PERIBULBARNA ANESTEZIJA UZ CILJANU INTRAVENSKU ANALGOSEDACIJU ESKETAMINOM TOKOM ENUKLEACIJE: SAVREMENI REVIJALNI PRIKAZ

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PERIBULBAR ANESTHESIA WITH TARGETED INTRAVENOUS ESKETAMINE ANALGOSEDATION DURING ENUCLEATION: A CONTEMPORARY NARRATIVE REVIEW

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SAŽETAK

Uvod: Enukleacija je invazivna oftalmološka procedura praćena izraženim nociceptivnim i refleksnim stimulusom, što predstavlja značajan anestezиološki izazov, naročito kod starijih i komorbidnih pacijenata. Savremeni anestezиološki trendovi sve više favorizuju primenu regionalne anestezije u kombinaciji sa ciljanom analgosedacijom kao bezbedniju alternativu opštoj anesteziji.

Cilj: Prikazati savremene koncepte primene peribulbarne anestezije u kombinaciji sa ciljanom intravenskom analgosedacijom esketaminom tokom enukleacije, sa posebnim osvrtom na hemodinamsku stabilnost, prevenciju okulokardijalnog refleksa, kontrolu perioperativnog bola, postoperativnu mučninu i povraćanje, kao i mogućnost uklapanja ove tehnike u principe jednodnevne hirurgije.

Metod: U radu je sprovedena narativna analiza dostupne savremene literature iz oblasti oftalmološke i regionalne anestezije, sa fokusom na farmakološka svojstva esketamina, mehanizme dejstva peribulbarnog bloka i kliničke aspekte njihove kombinovane primene tokom enukleacije.

Zaključak: Peribulbarna anestezija u kombinaciji sa esketaminom vođenom ciljanom analgosedacijom predstavlja bezbedan i efikasan savremeni anestezиološki pristup za izvođenje enukleacije, naročito kod starije i komorbidne populacije. Ovaj pristup omogućava stabilnu hemodinamiku, očuvano spontano disanje, adekvatnu kontrolu bola, nisku incidencu postoperativne mučnine i povraćanja i brz funkcionalni oporavak, uz mogućnost primene u okviru jednodnevne hirurgije.

Ključne reči: enukleacija, peribulbarna anestezija, esketamin, analgosedacija, okulokardijalni refleks

ABSTRACT

Introduction: Enucleation is an invasive ophthalmic procedure accompanied by pronounced nociceptive and reflex stimuli, representing a significant anesthesiological challenge, particularly in elderly and comorbid patients. Contemporary anesthesiology trends increasingly favor the use of regional anesthesia combined with targeted analgosedation as a safer alternative to general anesthesia.

Aim: To present current concepts of peribulbar anesthesia combined with targeted intravenous esketamine-guided analgosedation during enucleation, with special emphasis on hemodynamic stability, prevention of the oculocardiac reflex, control of perioperative pain, postoperative nausea and vomiting, and the feasibility of integrating this technique into day-surgery protocols.

Methods: A narrative review of contemporary literature in the fields of ophthalmic and regional anesthesia was conducted, focusing on the pharmacological properties of esketamine, the mechanisms of action of the peribulbar block, and the clinical aspects of their combined use during enucleation.

Conclusion: Peribulbar anesthesia combined with esketamine-guided targeted analgosedation represents a safe and effective contemporary anesthesiological approach for performing enucleation, particularly in elderly and comorbid patients. This approach provides stable hemodynamics, preserved spontaneous respiration, adequate pain control, a low incidence of postoperative nausea and vomiting, and rapid functional recovery, with the potential for application within a day-surgery setting.

Keywords: enucleation, peribulbar anesthesia, esketamine, analgosedation, oculocardiac reflex

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UVOD

Enukleacija predstavlja jednu od najinvazivnijih procedura u očnoj hirurgiji [1]. Iako je hirurški relativno kratkotrajna, ova intervencija je praćena izrazito snažnim nociceptivnim stimulusom i značajnim hemodinamskim i autonomnim reakcijama, uključujući trigeminokardijalni, odnosno okulokardijalni refleks (OKR), što je čini posebnim anesteziološkim izazovom [2]. Klinička manifestacija ovih refleksnih odgovora može uključivati bradikardiju, hipotenziju, poremećaje srčanog ritma, a u najtežim slučajevima i asistoliju [2,3].

