** Respiratory rate.
- **RSS:** Ramsy sedation score**.**
- **TCI:** Target-controlled infusion.
- **USA:** united States of America**.**
- **VD**: Volume of distribution.

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INTRODUCTION

Cataract surgery is the commonest ophthalmic surgical procedure and a local anaesthetic technique is usually preferred. Patient comfort, safety and low complication rates are the essentials of local anaesthesia. The anaesthetic requirements for ophthalmic surgery are dictated by the nature of the proposed surgery, the surgeon's preference and the patient's wishes. The provision of ophthalmic regional anaesthesia for cataract surgery varies worldwide. These may be chosen to eliminate eye movement or not and both non-akinetic and akinetic methods are widely used. [1-2]

Some drawbacks are linked with regional anaesthesia techniques: pain at the puncture site, fear of needles, and recall of the procedure. These factors stress the importance of sedation that offers analgesia, anxiolysis, and amnesia. Sedation has been shown to increase patient satisfaction during regional anaesthesia and may be considered as a means to increase the patient's acceptance of regional anaesthetic techniques. [3]

A multitude of sedative and analgesic agents are frequently used. Titration of anesthetic doses should be done cautiously and the patients should be continuously monitored. So far, an ideal intravenous anesthetic agent doesn't exist. [4] Ketofol is the combination of ketamine and Propofol in various concentrations and it has several ideal properties. It commonly used for several procedural sedation. Ketamine, a neuroleptic anesthetic agent, works on thalamocortical and limbic N-methyl-D-aspartate (NMDA) receptors.[5] Ketamine stimulates the cardiorespiratory system. A direct effect increases cardiac output, arterial blood pressure, heart rate and central venous pressures. Therefore, it is a valuable agent for hypotensive or

hypovolemic patients, but a less desirable agent in patients with ischemic heart disease or raised pulmonary vascular pressure. ketamine induces psychomimetic activity and emergence reactions in up to 30% of patients. In contrast, propofol, a sedative, hypnotic and anesthetic agent, is also an antagonist at N-methyl-D-aspartate receptors.[4] However, propofol has a narrow therapeutic range and risks of cardiovascular depression.[5] Combining these two agents; preserve sedation efficacy while minimizing their adverse effects, thus theoretically balance each other out when used together.

AIM OF WORK

A number of studies have demonstrated that the combination of ketamine and propofol (Ketofol) for sedation is safe and effective in different concentration. We compare the safety and efficacy of 4 concentrations of ketofol; group I ketofol in 1:1 ratio, group II 2:1, group III 3:1 and group IV ketofol in 4:1 ratio, given in bolus dose before the needle-based eye block and infusion although the operation.

We aimed to answer the following questions about ketofol use for ophthalmic surgery under local anesthesia; what is the optimal mixture ratio? What is the best dosing-regimen? And if a continuous infusion is appropriate?

ANATOMY

As with all anesthetic techniques, thorough knowledge of the anatomy is essential. Anatomy of the eye and its nerve supply is necessary for the safe practice of ophthalmic regional anesthesia.[6]

The anatomical features of the orbit permit the passage of needles into fibre-adipose compartments in the mid orbit avoiding close contact with the globe,major blood vessels, extraocular muscles and the lacrimal apparatus. [7]

The bony orbit

The orbit is an irregular four-sided pyramid with its apex pointing posteromedially and its base facing anteriorly. Seven bones conjoin to form the orbital structure; frontal, zygomatic, maxillary, ethmoidal, sphenoid, lacrimal and palatine bones.[8]

