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Review Article

Selection of induction agents for safe and effective rapid sequence intubation

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ABSTRACT

Rapid sequence intubation (RSI) is a critical procedure in emergency airway management, requiring rapid induction of unconsciousness and muscle relaxation to facilitate safe intubation. The choice of induction agent plays a pivotal role in optimizing outcomes, as each agent exhibits unique pharmacokinetic and pharmacodynamic profiles. Etomidate is frequently chosen for its hemodynamic stability, making it suitable for critically ill patients; however, concerns regarding adrenal suppression warrant caution in septic or prolonged critical illness cases. Ketamine is particularly advantageous in patients with reactive airway diseases or hypotension, owing to its bronchodilatory effects and ability to preserve respiratory drive, although its psychotomimetic side effects must be managed carefully. Propofol, characterized by its rapid onset and short duration, provides excellent intubating conditions but may cause significant hypotension, limiting its use in hemodynamically unstable patients. Thiopental, once widely used, is now less favored due to cardiovascular depression and prolonged recovery times. Patient-specific factors, including age, comorbidities, and clinical status, heavily influence agent selection. Pediatric and geriatric populations pose unique challenges, necessitating dose adjustments and close monitoring. Emerging agents like dexmedetomidine offer novel benefits such as sedation with preserved respiratory function, though slower onset limits its utility in emergency settings. The complexity of decision-making underscores the importance of understanding the nuances of each agent's efficacy and safety. Despite advancements in pharmacological options, limitations in evidence, variability in patient responses, and resource constraints highlight the need for individualized approaches and adaptable guidelines. Further research is essential to bridge gaps in knowledge and establish standardized practices to enhance safety and effectiveness in RSI across diverse clinical scenarios.

Keywords: Rapid sequence intubation, Induction agents, Pharmacokinetics, Emergency airway management, Patient-specific considerations

INTRODUCTION

Rapid sequence intubation (RSI) is a critical technique in emergency and elective airway management, combining rapid administration of an induction agent with a neuromuscular blocking drug to achieve rapid unconsciousness and muscle relaxation.[1] This approach minimizes the time between loss of protective airway reflexes and securing the airway, making it indispensable in situations such as trauma, respiratory failure, or altered mental status.[2] The choice of induction agent plays a pivotal role in the success and safety of RSI, influencing hemodynamic stability, airway reflex suppression, and overall patient outcomes.

Various agents, including etomidate, propofol, ketamine, and thiopental, have been employed for RSI, each with distinct pharmacodynamic and pharmacokinetic profiles. Etomidate is often favored for its hemodynamic stability, making it suitable for critically ill patients. However, its potential to suppress adrenal steroidogenesis raises concerns, especially with repeated dosing.[3] Propofol, a widely used induction agent, provides rapid onset and profound sedation but may induce significant hypotension, particularly in patients with compromised hemodynamic reserve.[4] Ketamine is another popular choice, offering a unique profile of sedation, analgesia, and bronchodilation, beneficial in scenarios involving bronchospasm or hypotension. Its association with increased intracranial pressure, once a concern, has been largely debunked, solidifying its role in RSI.[5] Thiopental, a barbiturate, while historically significant, has seen reduced use due to the availability of agents with better safety and efficacy profiles.

The selection of an induction agent is influenced not only by the drug's properties but also by patient-specific factors, including age, comorbidities, and the clinical scenario. For instance, propofol might be preferred in patients requiring deep sedation, while etomidate could be prioritized in hemodynamically unstable patients.[6] Furthermore, the debate around optimal induction agents underscores the need for evidence-based guidelines that balance efficacy and safety. Emerging evidence also highlights the role of adjuncts such as opioids and lidocaine in enhancing intubation conditions and minimizing adverse effects associated with RSI agents.[7] Despite advancements, gaps in comparative data and the diversity of clinical scenarios challenge the formulation of universal recommendations. This review aims to explore the pharmacological nuances, clinical efficacy, and safety profiles of different induction agents used in RSI, offering a comprehensive comparison to guide clinical practice.

REVIEW

The choice of induction agents for RSI is pivotal in balancing efficacy and safety across diverse clinical scenarios. Agents such as etomidate, ketamine, and propofol each possess unique pharmacological characteristics that cater to specific patient needs. Etomidate, for example, remains a cornerstone in RSI for hemodynamically unstable patients due to its minimal cardiovascular effects. However, its potential to suppress adrenal function raises concerns in critically ill patients, especially with repeated use or prolonged exposure.[3] This underscores the necessity of judicious agent selection tailored to individual clinical contexts.