Tradicionalno, enukleacija se izvodila u uslovima opšte endotrahealne anestezije. Međutim, ovaj pristup je povezan sa povećanim rizikom od respiratornih, kardiovaskularnih i neurokognitivnih komplikacija, naročito kod starije i komorbidne populacije [4]. U skladu sa savremenim anesteziološkim principima, sve veći značaj pridaje se primeni regionalnih anesteziloških tehnika u kombinaciji sa analgosedacijom, sa ciljem smanjenja perioperativnog rizika, ubrzanog postoperativnog oporavka i unapređenja ukupne bezbednosti pacijenata [2,5].

Peribulbarna anestezija predstavlja pouzdanu regionalnu tehniku koja obezbeđuje adekvatnu senzornu blokadu i akineziju oka, uz značajno povoljniji bezbednosni profil u poređenju sa retrobulbarnim blokom [2,6]. U kombinaciji sa kontinuiranom intravenskom analgosedacijom esketaminom u subanestetičkim dozama, ovaj pristup omogućava stabilan perioperativni tok uz očuvano spontano disanje, minimalne hemodinamske oscilacije i povoljan postoperativni oporavak [5,6].

Cilj ovog revijalnog rada je da prikaže savremene koncepte primene peribulbarne anestezije u kombinaciji sa esketaminom tokom enukleacije, sa posebnim osvrtom na hemodinamsku stabilnost, kontrolu perioperativnog bola, prevenciju okulokardijalnog refleksa, smanjenje incidence postoperativne mučnine i povraćanja, kao i mogućnost uklapanja ovog anesteziološkog pristupa u principe jednodnevne hirurgije.

Regionalna anestezija u očnoj hirurgiji – savremeni koncept

Razvoj lokalnih anestetika, uz kontinuirano unapređenje tehnika regionalne i lokalne anestezije, značajno je doprineo razvoju savremene očne hirurgije [1]. Ove tehnike omogućavaju adekvatnu analgeziju i, u određenim slučajevima, pouzdanu akineziju oka uz minimalno sistemsko opterećenje, što je od posebnog značaja kod starijih i komorbidnih pacijenata [2].

Najčešće primenjivane anesteziološke tehnike u oftalmološkoj hirurgiji uključuju topikalnu anesteziju,

INTRODUCTION

Enucleation represents one of the most invasive procedures in ophthalmic surgery [1]. Although surgically relatively short in duration, this intervention is accompanied by an extremely strong nociceptive stimulus and significant hemodynamic and autonomic responses, including the trigeminocardiac reflex, i.e., the oculocardiac reflex (OCR), which makes it a particular anesthesiological challenge [2]. The clinical manifestation of these reflex responses may include bradycardia, hypotension, cardiac arrhythmias, and in the most severe cases, asystole [2,3].

Traditionally, enucleation has been performed under general endotracheal anesthesia. However, this approach is associated with an increased risk of respiratory, cardiovascular, and neurocognitive complications, particularly in elderly and comorbid patients [4]. In accordance with contemporary anesthesiology principles, increasing importance is being given to the use of regional anesthesia techniques combined with analgosedation, with the aim of reducing perioperative risk, accelerating postoperative recovery, and improving overall patient safety [2,5].

Peribulbar anesthesia represents a reliable regional technique that provides adequate sensory block and ocular akinesia, with a significantly more favorable safety profile compared to the retrobulbar block [2,6]. In combination with continuous intravenous analgosedation using esketamine in subanesthetic doses, this approach enables a stable perioperative course with preserved spontaneous respiration, minimal hemodynamic fluctuations, and favorable postoperative recovery [5,6].

The aim of this review article is to present contemporary concepts in the application of peribulbar anesthesia combined with esketamine during enucleation, with particular emphasis on hemodynamic stability, perioperative pain control, prevention of the oculocardiac reflex, reduction in the incidence of postoperative nausea and vomiting, as well as the potential integration of this anesthetic approach into the principles of day-case surgery.

