Brief description of patient problem/setting : 46 year old male presents to the emergency department with an acute anterior shoulder dislocation confirmed on imaging. He is hemodynamically stable and neurovascularly intact. Intra-articular lidocaine is administered for analgesia however, the patient continues to experience significant pain. Procedural sedation is required to facilitate closed reduction. The emergency team must determine whether ketamine or propofol is the more appropriate sedative agent.

Search Question: In hemodynamically stable middle aged adults undergoing emergency department procedural sedation for shoulder dislocation reduction, does ketamine compared with propofol result in fewer respiratory and hemodynamic adverse events while maintaining similar procedural success and recovery time?

Question Type: What kind of question is this?

☐Prevalence ☐Screening ☐Diagnosis ☐Prognosis ☐**Treatment** ☐Harms

Assuming that the highest level of evidence to answer your question will be meta-analysis or systematic review, what other types of study might you include if these are not available (or if there is a much more current study of another type)?

I would include well-designed randomized controlled trials (RCTs) if a recent or high-quality meta-analysis were not available. RCTs are particularly appropriate for this question because they directly compare two interventions under controlled conditions and minimize confounding variables, such as differences in patient characteristics or provider technique. Since outcomes like respiratory events, hypotension, procedural success, and recovery time are objective and measurable, RCTs provide strong internal validity for determining safety and effectiveness. If high-quality RCTs were limited, I would consider prospective cohort studies conducted in the emergency department setting. These studies can still provide useful real-world data on adverse events and recovery times, especially in large patient populations.

PICO search terms:

P	I	C	O
Shoulder dislocation	Ketamine	Propofol	Respiratory depression
Procedural sedation	Ketalar	2,6-diisopropylphenol	Hypotension
Adults	Dissociative anesthetic	Diprivan	Procedural success
Emergency Medicine	NMDA receptor antagonist		Recovery time

			Length of stay
			Adverse events

Search Strategy

	Pubmed	**Cochrane Library**	**Google Scholar**
Search Terms	("anterior shoulder dislocation" OR "shoulder dislocation") AND ("procedural sedation") AND ("emergency department") AND (ketamine) AND (propofol) AND ("respiratory depression" OR hypotension OR "recovery time" OR "length of stay" OR "adverse events")	shoulder dislocation AND procedural sedation AND ketamine AND propofol	shoulder dislocation procedural sedation ketamine propofol emergency department
Filters	Publication date: last 10 years, Article types: Clinical Trial, Randomized Controlled Trial, Systematic Review, Meta-Analysis, English language, Humans, Adults (19+ years), MEDLINE indexed	Publication date: January 2016 - January 2026	Results were sorted by relevance and Reviewed articles
Results	**About 65**	**About 12**	**About 329**

After completing searches across PubMed, Cochrane, and Google Scholar, I gathered numerous articles across the 3 data bases. I first screened titles in the first 2-3 pages to exclude studies that clearly did not match my clinical question, including those focused solely on pediatric populations, operating room anesthesia, ICU sedation, or rapid sequence intubation. I then reviewed abstracts to determine whether the studies directly compared ketamine and propofol in adult emergency department procedural sedation settings. Priority was given to randomized controlled trials and systematic reviews published within the last 10 years. I specifically selected studies that reported outcomes relevant to my PICO question, including respiratory depression, hypotension, procedural success, and/or recovery time. When multiple studies addressed similar outcomes, preference was given to the most recent and highest level of evidence. However, it is important to note that recent high-quality head-to-head randomized trials directly comparing ketamine alone versus propofol alone in adult emergency department procedural sedation were

limited, one well-designed randomized clinical trial from 2010 was identified on google scholar that directly compared the two agents. Given its direct relevance to the clinical question and lack of more recent head-to-head trials, this study was included as an exception to provide the most accurate comparative evidence available.