Ketamine has gained traction due to its dual sedative and analgesic properties, alongside its bronchodilatory effects, which are advantageous in patients with reactive airway disease. Recent evidence has refuted previous concerns about its role in raising intracranial pressure, making it a viable option in neurologically compromised patients. Nevertheless, its psychotomimetic side effects necessitate caution in vulnerable populations.[5] Propofol offers rapid onset and effective sedation but is often associated with hypotension, limiting its use in hemodynamically compromised patients. The variation in agent profiles illustrates the complexity of decision-making in RSI, where optimizing patient outcomes hinges on a nuanced understanding of pharmacology and individual patient factors.

Pharmacokinetics and pharmacodynamics of common induction agents

Induction agents for RSI are chosen based on their ability to rapidly induce unconsciousness while maintaining hemodynamic stability. The pharmacokinetics and pharmacodynamics of these agents are pivotal in ensuring effective and safe airway management in diverse patient populations. Each agent's onset, duration of action, and side effect profile play critical roles in the decision-making process.

Etomidate is often used in RSI for its stability in cardiovascularly compromised patients. Its rapid onset of action is attributed to its high lipid solubility, which facilitates quick penetration of the blood-brain barrier. Etomidate’s clearance is primarily through hepatic metabolism and plasma esterases, leading to a short duration of effect. However, it is also associated with adrenal suppression, even after a single dose, due to its inhibition of 11-beta-hydroxylase, an enzyme critical for cortisol synthesis.[1] This makes its repeated use or use in sepsis patients a topic of caution.

Ketamine, another agent commonly employed in RSI, offers unique benefits due to its dual sedative and analgesic properties. It acts as an N-methyl-D-aspartate (NMDA) receptor antagonist and is metabolized in the liver via the cytochrome P450 system. Its active metabolite, norketamine, contributes to its prolonged effects. Ketamine’s preservation of respiratory drive and bronchodilatory properties make it advantageous in patients with reactive airway diseases or hypotension. Despite earlier concerns about its potential to increase intracranial pressure, recent evidence has largely dispelled

this notion, solidifying its role in trauma and critically ill patients.[5]

Propofol is a widely used agent known for its rapid onset due to high lipid solubility and short half-life, allowing for quick induction and recovery. However, propofol is associated with dose-dependent hypotension and myocardial depression, which are significant limitations in hemodynamically unstable patients. Its metabolism occurs predominantly in the liver, with extrahepatic clearance also contributing. The absence of analgesic properties necessitates the concurrent use of opioids when propofol is chosen as the induction agent.[4]

Thiopental, a barbiturate, has historical significance in RSI but has been largely replaced due to newer agents with better safety profiles. Its rapid redistribution from the central nervous system to peripheral tissues explains its short duration of action. Thiopental is metabolized hepatically, with a half-life that can be prolonged in patients with hepatic impairment. Although effective in reducing intracranial pressure, its use is limited by its potential to cause profound hypotension and respiratory depression.[3]

Emerging agents like dexmedetomidine have gained attention for their sedative and sympatholytic effects. Acting on alpha-2 adrenergic receptors, dexmedetomidine offers a unique profile by maintaining spontaneous ventilation while providing sedation. Its slower onset compared to traditional agents, however, limits its utility in emergent RSI scenarios but highlights potential in elective procedures where gradual induction is acceptable.[6] The pharmacokinetics and pharmacodynamics of these agents illustrate the complexity of their selection. Patient-specific factors such as age, comorbidities, and clinical presentation heavily influence the choice of induction agent. A nuanced understanding of each drug's properties and limitations is essential for optimizing RSI outcomes.

Efficacy and safety profiles in rapid sequence intubation

Evaluating the efficacy and safety of induction agents in RSI is crucial for optimizing outcomes, particularly in emergent situations. Etomidate remains a widely utilized agent, primarily due to its hemodynamic stability. Studies have consistently highlighted its minimal impact on blood pressure and heart rate, making it a preferred choice in critically ill patients. However, the association of etomidate with adrenal suppression, particularly through the inhibition of 11-beta-hydroxylase, raises concerns when used repeatedly or in septic shock scenarios. Despite this, its overall safety profile has positioned it as a key option in the RSI arsenal.[8]

Ketamine has garnered significant attention due to its unique ability to provide sedation, analgesia, and bronchodilation simultaneously. This agent is particularly advantageous in patients with reactive airway disease or hemodynamic instability. Unlike many induction agents, ketamine preserves respiratory drive, which can be lifesaving in specific clinical contexts. Concerns regarding its potential to raise intracranial pressure have been largely dispelled by recent data, further supporting its utility in trauma and neurocritical care settings. Adverse effects, including emergence phenomena and hypersalivation, have been noted but are generally manageable with adjunctive measures.[9]