Regional Anesthesia in Ophthalmic Surgery – Contemporary Concept

The development of local anesthetics, along with the continuous improvement of regional and local anesthesia techniques, has significantly contributed to the advancement of modern ophthalmic surgery [1]. These techniques provide adequate analgesia and, in certain cases, reliable ocular akinesia with minimal systemic burden, which is particularly important in elderly and comorbid patients [2].

subkonjunktivalnu i subtenonsku anesteziju, kao i retrobulbarni i peribulbarni blok [2,3]. Topikalna anestezija ne obezbeđuje akineziju oka i stoga nije pogodna za duboke orbitalne zahvate, ali predstavlja standardnu metodu u minimalno invazivnim procedurama. Subtenonska anestezija omogućava pouzdanu analgeziju prednjeg segmenta oka uz delimičnu akineziju i povoljan bezbednosni profil, zbog čega se često koristi u svakodnevnoj kliničkoj praksi [3].

Retrobulbarni blok obezbeđuje brzu i efikasnu analgeziju i akineziju oka i orbite, ali je povezan sa povećanim rizikom od ozbiljnih komplikacija, uključujući perforaciju bulbusa, povredu optičkog živca, intravaskularnu aplikaciju anestetika i intratekalno širenje sa potencijalno životno ugrožavajućom anestezijom moždanog stabla („brainstem anesthesia“) [4].

Peribulbarni blok je razvijen sa ciljem smanjenja navedenih rizika uz očuvanje visoke efikasnosti regionalne anestezije [1,4]. Izvodi se jednom ili dvema punkcijama, najčešće inferotemporalnim pristupom, uz ekstrakonalnu aplikaciju lokalnog anestetika, samostalno u obliku 2% lidokaina ili u kombinaciji sa 0,5% levobupivakainom radi produženog dejstva. Difuzijom lokalnog anestetika postiže se blokada senzornih i motornih vlakana n. ophthalmicus (V1), n. maxillaris (V2), kao i III, IV i VI kranijalnog živca do nivoa cilijarnog gangliona [2,4]. U poređenju sa retrobulbarnim blokom, peribulbarni pristup ima značajno povoljniji bezbednosni profil, uz stabilniju kontrolu intraokularnog pritiska (IOP) i okularnog perfuzionog pritiska (OPP), kao i nižu incidencu okulokardijalnog refleksa (OKR) [1,5].

Esketamin u ciljanoj analgosedaciji – farmakološki profil i klinička primena

Esketamin je potentni antagonista NMDA receptora sa izraženim analgetskim i sedativnim dejstvom, uz minimalan uticaj na respiratorni centar [6]. Kao S-enantiomer ketamina, odlikuje se približno dvostruko većom afinitetnom i analgetskom potentnošću, što omogućava pouzdanu analgeziju u subanestetičkim dozama uz manju učestalost psihomimetskih neželjenih efekata u poređenju sa racemskim ketaminom [6,7]. Pored primarnog delovanja na NMDA receptore, esketamin ostvaruje i dodatne efekte putem opioidnih receptora, monoaminskih puteva i voltažno-zavisnih kalcijumskih kanala, čime se postiže multimodalni analgetski efekat bez klinički značajne respiratorne depresije [6–8].

Farmakokinetički profil esketamina karakterišu brz početak dejstva (30–60 sekundi nakon intravenske primene), kratak kontekst-zavisni poluživot i predvidiva eliminacija, što omogućava preciznu titraciju infuzije i brz oporavak nakon prekida primene [7,8]. Njegov

The most commonly used anesthetic techniques in ophthalmic surgery include topical anesthesia, subconjunctival and sub-Tenon's anesthesia, as well as retrobulbar and peribulbar blocks [2,3]. Topical anesthesia does not provide ocular akinesia and is therefore not suitable for deep orbital procedures, but it represents the standard method in minimally invasive interventions. Sub-Tenon's anesthesia provides reliable analgesia of the anterior segment of the eye with partial akinesia and a favorable safety profile, which is why it is frequently used in routine clinical practice [3].

