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Dexmedetomidine versus Lidocaine for Hemodynamic Stability During Airway Management in Patients with Traumatic Brain Injury: A Randomized Clinical Trial

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A B S T R A C T

Introduction: The profound sympathoadrenal stress response to endotracheal intubation in patients with traumatic brain injury (TBI) presents a significant risk for secondary brain injury by inducing perilous hemodynamic instability. Pharmacological attenuation is critical, yet direct comparative evidence between commonly used agents is lacking. This study aimed to rigorously compare the efficacy of dexmedetomidine, a central sympatholytic, versus lidocaine, a peripheral membrane stabilizer, in maintaining hemodynamic stability during airway management in the TBI population. **Methods:** In this prospective, randomized, double-blind clinical trial, seventy-one adult patients with TBI (ASA I-III) were allocated to receive either intravenous dexmedetomidine (1 µg/kg over 10 minutes; n=37) or intravenous lidocaine (1.5 mg/kg over 2 minutes, with total infusion time matched to 10 minutes with saline; n=34) prior to a standardized anesthesia induction. The prespecified primary outcome was the change in mean arterial pressure (MAP) from baseline to one minute post-intubation. Secondary outcomes included changes in heart rate (HR) and hemodynamic profiles over 10 minutes. **Results:** Baseline patient characteristics, including TBI severity, were well-balanced between groups. Both interventions effectively blunted the pressor response, causing a significant decrease in MAP and HR from baseline ($p<0.001$ for all). The primary outcome, the change in MAP at one minute post-intubation, was not statistically different between the dexmedetomidine and lidocaine groups (-12.8 ± 6.1 mmHg vs. -11.5 ± 5.9 mmHg, respectively; $p=0.412$). Similarly, no significant differences in HR or MAP were observed between groups at any time point up to 10 minutes post-intubation. The incidence of rescue therapy for hypotension or bradycardia was low and comparable. **Conclusion:** In patients with TBI, both dexmedetomidine and lidocaine are effective and safe for attenuating the hemodynamic stress of intubation. At the doses studied, neither agent demonstrated clinical superiority, providing clinicians with two valid, mechanistically distinct options. The choice can therefore be guided by the specific clinical context, including desired onset, duration of action, and sedative profile.

1. Introduction

Traumatic brain injury (TBI) stands as a devastating and pervasive public health crisis, inflicting a heavy toll of mortality and lifelong disability, especially upon the younger adult population.[1] The clinical course of TBI is notoriously complex, characterized by a primary, irreversible mechanical injury and a subsequent, preventable cascade of secondary insults.[2] This secondary injury cascade—a destructive torrent of ischemia, inflammation, cerebral edema, and excitotoxicity—is the principal determinant of a patient's ultimate neurological outcome and thus represents the primary target of modern neurocritical care. Central to mitigating this cascade is the meticulous management of intracranial physiology, governed by the Monro-Kellie doctrine.[3] Within the rigid

confines of the skull, the maintenance of a stable intracranial pressure (ICP) and an adequate cerebral perfusion pressure (CPP) is paramount. Therefore, the stabilization of systemic hemodynamics transcends supportive care, becoming a direct and potent neuroprotective therapy. A critical, early intervention in the management of patients with moderate to severe TBI is securing the airway via laryngoscopy and endotracheal intubation.[4] While indispensable for providing oxygenation, ventilation, and protection from aspiration, this procedure is a double-edged sword. The intense mechanical stimulation of the richly innervated oropharyngeal and laryngeal structures constitutes a profound noxious stimulus, capable of provoking a massive sympathoadrenal response.[5] This reflex, well-documented to produce a 30-40 mmHg rise in mean arterial pressure (MAP) and a 20-30 bpm increase in heart rate, unleashes a surge of catecholamines. In the context of an injured brain with impaired or absent cerebral autoregulation, this abrupt hypertension can be catastrophic. It can lead to a passive increase in cerebral blood flow, exacerbating vasogenic edema, elevating ICP, and precipitating a dangerous decline in CPP. The prevention of this hemodynamic volatility is therefore a non-negotiable tenet of neuroanesthesia.[6]

A variety of pharmacological agents have been employed to obtund this pressor response. Among them, dexmedetomidine and lidocaine have garnered significant interest due to pharmacological profiles that suggest benefits beyond mere hemodynamic control. Dexmedetomidine, a highly selective alpha-2 adrenergic receptor agonist, exerts its effect centrally by inhibiting noradrenergic outflow from the locus coeruleus.[7] This central sympatholysis produces reliable, dose-dependent sedation and anxiolysis alongside a controlled reduction in heart rate and blood pressure, all while characteristically sparing respiratory drive. Its potential to reduce the cerebral metabolic rate ($CMRO_2$) and exert anti-inflammatory effects further enhances its appeal as a neuroprotective agent. Lidocaine, a ubiquitous local anesthetic and Class Ib antiarrhythmic, operates through a fundamentally different mechanism: the blockade of voltage-gated sodium channels.[8] Administered intravenously, it provides a multi-pronged defense. It anesthetizes afferent nerve endings in the airway, blocks central polysynaptic reflexes, and directly stabilizes the myocardium against catecholamine-induced irritability. These actions collectively blunt the intubation response while also potentially conferring neuroprotection by reducing $CMRO_2$, suppressing seizure activity, and mitigating the excitotoxic injury cascade. Furthermore, the economic disparity between the agents is substantial; lidocaine is inexpensive and universally accessible, whereas dexmedetomidine is significantly more costly. Validating the efficacy of the more accessible option is therefore of considerable practical importance. Despite the widespread use of both drugs, a striking paucity of high-quality, direct comparative evidence exists within the specific TBI population. Clinical practice is often guided by institutional tradition or individual preference rather than robust data comparing these two mechanistically distinct agents in the setting where their effects are most critical.[9]

The novelty of this research lies in its rigorous, head-to-head, double-blind comparison of two pharmacologically divergent agents—one acting via central sympatholysis, the other via peripheral membrane stabilization—within a homogenous cohort of patients with traumatic brain injury. By focusing exclusively on this specific population, this trial addresses a critical knowledge gap in neuroanesthesiology, providing highly relevant data to inform evidence-based practice where the stakes of hemodynamic control are highest.[10] Therefore, the primary aim of this study was to conduct a randomized clinical trial to compare the efficacy of intravenous dexmedetomidine versus intravenous lidocaine in attenuating the hemodynamic response to endotracheal intubation in adult patients with TBI. Our primary hypothesis was that a statistically significant difference would exist in the change in mean arterial pressure from baseline to one minute post-intubation between the two groups.