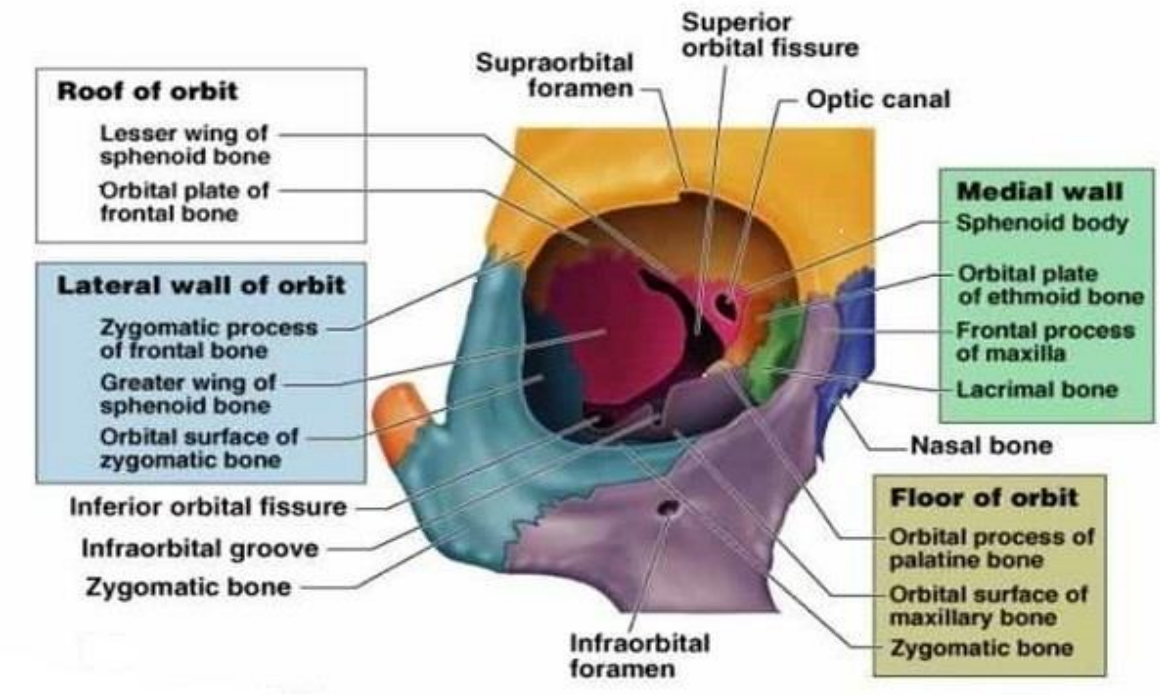

Figure 1: Anatomy of the bony orbit [9]

The apex lies near the medial end of superior orbital fissure and contains the optic canal, which communicates with middle cranial fossa. The_roof (superior wall) is formed by the orbital plate of the frontal bone and the lesser wing of sphenoid. The orbital surface presents medially by trochlear fovea and laterally by lacrimal fossa. [The optic foramen, which contains the optic nerve and the large ophthalmic artery, is at the apex. [8]

The floor (inferior wall) is formed by the orbital surface of maxilla, the orbital surface of zygomatic bone and the orbital process of palatine bone. Medially near the orbital margin is located the groove for naso-lacrimal duct. The medial wall is formed by the frontal process of maxilla, lacrimal bone, orbital plate of ethmoid and a small part of the body of the sphenoid.[The Lateral wall is formed by the orbital process of zygomatic and the orbital plate of greater wing of sphenoid. The bones meet at the zygomatico-sphenoid suture. The lateral wall is the thickest wall of the orbit.[7]

The annulus of Zinn, a fibrous ring arising from the superior orbital fissure, forms the apex. The base is formed by the surface of the cornea, the conjunctiva and the lids. Globe movements are controlled by the rectus muscles (inferior, lateral, medial and superior) and the oblique muscles (superior and inferior). The rectus muscles arise from the annulus of Zinn near the apex of the orbit and insert anterior to the equator of the globe, forming an incomplete cone. [7]

The volume of the adult orbit is 30 ml^3; whereas that of an average sized globe is 6.5 ml^3. The typical dimensions at the rim are 35 mm vertically and 40 mm horizontally. The depth of the orbit from the inferior orbital rim to the optic foramen ranges from 42 to 54 mm. The lateral orbital rim (Fig. 2) is set back 12 to 18 mm behind the cornea, allowing exposure of the globe to its equator.[11]