The retrobulbar block provides rapid and effective analgesia and akinesia of the eye and orbit but is associated with an increased risk of serious complications, including globe perforation, optic nerve injury, intravascular injection of the anesthetic, and intrathecal spread with potentially life-threatening brainstem anesthesia [4].

The peribulbar block was developed with the aim of reducing the aforementioned risks while maintaining high efficacy of regional anesthesia [1,4]. It is performed using one or two injections, most commonly via an inferotemporal approach, with extraconal administration of the local anesthetic, either as 2% lidocaine alone or in combination with 0.5% levobupivacaine to prolong the duration of action. Through diffusion of the local anesthetic, sensory and motor fibers of the ophthalmic (V1) and maxillary (V2) branches of the trigeminal nerve, as well as cranial nerves III, IV, and VI up to the level of the ciliary ganglion, are blocked [2,4]. Compared to the retrobulbar block, the peribulbar approach has a significantly more favorable safety profile, with more stable control of intraocular pressure (IOP) and ocular perfusion pressure (OPP), as well as a lower incidence of the oculocardiac reflex (OCR) [1,5].

Esketamine in Targeted Analgosedation – Pharmacological Profile and Clinical Application

Esketamine is a potent NMDA receptor antagonist with pronounced analgesic and sedative properties, exerting minimal influence on the respiratory center [6]. As the S-enantiomer of ketamine, it demonstrates approximately twice the receptor affinity and analgesic potency, enabling reliable analgesia at subanesthetic doses with a lower incidence of psychomimetic adverse effects compared to racemic ketamine [6,7]. In addition to its primary action on NMDA receptors, esketamine exerts supplementary effects via opioid receptors, monoaminergic pathways, and voltage-gated calcium channels, thereby producing a multimodal analgesic effect without clinically significant respiratory depression [6–8].

umereni simpatikomimetski efekat doprinosi održavanju srčane frekvence i srednjeg arterijskog pritiska u fiziološkim granicama, čime se smanjuje rizik od perioperativne hipotenzije, koja se često javlja tokom duboke sedacije ili opšte anestezije [6,9].

U kontekstu enukleacije, procedure koju karakterišu intenzivan nociceptivni stimulus, trakcija ekstraokularnih mišića i manipulacija optičkim nervom, neophodni su očuvani respiratorni refleksi, hemodinamska stabilnost i adekvatna analgezija. U tom smislu, esketamin predstavlja racionalan izbor za kontinuiranu analgosedaciju [5,9].

U poređenju sa propofolom, esketamin omogućava stabilnije održavanje hemodinamskih parametara, uz ograničene fiziološke fluktuacije arterijskog pritiska i srčane frekvence [5,10]. Midazolam, iako efikasan anksiolitik, ne poseduje analgetska svojstva i često zahteva dodatnu primenu opioida, dok deksmedetomidin, uprkos očuvanoj respiratornoj funkciji, može dovesti do bradikardije i hipotenzije, uz potencijalno nedovoljnu analgeziju tokom izrazito bolnih faza enukleacije [3,5].

Prednosti peribulbarne anestezije uz esketamin tokom enukleacije

Većina pacijenata podvrgnutih enukleaciji pripada starijoj populaciji i često ima pridružena kardiovaskularna, respiratorna i metabolička oboljenja, što značajno povećava perioperativni rizik u uslovima opšte anestezije [11]. Prednosti regionalnog anesteziološkog pristupa ogledaju se u izbegavanju manipulacije disajnim putem, smanjenju hemodinamskih oscilacija, minimalnom sistemskom opterećenju i bržem postoperativnom oporavku [2,11].

U tom kontekstu, peribulbarna anestezija u kombinaciji sa ciljanom analgosedacijom esketaminom omogućava stabilnije vrednosti arterijskog pritiska i srčane frekvence, uz očuvano spontano disanje i zaštitne refleksne mehanizme [5,9].