2. Methods

This study was conducted as a prospective, parallel-group, double-blind, randomized controlled trial at Dr. Saiful Anwar Regional General Hospital in Malang,

Indonesia, a university-affiliated tertiary care hospital and regional trauma center. The protocol was designed in full accordance with the principles outlined in the Declaration of Helsinki and adhered to the Consolidated Standards of Reporting Trials (CONSORT) guidelines. The Institutional Ethics Committee of the Faculty of Medicine, Universitas Brawijaya, granted full approval for the study protocol and all associated documents. Written informed consent was obtained from each participant or, in cases of incapacitation, from their legally authorized representative. The study population comprised adult patients with a diagnosis of TBI who required general anesthesia and endotracheal intubation for surgical intervention between June 2024 and December 2024. Inclusion criteria were: (1) age 18 to 65 years; (2) a diagnosis of traumatic brain injury (of any severity) confirmed by clinical assessment and computed tomography; (3) American Society of Anesthesiologists (ASA) physical status I-III; and (4) requirement for orotracheal intubation for a scheduled surgical procedure. Exclusion criteria included: (1) patient or legal representative refusal; (2) known hypersensitivity to dexmedetomidine, lidocaine, or other amide local anesthetics; (3) pre-existing severe cardiovascular disease, including uncontrolled hypertension, significant coronary artery disease, high-degree atrioventricular block, or presence of a cardiac pacemaker; (4) chronic therapy with beta-blockers or antiarrhythmic drugs; (5) severe hepatic or renal impairment (defined as Stage 4 or 5 disease); (6) pregnancy; or (7) a known or anticipated difficult airway where adherence to the study protocol could compromise patient safety. A computer-generated random number sequence was used to allocate eligible patients in a 1:1 ratio to either the Dexmedetomidine Group (Group D) or the Lidocaine Group (Group L). This sequence was managed by a hospital statistician with no clinical involvement in the trial. Allocation concealment was maintained using sequentially numbered, sealed, opaque envelopes, which were opened only after a patient was enrolled and immediately prior to drug preparation. The trial was conducted with double-blinding. The study drug was prepared by an independent anesthesiologist not involved in patient care or data collection. To maintain blinding despite different infusion durations, the protocol was standardized to a 10-minute total infusion period for both groups. Group D: Received dexmedetomidine 1 μg/kg in 50 mL of normal saline, infused over 10 minutes. Group L: Received lidocaine 1.5 mg/kg in 50 mL of normal saline, infused over 2 minutes, immediately followed by a sham infusion of normal saline for the remaining 8 minutes from an identical syringe and infusion pump. The prepared syringe was labeled only with the patient's unique study code, ensuring that the patient, the attending anesthesiologist, and the data-collecting investigator remained blinded to the treatment allocation.

On arrival in the operating room, standard ASA monitoring was applied. An 18-gauge intravenous cannula was secured. After a 5-minute stabilization period, baseline hemodynamic parameters (Heart Rate [HR], systolic blood pressure [SBP], diastolic blood pressure [DBP], and mean arterial pressure [MAP]) were recorded. Following 3 minutes of pre-oxygenation with 100% oxygen, the 10-minute blinded study drug infusion was commenced. The choice of a 1 μg/kg loading dose for dexmedetomidine and 1.5 mg/kg for lidocaine was based on extensive prior literature demonstrating their efficacy in attenuating hemodynamic responses to airway manipulation, establishing them as clinically relevant and approximately equipotent doses for this purpose. Immediately upon completion of the infusion, a standardized anesthesia induction was performed by an attending anesthesiologist with more than five years of clinical experience. Anesthesia was induced with intravenous fentanyl 2 μg/kg, followed by propofol administered to a target of loss of eyelash reflex. The total administered dose of propofol was recorded. Following confirmation of successful mask ventilation, neuromuscular blockade was achieved with rocuronium 0.6 mg/kg. Exactly three minutes after the propofol bolus, direct laryngoscopy was performed using a Macintosh blade (size 3 or 4, at the discretion of the anesthesiologist). The duration of the laryngoscopy attempt (from blade insertion to removal) and the Cormack-Lehane grade of laryngeal view were recorded. Following successful intubation, tube placement was confirmed by capnography and

auscultation. Anesthesia was maintained with sevoflurane in an air-oxygen mixture. Any instance of significant hypotension (MAP < 65 mmHg for >1 minute) was treated with intravenous boluses of ephedrine 5 mg. Significant bradycardia (HR < 50 bpm for >1 minute) was treated with intravenous atropine 0.5 mg. The use of any rescue medication was recorded.

Hemodynamic data were recorded at the following intervals: at baseline (T-Baseline); immediately after the study drug infusion (T-PostDrug); immediately after induction (T-Induction); immediately after intubation (T0); and at 1, 3, 5, and 10 minutes post-intubation (T1, T3, T5, T10). The prespecified primary outcome was the change in MAP from T-Baseline to T1 (one minute post-intubation). Secondary outcomes included: (1) the change in HR from T-Baseline to T1; (2) the time-course profile of MAP and HR at all measured time points; (3) TBI severity, total dose of induction agents, and procedural data (laryngoscopy duration, Cormack-Lehane grade); and (4) the incidence of adverse events and the requirement for rescue vasoactive medications. Based on an a-priori power calculation, a sample size of 30 patients per group was required to detect a 10 mmHg difference in MAP with 80% power and an alpha of 0.05. We enrolled 71 patients to account for potential protocol deviations. Data were analyzed using SPSS Statistics Version 26.0. Normality was assessed with the Shapiro-Wilk test. As hemodynamic data were not normally distributed, non-parametric tests were used. Continuous variables were presented as mean ± standard deviation (SD) and compared using the Mann-Whitney U test. Categorical variables were presented as frequencies (percentages) and compared using the Chi-squared or Fisher's exact test. Within-group changes from baseline were analyzed using the Wilcoxon signed-rank test. The relationship between drug administration and hemodynamic change was assessed with Spearman's rank correlation, and a multivariable linear regression model was used to assess the independent predictive value of each intervention. A two-tailed p-value < 0.05 was considered statistically significant.