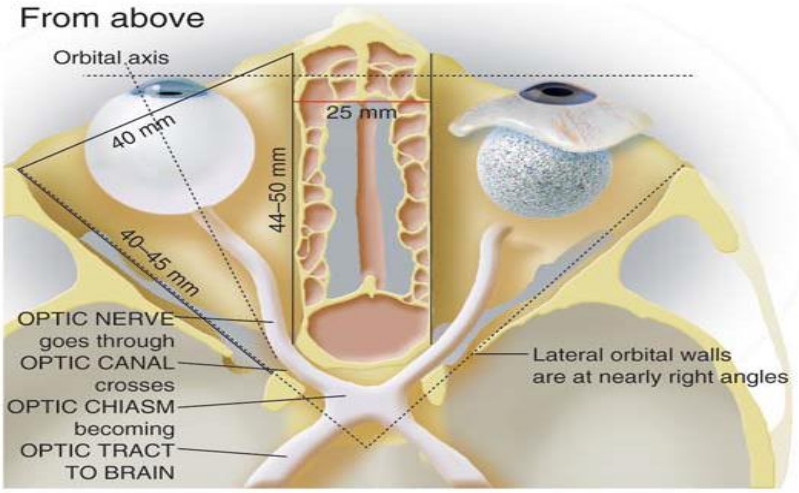

Figure 2: Orientation of the orbital walls, and normal globe position [3]

The Orbital Septum

A thin sheet of connective tissue called the orbital septum encircles the orbit as an extension of the periosteum of the roof and the floor of the orbit. It also attaches to the anterior surface of the levator muscle. Posterior to the orbital septum is the orbital fat. In both the upper and lower eyelids, the orbital septum attaches to the apponeurosis. The orbital septum thus provides a barrier to anterior or posterior extravasation of blood or the spread of inflammation.[12]

Extraocular muscles

Each orbit contains 6 extraocular muscles that function together to move the eye: 4 recti muscles (superior, inferior, lateral, medial) and 2 oblique muscles (superior, inferior). The levator palpebrae muscle elevates the upper lid Traditionally, the four recti muscles, along with connective tissue septa, were believed to create a defined compartment known as the orbital cone. This so-called cone extends from the rectus muscle origins around the optic foramen at the apex of the orbit to the attachment of the muscles to the globe anteriorly.[7] Within the annulus and the *muscle cone* lie the optic nerve (II), the oculomotor nerves (III containing both superior and inferior branches), the abducent nerve (VI nerve), the nasociliary nerve (a branch of V nerve), the ciliary ganglion and vessels. .[10]

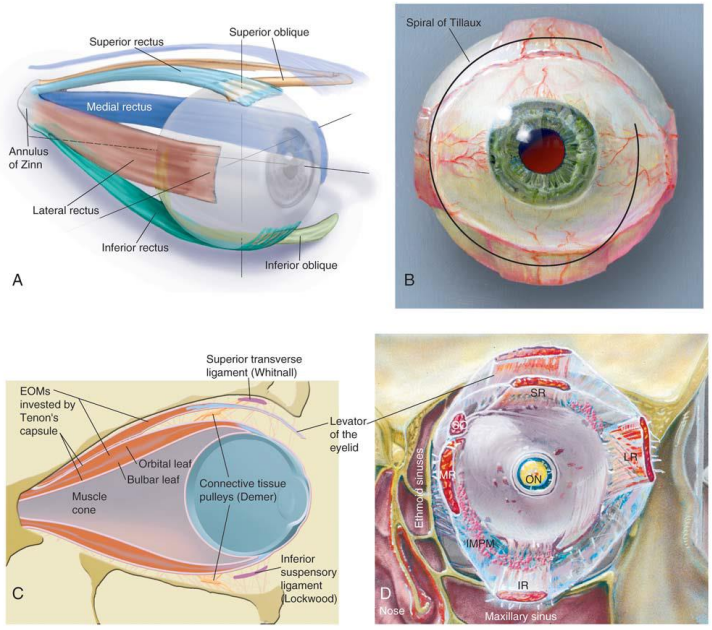

Figure 3: Extraocular muscles (EOMs). **A.** EOMS of the right eye viewed from antero-lateral, color coded by their cranial nerve innervation. **B.** Posterior Tenon's capsule around and between the EOMs. **C.** Tenon's capsule and the muscle cone. **D.** Posterior view of muscle cone; Tenon's capsule continues posteriorly adherent to the globe to eventually encircle the optic nerve. [10]