Results found:

Article #1: Safety of procedural sedation in emergency department settings among the adult population: a systematic review and meta-analysis of randomized controlled trials

Khan, M. T., Khan, A. R., Rohail, S., Raza, F. A., Ahmed, S., Siddiqui, A., Kumar, J., Yasinzai, A. Q. K., Sohail, A. H., & Goyal, A. (2024). Safety of procedural sedation in emergency department settings among the adult population: a systematic review and meta-analysis of randomized controlled trials. *Internal and emergency medicine*, *19*(5), 1385–1403. https://doi.org/10.1007/s11739-024-03697-2

Abstract

Procedural sedation and analgesia (PSA) are a common practice in emergency departments (EDs), aiming to alleviate pain, anxiety, and discomfort during various medical procedures. We have undertaken a systematic review and meta-analysis with the aim of assessing the incidence of adverse events associated with PSA, including those related to individual drugs and various drug combinations. The study adhered to PRISMA guidelines for a systematic review and meta-analysis of adverse events in ED sedation. A comprehensive search strategy was employed across ten databases, supplemented by searches on clinicaltrials.gov and manual reviews of reference lists. Data extraction focused on medication administration and adverse events. The study considered four types of adverse events: cardiac, respiratory, gastrointestinal, and neurological. Only randomized controlled trials (RCTs) focusing on PSA administered to adult patients within the ED setting were included. The statistical analysis employed OpenMeta Analyst to conduct a one-arm meta-analysis, with findings presented alongside their corresponding 95% Confidence Intervals. Forest plots were constructed to combine and evaluate results, and sensitivity analyses were performed to identify sources of heterogeneity. From a literature search of 4246 records, 32 RCTs were deemed suitable for this meta-analysis. The analysis included 6377 procedural sedations. The most common adverse event was hypoxia, with an incidence rate of 78.5 per 1000 sedations (95% CI = 77.5-133.5). This was followed by apnea and hypotension, with incidence rates of 31 (95% CI = 19.5-41.8) and 28.1 (95% CI = 17.4-38.9) per 1,000 sedations, respectively. Agitation and vomiting each occurred in 15.6 per 1,000 sedations (95% CI = 8.7-22.6). Severe adverse events were rare, with bradycardia observed in 16.7 per 1,000 sedations, laryngospasm in 2.9 per 1,000 sedations (95% CI = - 0.1 to 6), intubation in 10.8 per 1,000 sedations (95% CI = 4-17), and aspiration in 2.7 per 1,000 sedations (95% CI = - 0.3 to 5.7). Ketamine is found to be the safest option in terms of respiratory adverse

events, with the lowest rates of apnea and hypoxia, making it the least respiratory depressant among the evaluated drugs. Etomidate has the least occurrence of hypotension when used alone. Propofol has the highest incidence of hypotension when used alone and ranks second in hypoxia-related adverse events after midazolam. Using combinations of sedating agents, such as propofol and ketamine, has been found to offer several advantages over single drugs, especially in reducing adverse events like vomiting, intubation difficulty, hypotension, bradycardia, and laryngospasm. The combination significantly reduces the incidence of hypotension compared to using propofol or ketamine individually. Despite the regular use of procedural sedation, it can sometimes lead to serious adverse events. Respiratory issues like apnea and hypoxia, while not common, do occur more often than cardiovascular problems such as hypotension. However, the least frequent respiratory complications, which can also pose a threat to life, include laryngospasm, aspiration, and intubation. These incidents are extremely rare.

Key Points:

- There was significant variability in how hypoxia was defined across studies (some used <90%, others <92–95%). This contributed to high heterogeneity ($I^2 = 80\%$) for respiratory outcomes and is important when interpreting the pooled hypoxia rates.
- In the pooled analysis, propofol had the highest hypotension rate among single agents (55.7 per 1,000 sedations), confirming its known vasodilatory effects and tendency to lower blood pressure.
- Ketamine demonstrated the lowest hypoxia rate (20.8 per 1,000 sedations) among single agents, reinforcing its profile as the least respiratory depressant medication.
- Despite differences in respiratory event detection, severe respiratory complications such as intubation, aspiration, and laryngospasm were extremely rare across all agents, suggesting that life-threatening events are uncommon when proper monitoring is used.
- Ketamine was associated with higher agitation rates (61.8 per 1,000) compared to propofol (16.5 per 1,000), highlighting a clinically relevant difference in recovery profile.
- Vomiting was also more common with ketamine (61.8 per 1,000) compared to propofol (16.5 per 1,000), which may impact patient comfort and post-procedure experience.
- The ketamine + propofol combination (ketofol) demonstrated significantly lower hypotension rates (9.8 per 1,000) compared to either drug alone, suggesting a balancing cardiovascular effect when combined.
- In a sensitivity analysis including studies that used capnography or end-tidal CO_2 monitoring, respiratory event detection increased, suggesting that improved monitoring may identify more subclinical events rather than true clinical deterioration.
- Subgroup analysis showed that procedure type influenced adverse event rates, and heterogeneity decreased when orthopedic and cardiac procedures were analyzed separately. This indicates that complication rates may depend partly on the type of procedure performed.