3. Results

Figure 1 showed the transparent and systematic flow of participants through each stage of this prospective, randomized clinical trial, in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guidelines. The process began with an initial cohort of 80 patients with traumatic brain injury who were assessed for eligibility. Of these, 9 patients were excluded from participation: 5 did not meet the specified inclusion criteria, 2 declined to provide consent, and 2 were excluded for other reasons. This rigorous screening process resulted in a final study of 71 eligible patients who were successfully randomized into one of two treatment arms. The randomization process was balanced, with 37 patients allocated to the Dexmedetomidine Group and 34 patients allocated to the Lidocaine Group. It is crucial to note that there was perfect adherence and follow-up in both arms of the trial; all 37 patients in the dexmedetomidine arm and all 34 patients in the lidocaine arm received their allocated intervention as per the protocol. Finally, the diagram confirms the integrity of the analysis phase, demonstrating that all participants who were randomized and received an intervention were included in the final statistical analysis. The analysis cohort was complete, with 37 patients analyzed in the Dexmedetomidine Group and 34 patients analyzed in the Lidocaine Group. This absence of post-randomization attrition strengthens the internal validity of the study's findings, ensuring that the results are based on the complete data from all participants as originally allocated.

Figure 2 showed a detailed comparative analysis of the demographic, clinical, and baseline hemodynamic characteristics of the 71 patients enrolled in the trial, confirming the success of the randomization process. The data illustrate that the two study arms—Lidocaine (n=34) and Dexmedetomidine (n=37)—were exceptionally well-matched, providing a robust and unbiased foundation for comparing the interventions. Demographically, the mean age was nearly identical between the groups, with the Lidocaine group averaging 33.7 ± 14.8 years and the Dexmedetomidine group averaging 32.4 ± 15.8 years (p=0.721).

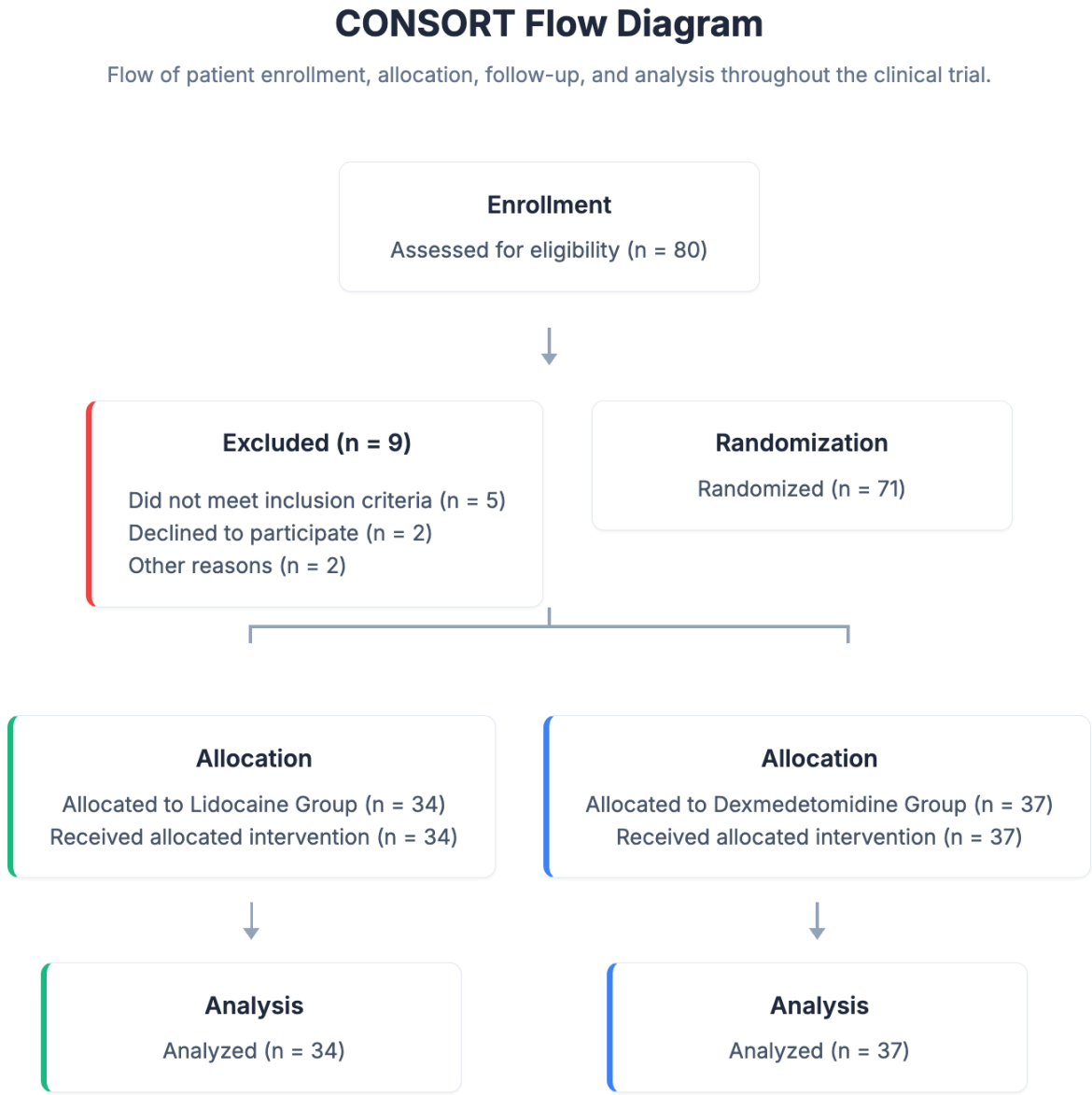

Figure 1. CONSORT flow diagram.

Similarly, gender distribution was comparable, with a male predominance in both the Lidocaine (79.4%) and Dexmedetomidine (78.4%) groups (p=0.915). Crucially, the clinical severity of the brain injuries was also balanced. The distribution of mild, moderate, and severe traumatic brain injury (TBI) based on the Glasgow Coma Scale was statistically indistinguishable between the cohorts (p=0.887). The baseline hemodynamic status, a critical starting point for this study, showed no significant differences. The mean Heart Rate was 92.2 bpm in the Lidocaine group and 91.4 bpm in the Dexmedetomidine group (p=0.764). Likewise, the baseline Mean Arterial Pressure was virtually identical at 98.0 mmHg and 97.0 mmHg for the Lidocaine and Dexmedetomidine groups, respectively (p=0.449). In summary, the complete absence of statistically significant differences across all measured baseline parameters confirms that the randomization was effective. This ensures that any subsequent hemodynamic changes observed during the study can be confidently attributed to the pharmacological effects of the assigned interventions rather than pre-existing disparities between the groups.