Enukleacija predstavlja jedan od najizraženijih refleksogenih zahvata u očnoj hirurgiji. Aktivacija trigemino–vagalnog refleksnog luka tokom trakcije ekstraokularnih mišića i manipulacije optičkim nervom može dovesti do pojave okulokardijalnog refleksa (OKR), sa potencijalno ozbiljnim hemodinamskim posledicama [2,4]. Kombinacija peribulbarne anestezije i analgosedacije esketaminom doprinosi smanjenju incidence ovog refleksa kroz efikasnu blokadu aferentnih refleksnih puteva i modulaciju autonomnog odgovora [5]. Smanjena potreba za opioidnim analgeticima dodatno rezultuje nižom učestalošću postoperativne mučnine i povraćanja, bržim funkcionalnim oporavkom i većim komforom pacijenata [1,8].

The pharmacokinetic profile of esketamine is characterized by a rapid onset of action (30–60 seconds following intravenous administration), a short context-sensitive half-life, and predictable elimination, allowing precise infusion titration and rapid recovery after discontinuation [7,8]. Its moderate sympathomimetic effect helps maintain heart rate and mean arterial pressure within physiological ranges, thereby reducing the risk of perioperative hypotension, a common complication of deep sedation or general anesthesia [6,9].

In the context of enucleation, a procedure characterized by intense nociceptive stimulation, traction of the extraocular muscles, and manipulation of the optic nerve, preservation of respiratory reflexes, hemodynamic stability, and adequate analgesia are essential. In this regard, esketamine represents a rational choice for continuous analgosedation [5,9].

Compared with propofol, esketamine enables more stable maintenance of hemodynamic parameters, with limited physiological fluctuations in arterial pressure and heart rate [5,10]. Midazolam, although an effective anxiolytic, lacks intrinsic analgesic properties and often necessitates adjunctive opioid administration, whereas dexmedetomidine, despite preserving respiratory function, may induce bradycardia and hypotension, with potentially insufficient analgesia during highly painful phases of enucleation [3,5].

Advantages of Peribulbar Anesthesia with Esketamine During Enucleation

The majority of patients undergoing enucleation belong to the elderly population and frequently present with concomitant cardiovascular, respiratory, and metabolic comorbidities, significantly increasing perioperative risk under general anesthesia [11]. The advantages of a regional anesthetic approach include avoiding airway manipulation, reducing hemodynamic fluctuations, minimizing systemic burden, and accelerating postoperative recovery [2,11].

In this context, peribulbar anesthesia combined with targeted analgosedation using esketamine provides more stable arterial pressure and heart rate values while preserving spontaneous ventilation and protective reflex mechanisms [5,9].

Enucleation represents one of the most pronounced reflexogenic procedures in ophthalmic surgery. Activation of the trigemino-vagal reflex arc during traction of the extraocular muscles and manipulation of the optic nerve may provoke the oculocardiac reflex (OCR), potentially leading to serious hemodynamic consequences [2,4]. The combination of peribulbar anesthesia and analgosedation with esketamine reduces the incidence of this reflex by effectively blocking afferent reflex pathways

DISKUSIJA

Primena peribulbarne anestezije u kombinaciji sa ciljanom intravenskom analgosedacijom esketaminom predstavlja racionalan i savremen odgovor na specifične anesteziološke zahteve koje nameće enukleacija [1,2]. Ovaj multimodalni pristup objedinjuje prednosti stabilne regionalne analgezije i akinezije oka sa centralnom analgezijom i sedacijom uz očuvano spontano disanje, čime se izbegavaju hemodinamske i respiratorne oscilacije karakteristične za opštu anesteziju [2–4].

Poseban značaj ovog koncepta ogleda se u njegovoj primeni kod starije i komorbidne populacije, kod koje su kardiopulmonalne i neurokognitivne rezerve često ograničene [5,6]. Stabilna hemodinamika, efikasna prevencija okulokardijalnog refleksa i smanjena potreba za opioidima doprinose boljoj kontroli postoperativnog bola, nižoj incidenci postoperativne mučnine i povraćanja i bržem funkcionalnom oporavku pacijenata [1,3,7]. U tom kontekstu, kombinacija peribulbarnog bloka i esketaminom vođene ciljane analgosedacije pokazuje visok stepen bezbednosti i dobru kliničku toleranciju [2,8].