- Importantly, the authors conclude that no single drug was superior across all safety domains. Each agent has a distinct adverse event profile, and sedation choice should be individualized based on patient stability, comorbidities, and procedure type.

This article is a systematic review and meta-analysis of randomized controlled trials (RCTs) focused specifically on adult procedural sedation in the emergency department. I chose this study because it represents the highest level of evidence available for evaluating safety outcomes between commonly used sedative agents. Unlike individual trials that may be limited by small sample sizes, this meta-analysis pools data from 32 RCTs and over 6,000 sedations, which strengthens the reliability of its findings. It directly examines clinically relevant adverse events such as hypoxia, apnea, hypotension, agitation, and vomiting. Additionally, the authors only included RCTs and excluded observational studies, which improves methodological quality and reduces bias. Since it was published in 2024, it also reflects more modern ED sedation practices and monitoring standards. Overall, I selected this article because it provides strong, up-to-date, and high-level evidence to support a safety comparison between ketamine and propofol in adult emergency department procedural sedation.

<u>Article #2:</u> Randomized Clinical Trial of Propofol Versus Ketamine for Procedural Sedation in the Emergency Department

Miner, J.R., Gray, R.O., Bahr, J., Patel, R. and McGill, J.W. (2010), Randomized Clinical Trial of Propofol Versus Ketamine for Procedural Sedation in the Emergency Department. Academic Emergency Medicine, 17: 604-611.
https://doi-org.york.ezproxy.cuny.edu/10.1111/j.1553-2712.2010.00776.x

Abstract

Objectives: The objective was to compare the occurrence of respiratory depression, adverse events, and recovery duration of propofol versus ketamine for use in procedural sedation in the emergency department (ED).

Methods: This was a randomized nonblinded prospective clinical trial of adult patients undergoing procedural sedation for painful procedures in the ED. Patients with pain before the procedure were treated with intravenous (IV) morphine sulfate until their pain was adequately treated at least 20minutes before starting the procedure. Patients were randomized to receive either propofol 1 mg/kg IV followed by 0.5 mg/kg every 3 minutes as needed or ketamine 1.0 mg/kg IV followed by 0.5 mg/kg every 3 minutes as needed. Doses, vital signs, nasal end-tidal CO2 (ETCO2), and pulse oximetry were recorded. Subclinical respiratory depression was defined as a change in ETCO2 of >10 mm Hg, an oxygen saturation of <92% at any time, or an absent ETCO2 waveform at any time. Clinical interventions related to respiratory depression were noted during the procedure, including the addition of or increase in the flow rate of supplemental oxygen, the use of a bag-valve mask apparatus, airway repositioning, or stimulation to induce breathing. After the procedure, patients were asked if they experienced pain during the procedure and had recall of the procedure. Physicians were asked to describe any adverse events or the occurrence of recovery agitation.

Results: One-hundred patients were enrolled; 97 underwent sedation and were included in the analysis. Fifty patients received propofol and 47 received ketamine. Subclinical respiratory depression was seen in 20 of 50 patients in the propofol group and 30 of 47 patients in the ketamine group (p = 0.019, effect size 22.8%; 95% CI = 4.0% to 43.6%). Clinical interventions related to respiratory depression were used in 26 of 50 propofol patients and 19 of 47 ketamine patients (p = 0.253, effect size = −13.7%; 95% CI = −33.8% to 6.4%). The median times of the procedures were 11 minutes (range = 4 to 33 minutes) for the ketamine group versus 10 minutes (range = 5 to 33 minutes) for the propofol group (p = 0.256). The median time to return to baseline mental status after the procedure was completed was 14 minutes (range = 2 to 47 minutes) for the ketamine group and 5 minutes (range = 1 to 32 minutes) for the propofol group (p < 0.001). Pain during the procedure was reported by 3 of 50 patients in the propofol group and 1 of 47 patients in the ketamine group (effect size = −3.9%, 95% confidence interval [CI] = −11.9 to 4.1). Recall of some part of the procedure was reported by 4 of 50 patients in the propofol group and 6 of 47 patients in the ketamine group (effect size = 4.8%, 95% CI = −7.6% to 17.1%). Forty-eight of 50 procedures were successful in the propofol group and 43 of 47 in the ketamine group (p = 0.357, effect size = 0.3%; 95% CI = −7.8% to 8.4%). Recovery agitation was reported in 4 of 50 in the propofol group and 17 of 47 in the ketamine group (effect size = 28.2%, 95% CI = 12.4% to 43.9%).