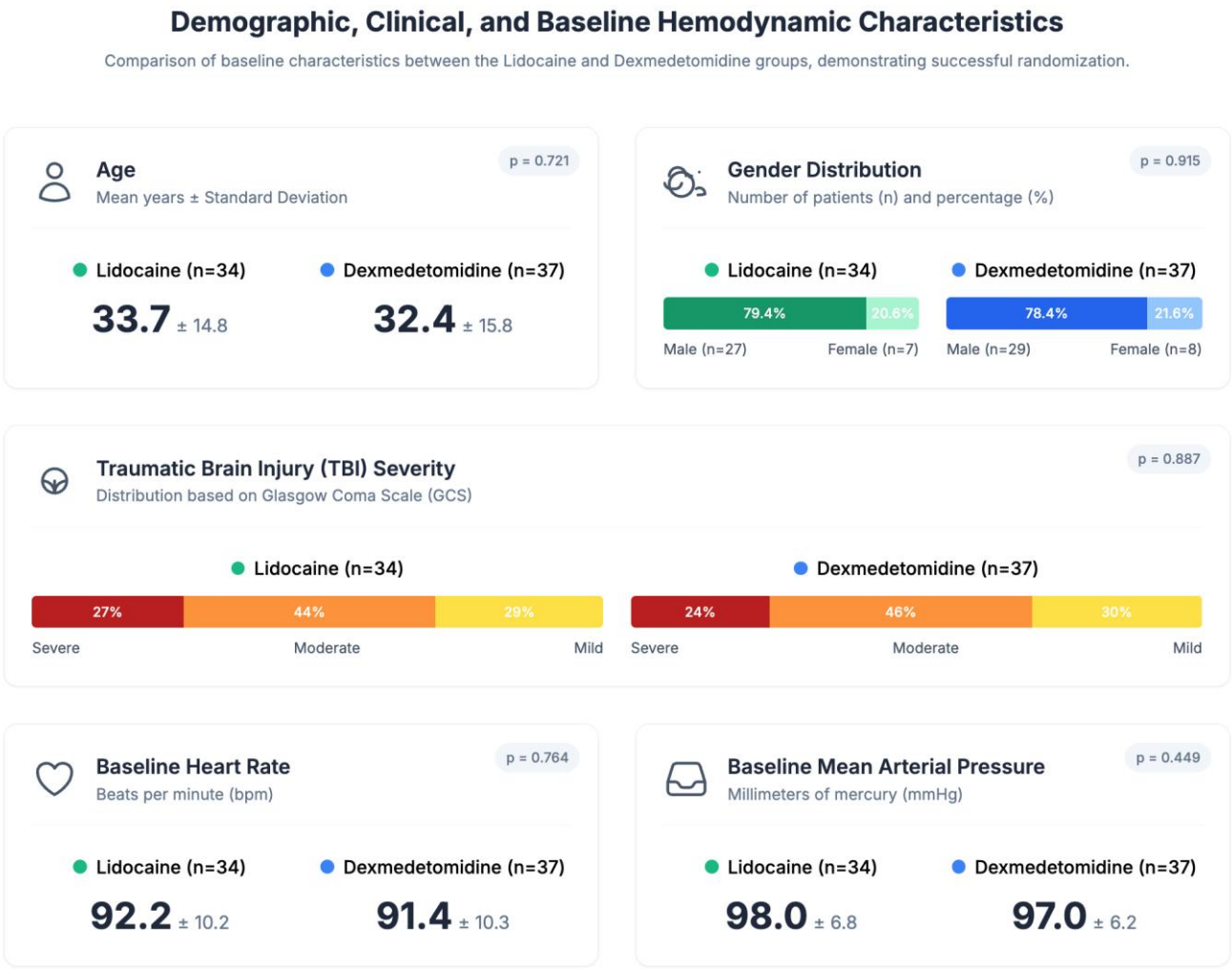

Figure 2. Demographic, clinical, and baseline hemodynamic characteristics.

Figure 3 showed a comparative analysis of key anesthetic and procedural variables, confirming that the technical aspects of anesthesia induction and intubation were remarkably consistent between the two study groups. This consistency is crucial as it minimizes potential confounding factors, ensuring that the observed hemodynamic outcomes can be attributed to the study medications themselves.The depth of anesthesia at induction was virtually identical, with no significant difference in the mean propofol dose administered. The Lidocaine group required 2.1 ± 0.4 mg/kg of propofol, while the Dexmedetomidine group required a nearly identical 2.0 ± 0.5 mg/kg (p=0.511). Furthermore, the degree of noxious stimulus during airway manipulation was also equivalent. The mean duration of laryngoscopy was 18.3 seconds in the Lidocaine group and 17.9 seconds in the Dexmedetomidine group, a negligible difference (p=0.689). The anatomical difficulty of intubation, as assessed by the Cormack-Lehane grading system, was also well-matched. The distribution of Grade I and Grade II views was statistically similar between the Lidocaine (73.5% Grade I) and Dexmedetomidine (75.7% Grade I) groups (p=0.913). This procedural uniformity ensures that the stimulus provoking the hemodynamic response was equivalent for all patients in the trial.