Propofol, a cornerstone in anesthesia practice, offers rapid onset and recovery due to its favorable pharmacokinetics. However, its propensity to cause hypotension and myocardial depression limits its use in hemodynamically compromised patients. While propofol lacks intrinsic analgesic properties, its profound sedative effects provide excellent intubating conditions. In non-critical settings, its efficacy is unmatched, but clinicians must weigh its risks against patient-specific factors such as baseline hemodynamic stability.[4,10]

Thiopental, a barbiturate, has a long-standing history in RSI but has seen reduced use in modern practice due to safety concerns. Its rapid onset and ability to reduce intracranial pressure make it useful in neurocritical scenarios. However, thiopental's potential for significant cardiovascular depression and prolonged recovery time, particularly in patients with hepatic impairment, has shifted preference towards newer agents with superior safety profiles.[6,11]

Dexmedetomidine is emerging as a novel option in RSI, particularly for its sedative and sympatholytic properties. By acting on alpha-2 adrenergic receptors, it offers sedation without respiratory depression, which can be valuable in specific patient populations. However, its slower onset compared to traditional agents limits its utility in emergent intubations. Additionally, concerns about bradycardia and hypotension require careful monitoring when dexmedetomidine is administered.[12]

Recent studies have also explored the role of combination strategies to optimize intubating conditions while mitigating adverse effects. For instance, the addition of opioids such as fentanyl to induction agents can blunt the sympathetic response to laryngoscopy and reduce hemodynamic perturbations. However, these combinations require careful dose titration to avoid complications like prolonged apnea or excessive sedation, underscoring the importance of tailoring therapy to individual patients' needs.[13]

Patient-specific considerations and optimal agent selection

Selecting the ideal induction agent for RSI requires careful consideration of the patient's physiological and pathological state. Etomidate is commonly used for patients with hemodynamic instability due to its minimal effects on cardiovascular parameters. However, its potential for adrenal suppression, even after a single dose,

makes it less favorable for septic patients or those with prolonged critical illness.[14]

For patients with reactive airway diseases, ketamine provides distinct advantages due to its bronchodilatory effects and maintenance of respiratory drive. It is also beneficial for patients who are hypotensive, as it typically increases systemic vascular resistance and blood pressure. Nonetheless, ketamine's psychotomimetic side effects require caution, especially in patients with a history of psychiatric disorders.[15]

Propofol offers rapid onset and recovery but is associated with dose-dependent hypotension, making it unsuitable for hemodynamically unstable patients. It is, however, an excellent choice for elective cases where cardiovascular stability is less of a concern. Its short duration of action and antiemetic properties further enhance its utility in specific clinical settings.[16]

In neurocritical cases, thiopental's ability to decrease intracranial pressure is advantageous. However, its longer half-life and significant cardiovascular depressant effects limit its use in scenarios requiring rapid emergence or in patients with cardiac dysfunction.[17] Moreover, dexmedetomidine is emerging as a choice for scenarios requiring preserved respiratory drive and mild sedation. While its slower onset limits its use in emergent RSI, its ability to provide sedation without significant respiratory depression offers promise in cases where gradual intubation is feasible.[18]

Pediatric and geriatric patients present unique challenges in RSI, with altered pharmacokinetics and pharmacodynamics due to age-related physiological changes. In children, the immature hepatic and renal systems require careful dose adjustment to avoid toxicity. Similarly, in the elderly, reduced metabolic clearance and increased sensitivity to sedative agents necessitate lower doses and closer monitoring.[19]

The selection of induction agents for RSI is influenced by a multitude of patient-specific and situational factors, which limits the ability to generalize recommendations universally. Variability in individual patient responses, influenced by comorbid conditions, concurrent medications, and physiological reserves, complicates direct comparisons among agents. Additionally, much of the evidence supporting the use of specific agents is derived from retrospective studies or controlled environments, which may not fully capture the complexities of emergent clinical scenarios. The risk-benefit profiles of certain agents, such as etomidate's adrenal suppression or propofol's hypotensive effects, require further study in diverse patient populations to better delineate their impact on long-term outcomes. Lastly, limitations in access to specific agents in resource-constrained settings may necessitate compromises in agent selection, underscoring the need for adaptable, context-specific guidelines.