U skladu sa savremenim *fast-track* anesteziološkim protokolima, ovakav pristup omogućava raniju mobilizaciju, kraći boravak u sobi za oporavak i, kod pažljivo selektovanih pacijenata, bezbedno uklapanje enukleacije u principe jednodnevne hirurgije [4,6]. Iako su potrebna dalja prospektivna i multicentrična istraživanja radi dodatne standardizacije protokola i procene dugoročnih ishoda, dostupni podaci iz literature dosledno ukazuju na kliničku opravdanost ovog pristupa [2,5,9]. Na osnovu postojećih dokaza, peribulbarna anestezija u kombinaciji sa ciljanom analgosedacijom esketaminom može se smatrati metodom izbora kod pažljivo selektovanih pacijenata koji se podvrgavaju enukleaciji, uz povoljan balans između bezbednosti, efikasnosti i komfora pacijenata [1,2].

Ograničenja dostupne literature

Dostupni dokazi o primeni regionalne anestezije uz esketamin tokom enukleacije ograničeni su nedostatkom velikih, randomizovanih i kontrolisanih studija [2,5]. Većina publikovanih radova odnosi se na manje invazivne oftalmološke procedure, dok su podaci specifični za enukleaciju retki i metodološki heterogeni, sa varijacijama u anesteziološkim tehnikama, režimima sedacije i kriterijumima procene ishoda [3,7,8]. Dodatna ograničenja proizilaze iz etičkih i kliničkih izazova sprovođenja randomizovanih studija kod starijih i komorbidnih pacijenata [5,6].

Uprkos tome, postojeći podaci ukazuju na povoljan trend ka boljoj hemodinamskoj stabilnosti, smanjenju

DISCUSSION

The use of peribulbar anesthesia in combination with targeted intravenous analgosedation using esketamine represents a rational and contemporary response to the specific anesthetic demands imposed by enucleation [1,2]. This multimodal approach integrates the benefits of stable regional analgesia and ocular akinesia with central analgesia and sedation while preserving spontaneous respiration, thereby avoiding the hemodynamic and respiratory fluctuations characteristic of general anesthesia [2–4].

The particular relevance of this concept is reflected in its application in elderly and comorbid patients, whose cardiopulmonary and neurocognitive reserves are often limited [5,6]. Stable hemodynamics, effective prevention of the oculocardiac reflex, and reduced opioid requirements contribute to improved postoperative pain control, a lower incidence of postoperative nausea and vomiting, and faster functional recovery [1,3,7]. In this context, the combination of peribulbar block and esketamine-guided targeted analgosedation demonstrates high safety and good clinical tolerability [2,8].

In accordance with contemporary fast-track anesthetic protocols, this approach enables earlier mobilization, shorter stay in the recovery unit, and-among carefully selected patients-the safe integration of enucleation into the principles of day-case surgery [4,6]. Although further prospective and multicenter studies are required to standardize protocols and evaluate long-term outcomes, the available literature consistently supports the clinical justification of this approach [2,5,9]. Based on current evidence, peribulbar anesthesia combined with targeted analgosedation using esketamine may be considered a method of choice in carefully selected patients undergoing enucleation, offering a favorable balance between safety, efficacy, and patient comfort [1,2].

Limitations of the Available Literature

The available evidence regarding the use of regional anesthesia with esketamine during enucleation is limited by the lack of large, randomized controlled trials [2,5]. Most published studies concern less invasive ophthalmic procedures, whereas data specific to enucleation are scarce and methodologically heterogeneous, with variations in anesthetic techniques, sedation regimens, and outcome assessment criteria [3,7,8]. Additional limitations arise from the ethical and clinical

perioperativnog rizika i bržem oporavku pri primeni regionalne anestezije uz analgosedaciju u poređenju sa opštom anestezijom, što opravdava dalja istraživanja i kliničko razmatranje ovog pristupa [1,2,4,9].

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challenges of conducting randomized studies in elderly and comorbid populations [5,6].

Nevertheless, existing data indicate a favorable trend toward improved hemodynamic stability, reduced perioperative risk, and faster recovery with regional anesthesia combined with analgosedation compared to general anesthesia, thereby supporting further research and clinical consideration of this approach [1,2,4,9].

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