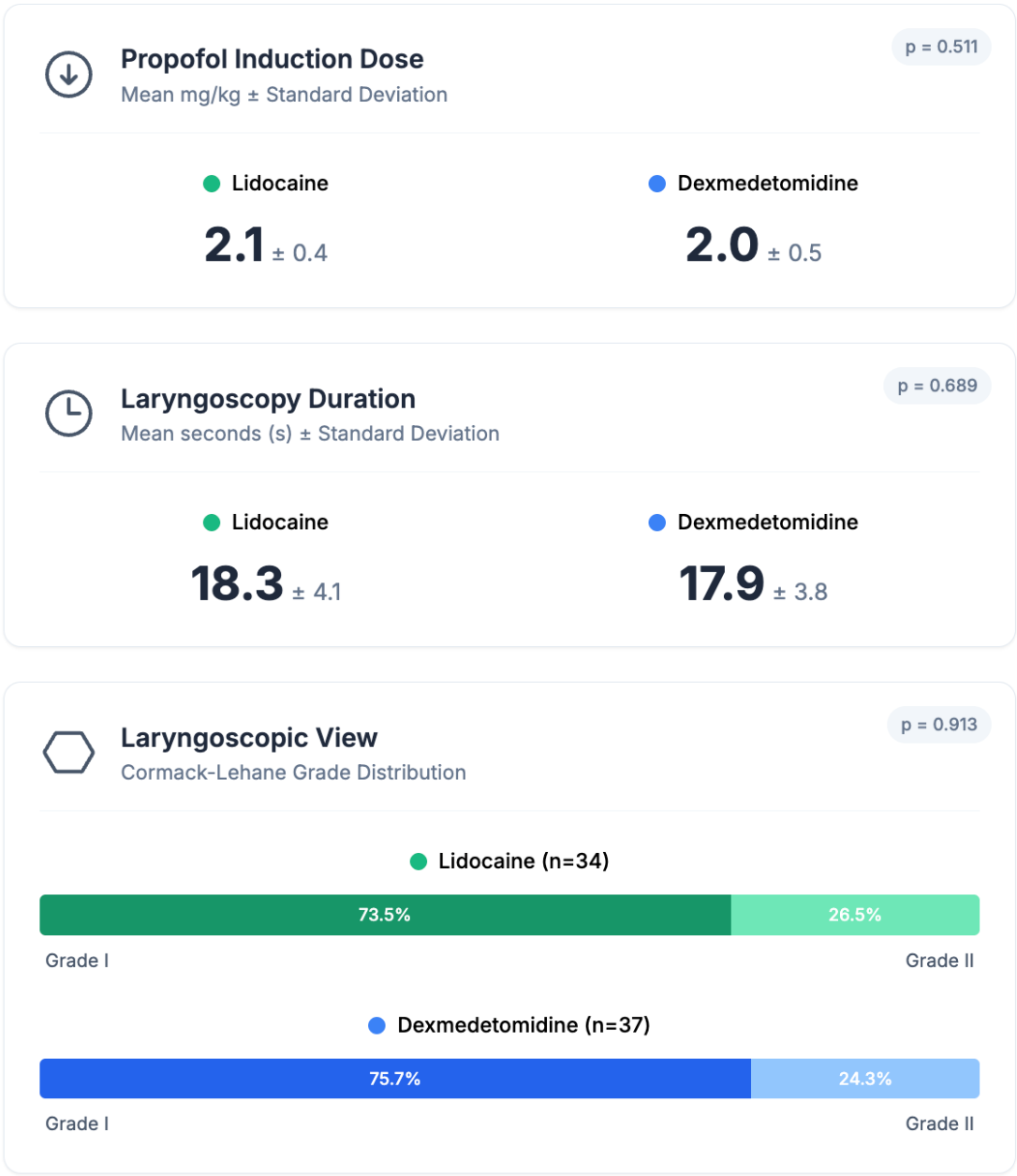

Figure 3. Anesthetic and procedural data.

Figure 4 showed a comprehensive summary of the hemodynamic outcomes, presenting both a graphical time-course and detailed numerical data for mean arterial pressure (MAP) and heart rate (HR) for both study groups. The visual data clearly illustrate that both dexmedetomidine and lidocaine effectively blunted the expected hypertensive and tachycardic response to intubation. The line graphs reveal remarkably parallel trajectories for both MAP and HR between the two groups. Following baseline measurements, both vitals decreased at the time of intubation (T0) and reached their lowest point one minute post-intubation (T1), with

MAP in the mid-80s mmHg and HR in the low-80s bpm. Subsequently, a gradual and controlled return towards baseline was observed over the 10-minute monitoring period, with the hemodynamic profiles of the two groups remaining closely aligned throughout. The accompanying tables provide the precise numerical data (mean ± SD) that underpins the graphs. The primary endpoint analysis, focused on the change in MAP at one minute post-intubation, yielded a p-value of 0.412, confirming the lack of a statistically significant difference between the two interventions. This finding robustly demonstrates that, at the doses studied, both dexmedetomidine and lidocaine possess comparable efficacy in maintaining hemodynamic stability during the critical peri-intubation period in patients with traumatic brain injury.

Figure 4. Hemodynamic outcomes over time.

Figure 5 showed a clear and reassuring safety profile for both study interventions, detailing the incidence of clinically significant adverse events and the corresponding need for rescue therapies. The data indicates that both dexmedetomidine and lidocaine were well-tolerated, with a very low and statistically comparable rate of hemodynamic complications. Specifically, the incidence of hypotension (defined as a MAP < 65 mmHg requiring intervention) was minimal. In the Lidocaine group, only 2 patients (5.9%) required

rescue ephedrine, while 3 patients (8.1%) in the Dexmedetomidine group experienced a similar event. This minor difference was not statistically significant ($p > 0.99$), demonstrating an equivalent risk profile for this adverse event. Similarly, the incidence of bradycardia (defined as a HR < 50 bpm requiring intervention) was also very low and similar between the groups. Only 1 patient (2.9%) in the Lidocaine group and 2 patients (5.4%) in the Dexmedetomidine group required rescue atropine. Once again, this difference was not statistically significant ($p > 0.99$). The overall low number of events underscores the safety of both agents when used for attenuating the intubation response in TBI patients.