CONCLUSION

In the context of rapid sequence intubation, the selection of induction agents must balance efficacy, safety, and patient-specific factors. Agents like etomidate, ketamine, and propofol offer distinct advantages but are associated with unique limitations that require careful consideration. Tailoring the choice of agent to the clinical scenario ensures optimal outcomes while minimizing adverse effects. Ongoing research and evidence-based guidelines are essential to refine agent selection and improve patient care in RSI.

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REFERENCES

1. Sagarin MJ, Chiang V, Sakles JC, Barton ED, Wolfe RE, Vissers RJ, et al; National Emergency Airway Registry (NEAR) investigators. Rapid sequence intubation for pediatric emergency airway management. Pediatr Emerg Care. 2002;18(6):417-23.
2. Weingart SD, Levitan RM. Preoxygenation and prevention of desaturation during emergency airway management. Ann Emerg Med. 2012;59(3):165-75.
3. Cuthbertson BH, Sprung CL, Annane D, Chevret S, Garfield M, Goodman S, et al. The effects of etomidate on adrenal responsiveness and mortality in patients with septic shock. Intensive Care Med. 2009;35(11):1868-76.
4. Marik PE. Propofol: therapeutic indications and side-effects. Curr Pharm Design. 2004;10(29):3639-49.
5. Green SM, Andolfatto G, Krauss BS. Ketamine and intracranial pressure: no contraindication except hydrocephalus. Ann Emerg Med. 2015;65(1):52-4.
6. Gropper MA, Eriksson LI, Fleisher LA, Wiener-Kronish JP, Cohen NH, Leslie K. Miller's anesthesia, 2-volume set E-book. Elsevier Health Sciences. 2019.
7. Schwarz M, Rivera G, Hammond M, Silman Z, Jackson K, Kofke WA. Acousto-optic cerebral blood flow monitoring during induction of anesthesia in humans. Neurocrit Care. 2016;24:436-41.
8. Paknezhad SP, Shahsavarinia K, Ghojazadeh M, Jangjou Esfahlan F, Soleimanpour M, Sanaie S, et al. The Role of Etomidate for Rapid Sequence Intubation in Emergency Medicine: A Systematic Review. Arch Anesth Crit Care. 2024 (In Press).
9. Baekgaard JS, Eskesen TG, Sillesen M, Rasmussen LS, Steinmetz J. Ketamine as a rapid sequence induction agent in the trauma population: a systematic review. Anesth Anal. 2019;128(3):504-10.
10. Sahinovic MM, Struys MM, Absalom AR. Clinical pharmacokinetics and pharmacodynamics of propofol. Clin Pharmacokinet. 2018;57(12):1539-58.

11. Perier F, Chateauneuf AL, Jacq G, Holleville M, Schnell D, Merceron S, et al; ICTAL Study Group. Comparison of etomidate and sodium thiopental for induction during rapid sequence intubation in convulsive status epilepticus: A retrospective single-center study. Seizure. 2018;61:170-6.
12. Zhang X, Bai Y, Shi M, Ming S, Jin X, Xie Y. Effect of different administration and dosage of dexmedetomidine in the reduction of emergence agitation in children: a meta-analysis of randomized controlled trials with sequential trial analysis. Transl Pediatr. 2021;10(4):929.
13. Paknezhad S, Serati E, Esfanjani RM, Soleimanpour M, Soleimanpour H. Effects of fentanyl versus remifentanil pretreatment on the QTc interval in patients undergoing rapid sequence intubation: a randomized clinical trial. Anesthesiol Pain Med. 2022;12(5).
14. Shahzad K, Ethan A, Said A, Alexander D. Anesthesia and Surgical Interventions in Emergency Cases. Anesth Surg Interv Emerg Cases. 2023;83:159.
15. Gustafson KA, Brown AS. Neuromuscular Blocking Agents: Use and Controversy in the Hospital Setting. US Pharm. 2017;42(1):HS16-20.
16. Celmins L. Pharmacology for Rapid Sequence Intubation (RSI) Airway Management in Trauma Patients. J Med Insight. 2024;2024(6).
17. Erstad BL, Barletta JF. Drug dosing in the critically ill obese patient—a focus on sedation, analgesia, and delirium. Crit Care. 2020;24(1):315.
18. Pankey JA, Christofferson S, Barrick G, Knettel BA, Knettel C. Effect of paralytic agents on post-intubation sedation in the emergency department. Hosp Pharm. 2022;57(6):759-66.
19. Duncan L, Correia M, Mogane P. A survey of paediatric rapid sequence induction in a Department of Anaesthesia. Children. 2022;9(9):1416.

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