Conclusions: This study detected a higher rate of subclinical respiratory depression in patients in the ketamine group than the propofol group. There was no difference in the rate of clinical interventions related to respiratory depression, pain, or recall of the procedure between the groups. Recovery agitation was seen more frequently in patients receiving ketamine than in those receiving propofol. The time to regain baseline mental status was longer in the ketamine group than the propofol group. This study suggests that the use of either ketamine or propofol is safe and effective for procedural sedation in the ED.

Key Points:

- Ketamine showed a higher rate of monitor-detected respiratory changes ($ETCO_2$ shifts, brief desaturations), however, there was no significant difference in clinically meaningful airway interventions between ketamine and propofol. This suggests that the monitor findings did not necessarily reflect dangerous respiratory compromise.
- Procedural success was nearly identical (96% with propofol vs 95.7% with ketamine), reinforcing that either agent is effective for ED procedures such as fracture or dislocation reductions.
- Median time to return to baseline mental status was 5 minutes with propofol versus 14 minutes with ketamine. This difference is clinically meaningful in a busy emergency department setting.

- Ketamine was associated with substantially higher rates of recovery agitation (36% vs 8%). Some patients required additional medication (midazolam) to manage agitation. This likely contributed to longer recovery times.
- While propofol is known to decrease blood pressure, episodes of hypotension in this study were brief and resolved with IV fluids. No patients experienced serious complications related to blood pressure changes.
- Patients receiving propofol often required multiple doses during the procedure, while ketamine more frequently achieved adequate sedation with fewer redoses. This reflects the shorter duration and titratable nature of propofol.
- The authors note that propofol lacks intrinsic analgesic properties, whereas ketamine provides both analgesia and amnesia. This may explain the slightly higher reports of procedural pain in the propofol group, even if patients did not recall it later.
- There were no intubations, aspirations, arrhythmias, or transfers to higher levels of care, supporting the overall safety of both agents when used appropriately in monitored ED settings.
- Treating physicians knew which medication was being administered, which may have influenced supplemental oxygen use or intervention decisions. This is an important consideration when interpreting the results.

This is a Prospective Randomized Clinical Trial. I chose this article because it directly compares ketamine and propofol head-to-head in adult emergency department procedural sedation. Even though this study was published in 2010 and is older than 10 years, it remains highly relevant because there are very limited high-quality randomized controlled trials that directly compare ketamine and propofol alone in the ED setting. Most newer studies focus on ketofol (ketamine + propofol) or compare agents against other opioid regimens. Since my PICO question specifically compares ketamine versus propofol in adults undergoing ED procedural sedation, this trial remains one of the strongest direct comparisons available. This study evaluates clinically meaningful outcomes including respiratory adverse events, hypotension, recovery time, procedural success, and emergence reactions all of which directly answer my question. It was conducted in the emergency department and included adult patients undergoing procedures such as orthopedic reductions, which closely aligns with my clinical scenario. Although it is a single-center study and not blinded, it is a randomized clinical trial with clear outcome reporting and remains widely cited in the emergency medicine literature. Given the limited availability of more recent head-to-head RCTs comparing ketamine and propofol alone, this article remains an important and clinically relevant source of evidence for my analysis.

<u>Article #3:</u> Pharmacological agents for procedural sedation and analgesia in the emergency department and intensive care unit: a systematic review and network meta-analysis of randomised trials

Sharif, S., Kang, J., Sadeghirad, B., Rizvi, F., Forestell, B., Greer, A., Hewitt, M., Fernando, S. M., Mehta, S., Eltorki, M., Siemieniuk, R., Duffett, M., Bhatt, M., Burry, L., Perry, J. J., Petrosoniak, A., Pandharipande, P., Welsford, M., & Rochwerg, B. (2024). Pharmacological agents for procedural sedation and analgesia in the emergency department and intensive care unit: a systematic review and network meta-analysis of randomised trials. *British journal of anaesthesia*, *132*(3), 491–506. https://doi.org/10.1016/j.bja.2023.11.050

Abstract

Background: We aimed to evaluate the comparative effectiveness and safety of various i.v. pharmacologic agents used for procedural sedation and analgesia (PSA) in the emergency department (ED) and ICU. We performed a systematic review and network meta-analysis to enable direct and indirect comparisons between available medications.