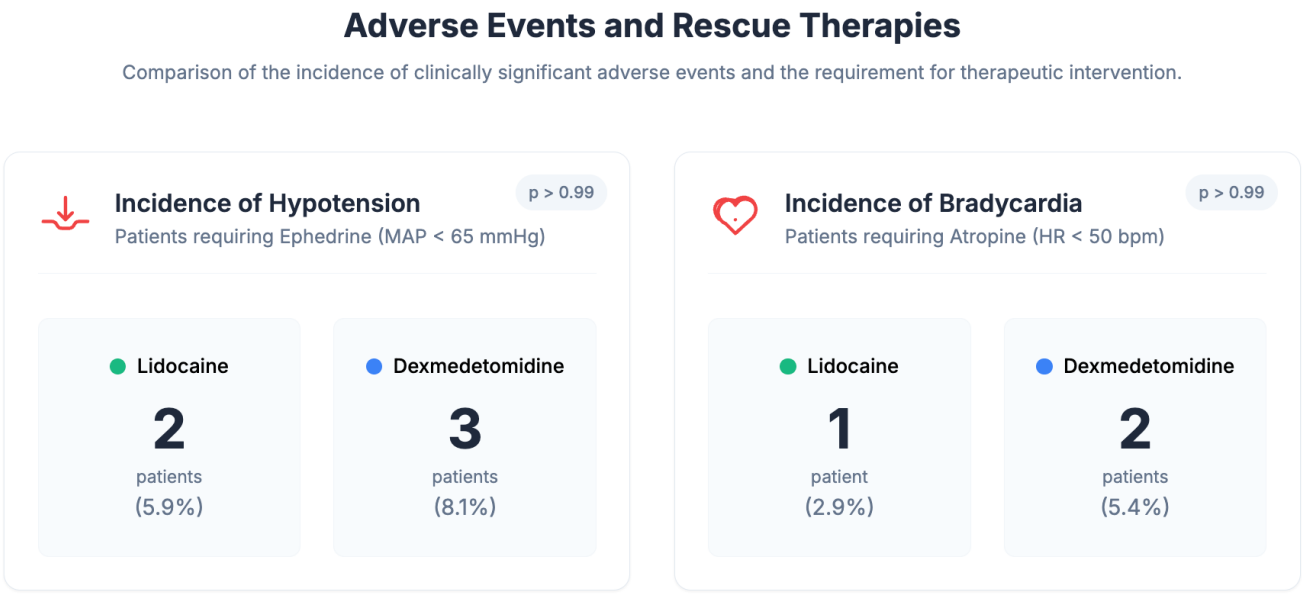

Figure 5. Adverse events and rescue therapies.

4. Discussion

This prospective, randomized, double-blind clinical trial was conceived to resolve a persistent and critical question in clinical neuroanesthesiology: in patients with traumatic brain injury, does the central sympatholysis of dexmedetomidine offer superior hemodynamic control during endotracheal intubation compared to the peripheral membrane stabilization of lidocaine? Our investigation yielded a clear and clinically significant primary finding: at the studied doses, there was no statistically significant difference between the two agents.[11] Both dexmedetomidine and lidocaine were profoundly effective at attenuating the hazardous sympathoadrenal reflex to airway manipulation, and both demonstrated an excellent safety profile. This result, establishing clinical equipoise between two pharmacologically distinct strategies, provides a robust evidence base that empowers clinicians with valuable flexibility in this high-stakes environment. The fundamental success of both interventions lies in their ability to disrupt the pathophysiological arc of the intubation stress response.[12] This reflex begins with intense mechanical stimulation of afferent nerve endings in the laryngopharynx, a signal that travels via the glossopharyngeal and vagus nerves to the nucleus tractus solitarius in the brainstem. This input triggers a powerful efferent sympathetic discharge, originating largely from the locus coeruleus, resulting in a surge of circulating catecholamines that drives the characteristic and dangerous spike in heart rate and blood pressure.[13] Our study demonstrates that this reflex can be effectively intercepted at two entirely different points. Dexmedetomidine acts centrally, at the

very origin of the sympathetic outflow. As a potent alpha-2 agonist, it binds to presynaptic autoreceptors in the locus coeruleus, powerfully inhibiting the release of norepinephrine. This action is akin to turning down the master rheostat of the sympathetic nervous system, producing a global, controlled state of sympatholysis that prevents the efferent surge.[14] Lidocaine, conversely, mounts a multi-pronged attack largely at the periphery. Its primary action as a sodium channel blocker allows it to function as a potent topical and systemic anesthetic. It directly blocks the initiation of the afferent signal from the airway mucosa, preventing the "danger" signal from ever reaching the brainstem. Concurrently, its systemic effects stabilize neuronal membranes throughout the central nervous system, raising the threshold for reflex processing, while its Class Ib antiarrhythmic properties directly stabilize the myocardium, making it less susceptible to the effects of any catecholamines that are released. The fact that dexmedetomidine's central modulation and lidocaine's peripheral and end-organ blockade produced statistically indistinguishable hemodynamic outcomes is a remarkable demonstration of pharmacological convergent evolution. It suggests that for this specific, potent, but transient stimulus, either disabling the central alarm system or cutting the peripheral wires leading to it are equally effective strategy.[15]

A crucial aspect of our findings is not just the prevention of hypertension, but the controlled and modest reduction in hemodynamics from baseline observed in both groups. This is the ideal clinical outcome. The goal is not to induce hypotension, which is a potent cause of secondary brain injury, but to maintain the patient within a narrow, neuroprotective hemodynamic corridor. Both agents achieved this, lowering the MAP to a nadir in the mid-80s mmHg, a level that ensures adequate cerebral perfusion in most circumstances while avoiding the risks of hypertension. The analysis of our time-course data, as visualized in Figures 2 and 3, further reinforces the finding of comparable efficacy. The hemodynamic trajectories of the two groups were virtually superimposable throughout the 10-minute post-intubation period. This indicates that even the subtle pharmacokinetic differences between the drugs—lidocaine's rapid onset and shorter duration versus dexmedetomidine's slower onset and more prolonged effect—did not translate into a clinically significant difference in the hemodynamic profile during this critical initial phase of anesthesia. The context of TBI physiology is essential to interpreting these results. A key feature of the injured brain is the impairment or complete loss of cerebral autoregulation.[16] In a healthy brain, cerebral blood flow (CBF) remains constant across a wide range of mean arterial pressures (typically 60-160 mmHg). In TBI, this mechanism is often defective, rendering CBF passively dependent on blood pressure. In this pressure-passive state, a hypertensive surge directly translates to increased cerebral blood volume, elevated ICP, and potential cerebral hyperemia, while hypotension leads directly to cerebral ischemia. The stable hemodynamic platform provided by both dexmedetomidine and lidocaine is therefore of paramount importance, as it protects the brain from the devastating consequences of both extremes. By maintaining a stable MAP, these drugs help to maintain a stable CPP and a less volatile intracranial environment, which is the cornerstone of preventing secondary ischemic and edematous injury.[17] While our primary analysis revealed no difference, our secondary regression analysis offered a subtle but intriguing insight. Dexmedetomidine demonstrated a numerically stronger and more statistically robust correlation with the observed reduction in heart rate and blood pressure. While this did not result in a different group average, it may suggest a more uniform and predictable dose-response relationship for dexmedetomidine. This is pathophysiologically plausible. A central, global suppression of sympathetic tone may be less subject to inter-patient variability than a peripheral blockade, which could be influenced by minor differences in laryngoscopy technique or individual anatomical sensitivity. For the clinician seeking the most reliable and consistent agent, this may be a point in favor of dexmedetomidine, though this interpretation remains speculative and requires further study.[18]

The finding of clinical equipoise between these two agents has immediate and practical implications for clinical practice. The decision of which agent to use can now be confidently shifted from a question of "which is

better for blood pressure?" to a more nuanced consideration of secondary properties and logistics. Dexmedetomidine, with its 10-minute infusion time, is ideally suited for controlled intubations where its sedative, anxiolytic, and analgesic properties can be fully leveraged to ensure a smooth, opioid-sparing anesthetic course.[19] Its prolonged duration of action is a distinct advantage for providing continued stability during transport or subsequent procedures. Lidocaine, with its rapid onset, short duration, and low cost, is the superior choice for more urgent or rapid sequence scenarios. It is perfect for obtunding the brief stimulus of intubation without inducing prolonged sedation, which is particularly advantageous if a rapid neurological assessment is required post-procedure. Our study validates the clinician's ability to tailor the pharmacological approach to the individual patient's needs, armed with the knowledge that the primary neuroprotective goal of hemodynamic stability will be met with either choice.[20]

Figure 6. Pathophysiological mechanisms and clinical outcomes.

Figure 6 showed a compelling schematic that visually synthesizes the core findings of the study, illustrating the distinct pathophysiological pathways through which dexmedetomidine and lidocaine achieve a comparable clinical outcome. The diagram serves as a powerful conceptual summary, narrating the journey

from a common clinical challenge to a shared, successful therapeutic result, despite the use of two fundamentally different pharmacological strategies. At the apex of the diagram is the inciting event: The clinical challenge, this represents the noxious stimulus of direct laryngoscopy and endotracheal intubation, a routine but profoundly stimulating procedure in anesthesia. As depicted, this stimulus triggers a massive sympathetic surge. This is not a trivial response; it is a powerful, primitive reflex designed to prepare the body for a perceived threat. The mechanical manipulation of the highly innervated structures of the oropharynx, larynx, and trachea activates afferent fibers of the glossopharyngeal and vagus nerves. These signals converge on the brainstem, specifically the nucleus tractus solitarius, which in turn activates sympathetic outflow centers like the locus coeruleus. The result is a sudden and massive release of catecholamines—epinephrine and norepinephrine—into the bloodstream. This surge has immediate and widespread effects: it causes peripheral vasoconstriction, dramatically increasing systemic vascular resistance; it increases myocardial contractility (positive inotropy); and it accelerates the heart rate (positive chronotropy). The combination of these effects leads to the dangerous increases in both mean arterial pressure (MAP) and heart rate (HR) that this study aimed to prevent. In a patient with a traumatic brain injury, whose cerebral autoregulation is often impaired, such a hypertensive surge can be catastrophic, leading to increased cerebral blood volume, elevated intracranial pressure, and a cascade of secondary ischemic and edematous injuries. Pathway 1: Dexmedetomidine, as a "top-down" approach that acts via central sympatholysis. Dexmedetomidine is a potent and highly selective alpha-2 adrenergic receptor agonist. Its primary site of action is not in the periphery but deep within the central nervous system, specifically at the presynaptic nerve terminals in the locus coeruleus of the brainstem.[19] This area is effectively the command-and-control center for the sympathetic nervous system. The alpha-2 receptors on these neurons function as autoreceptors—a crucial negative feedback mechanism. When stimulated by norepinephrine, they inhibit further release of the neurotransmitter. Dexmedetomidine hijacks this natural braking system. By directly stimulating these receptors, it potently inhibits presynaptic norepinephrine release from the nerve endings. This action effectively turns down the gain on the entire sympathetic nervous system at its source. The result, as the figure notes, is a global reduction of sympathetic tone. This central inhibition explains its profound clinical effects: the decreased stimulation of the heart's beta-1 receptors leads to a lower heart rate, and the reduced stimulation of alpha-1 receptors in the peripheral vasculature leads to vasodilation and a lower mean arterial pressure. This single, elegant mechanism provides a stable, controlled hemodynamic environment. Pathway 2: Lidocaine is depicted as a "bottom-up" and "end-organ" strategy that works through Peripheral & Membrane Stabilization. Lidocaine's mechanism is fundamentally different, targeting voltage-gated sodium channels rather than specific neurotransmitter receptors. Its efficacy comes from a multi-pronged attack on the reflex arc. First, by blocking Na^+ channels in peripheral afferent nerves from the airway, it acts as a topical anesthetic on a systemic level. It prevents the very initiation and propagation of the noxious signal from the laryngoscope blade and endotracheal tube, effectively cutting the wire of the alarm before the signal can reach the brainstem. Second, lidocaine that reaches the central nervous system suppresses central reflex processing by stabilizing neuronal membranes and raising the threshold for firing, making the brainstem less reactive to any signals that do get through. Finally, lidocaine has direct effects on the heart. As a Class Ib antiarrhythmic, it directly stabilizes the myocardial membrane, making the cardiac muscle cells themselves less excitable and less responsive to the effects of any catecholamines that may have been released. This culmination of afferent blockade, central suppression, and end-organ protection provides a robust defense against the sympathetic surge. The most insightful part of the diagram is the convergence of these two distinct pathways onto a single observed clinical outcome. Despite one drug working centrally and the other peripherally, the study found that both pathways led to Comparable hemodynamic attenuation. Both strategies

were successful in producing a stable MAP and HR, preventing the dangerous pressor response.[20] This clinical equipoise is underscored by the final, crucial piece of information: No significant difference was found between the groups ($p > 0.05$). This visual representation elegantly demonstrates the core conclusion of the research: that for this specific clinical challenge, targeting either the central command center or the peripheral signaling network is both equally valid and effective strategies, providing clinicians with valuable, evidence-based flexibility in managing these high-risk patients.

This study is not without limitations. As a single-center trial, its external validity may be limited. Although adequately powered for its primary endpoint, the sample size may have been insufficient to detect very small differences between the groups, and the trend towards a more consistent effect with dexmedetomidine could potentially have reached significance in a larger cohort. The most significant limitation, however, is the absence of invasive ICP monitoring. Directly correlating systemic hemodynamic data with real-time ICP and CPP measurements would provide a far more complete picture of the true neurophysiological impact of these drugs and is the most important avenue for future research in this area. This rigorous investigation provides compelling evidence that both dexmedetomidine and lidocaine are effective and safe interventions for securing the airway in patients with traumatic brain injury. By demonstrating that two fundamentally different pharmacological pathways converge on a similar, desirable clinical outcome, this study enhances our scientific understanding and provides invaluable, evidence-based support for clinical flexibility. It confirms that the modern neuroanesthesiologist has two excellent tools at their disposal, and the art of practice lies in selecting the right tool for the specific clinical circumstances to provide the safest possible journey for the injured brain.

5. Conclusion

This randomized clinical trial demonstrates that for the attenuation of the hemodynamic stress response to endotracheal intubation in adult patients with traumatic brain injury, intravenous dexmedetomidine (1 μg/kg) and intravenous lidocaine (1.5 mg/kg) are comparably effective and safe. Both drugs successfully blunted the expected rise in heart rate and mean arterial pressure without causing significant adverse events. The choice between these two agents can be tailored to the specific clinical context, considering factors such as the desired speed of onset, duration of action, need for postoperative sedation, and cost.

6. References

1. Kostadinov I, Avsenik J, Osredkar J, Jerin A, Gradisek P. Effect of stellate ganglion block on brain hemodynamics and the inflammatory response in moderate and severe traumatic brain injury: a pilot study. Reg Anesth Pain Med. 2025.
2. Lalenoh DC, Yulianti Bisri D. Glasgow coma scale improvement after lidocaine infusion in moderate traumatic brain injury. J Anesth Clin Res. 2016; 7(8).
3. Letson HL, Dobson GP. Adenosine, lidocaine, and Mg^{2+} (ALM) resuscitation fluid protects against experimental traumatic brain injury. J Trauma Acute Care Surg. 2018; 84(6): 908–16.
4. Dehnadi Moghadam A, Hasanzadeh H, Dehnadi Moghadam F. Evaluation of the effect of intranasal lidocaine in the treatment of spasticity in patients with traumatic brain injury. Anesth Pain Med. 2021; 11(4): e115849.
5. Karakaya D, Cakir-Aktas C, Uzun S, Soylemezoglu F, Mut M. Tailored therapeutic doses of dexmedetomidine in evolving neuroinflammation after traumatic brain injury. Neurocrit Care. 2022; 36(3): 802–14.
6. Xu J, Xiao Q. Assessment of the effects of dexmedetomidine on outcomes of traumatic brain injury using propensity score analysis. BMC Anesthesiol. 2022; 22(1): 280.
7. Jeon S, Baik J, Kim J, Lee J, Do W, Kim E, et al. Intrathecal dexmedetomidine attenuates mechanical allodynia through the downregulation of brain-derived neurotrophic factor in a mild traumatic brain injury rat

model. Korean J Anesthesiol. 2023; 76(1): 56–66.
8. Yousef IA, Mansour HS, Mahran MM, Aly AM. Effect of dexmedetomidine on Glasgow coma scale in patients with traumatic brain injury: an observational study. Minia J Med Res. 2024.
9. Hatfield J, Soto AL, Kelly-Hedrick M, Kaplan S, Komisarow JM, Ohnuma T, et al. Safety, efficacy, and clinical outcomes of dexmedetomidine for sedation in Traumatic brain injury: a scoping review. J Neurosurg Anesthesiol. 2024; 36(2): 101–8.
10. Deng Z, Gu Y, Luo L, Deng L, Li Y, Huang W. The effect of dexmedetomidine on the postoperative recovery of patients with severe traumatic brain injury undergoing craniotomy treatment: a retrospective study. Eur J Med Res. 2024; 29(1): 256.
11. Wongsripuemtet P, Ohnuma T, Temkin N, Barber J, Komisarow J, Manley GT, et al. Association of early dexmedetomidine exposure with brain injury biomarker levels following moderate - Severe traumatic brain injury: a TRACK-TBI study. J Clin Neurosci. 2024; 126: 338–47.
12. Sohn J-T. Dexmedetomidine for craniotomy in traumatic brain injury. Am J Ther. 2025; 32(4): e355–6.
13. Wang Y-Q, Zhang X-J, Zhou D, Li Q, Liu X. Effect of dexmedetomidine on posttraumatic stress disorder in traumatic brain injury patients undergoing emergency craniotomy surgery: a retrospective study. Int J Clin Pract. 2025; 2025(1).
14. Kang P, Gao Y, Zheng J, Chen J, Li Z, Cong G. Dexmedetomidine repairs behavioral deficits through miR-365a-3p/G3BP2 axis and Nrf2/Keap1 signaling pathway in traumatic brain injury. Mol Cell Toxicol. 2025.
15. Alaifan T, Sakhakhni A, Khojah A, Alraddadi EA, Alkhaibary A, Alqahtani AM. Impact of dexmedetomidine on hospital and intensive care unit stay duration in adult traumatic brain injury patients: a systematic review. Drug Healthc Patient Saf. 2025; 17: 157–71.
16. Khallaf M, Thabet AM, Ali M, Sharkawy E, Abdel-rehim S. The effect of dexmedetomidine versus propofol in traumatic brain injury: evaluation of some hemodynamic and intracranial pressure changes. Egypt J Neurosurg. 2019; 34(1).
17. Dong J, Liu L, Liu J, Peng Y. Clinical observation of hemodynamic and cerebral protective effects of different doses of dexmedetomidine in patients with traumatic brain injury. J Biosci Med (Irvine). 2023; 11(02): 146–51.
18. Chandar Chinnarasan V, Bidkar PU, Swaminathan S, Mani M, Vairappan B, Chatterjee P, et al. Comparison of dexmedetomidine versus fentanyl-based total intravenous anesthesia technique on the requirement of propofol, brain relaxation, intracranial pressure, neuronal injury, and hemodynamic parameters in patients with acute traumatic subdural hematoma undergoing emergency craniotomy: a randomized controlled trial. Surg Neurol Int. 2024; 15: 462.
19. Lin C-C, Yu J-H, Lin C-C, Li W-C, Weng Y-M, Chen S-Y. Postintubation hemodynamic effects of intravenous lidocaine in severe traumatic brain injury. Am J Emerg Med. 2012; 30(9): 1782–7.
20. Singh S, Chouhan RS, Bindra A, Radhakrishna N. Comparison of effect of dexmedetomidine and lidocaine on intracranial and systemic hemodynamic response to chest physiotherapy and tracheal suctioning in patients with severe traumatic brain injury. J Anesth. 2018; 32(4): 518–23.