Methods: We searched Medline, EMBASE, Cochrane, and PubMed from inception to 2 March 2023 for RCTs comparing two or more procedural sedation and analgesia medications in all patients (adults and children >30 days of age) requiring emergent procedures in the ED or ICU. We focused on the outcomes of sedation recovery time, patient satisfaction, and adverse events (AEs). We performed frequentist random-effects model network meta-analysis and used the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) approach to rate certainty in estimates.

Results: We included 82 RCTs (8105 patients, 78 conducted in the ED and four in the ICU) of which 52 studies included adults, 23 included children, and seven included both. Compared with midazolam-opioids, recovery time was shorter with propofol (mean difference 16.3 min, 95% confidence interval [CI] 8.4-24.3 fewer minutes; high certainty), and patient satisfaction was better with ketamine-propofol (mean difference 1.5 points, 95% CI 0.3-2.6 points, high certainty). Regarding AEs, compared with midazolam-opioids, respiratory AEs were less frequent with ketamine (relative risk [RR] 0.55, 95% CI 0.32-0.96; high certainty), gastrointestinal AEs were more common with ketamine-midazolam (RR 3.08, 95% CI 1.15-8.27; high certainty), and neurological AEs were more common with ketamine-propofol (RR 3.68, 95% CI 1.08-12.53; high certainty).

Conclusion: When considering procedural sedation and analgesia in the ED and ICU, compared with midazolam-opioids, sedation recovery time is shorter with propofol, patient satisfaction is better with ketamine-propofol, and respiratory adverse events are less common with ketamine.

Key Points:

- This was a network meta-analysis which means the authors compared multiple drugs simultaneously, even if two drugs were never directly compared in a head-to-head trial.

- Propofol consistently ranked among the fastest for recovery time. The Recovery was about 9-16 minutes shorter compared to several other regimens. The authors defined a 5-minute difference as clinically meaningful and propofol exceeded that threshold.
- Ketamine-propofol (ketofol) had fewer respiratory adverse events than propofol alone. When directly compared, propofol alone had more respiratory events than ketofol (RR ~1.37, moderate certainty). This suggests ketamine may provide some respiratory protective effect when combined.
- Propofol especially when combined with opioids) was associated with more cardiac adverse events.This mainly reflects hypotension and bradycardia.
- Nausea and vomiting were significantly more common with ketamine compared to some other regimens. This is clinically relevant for discharge comfort and patient experience.
- Neurological adverse events such as agitation, hallucinations were higher with ketamine-containing regimens. Compared to ketamine, propofol had significantly fewer neurological adverse events
- The authors performed subgroup analyses and did not find major differences between adult and pediatric populations in relative effects.
- Even though the study is large, some comparisons were downgraded for imprecision. So while trends are clear, not every comparison is definitive.
- The authors emphasize the importance of individualized decision-making based on airway status, hemodynamics, procedure type, and recovery priorities.

This is a Systematic Review and Network Meta-Analysis of Randomized Controlled Trials. I chose this article because it represents the highest level of evidence available on procedural sedation medications in the emergency department. It includes 82 randomized controlled trials with 8,105 patients, which makes it both large and methodologically strong. Unlike a simple meta-analysis, this was a network meta-analysis, meaning it compared multiple sedation agents at once using both direct and indirect comparisons. That allowed for stronger overall conclusions about ketamine, propofol, and combination regimens. This article was relevant to my PICO question because it evaluates recovery time, respiratory adverse events, cardiac adverse events, gastrointestinal effects, and neurological adverse events which were all outcomes that directly relate to my comparison of ketamine versus propofol in adult ED procedural sedation. Although it includes some ICU data as well, the majority of studies were conducted in the emergency department (78 out of 82), which makes it applicable to my setting.

What is the clinical "bottom line" derived from these articles in answer to your question?

Based on the reviewed evidence, propofol would be the preferred agent for this 46 year old hemodynamically stable patient requiring procedural sedation for shoulder reduction. Both ketamine and propofol are safe and effective, with similar procedural success rates. The main

differences are in their side effect profiles and recovery characteristics. Respiratory safety appears comparable in stable adults when appropriate monitoring is used. While propofol is more likely to cause hypotension, these episodes are typically brief and manageable in otherwise healthy patients. The most clinically meaningful difference is the recovery profile. Propofol is associated with significantly faster return to baseline mental status and less recovery agitation compared to ketamine. Ketamine, although hemodynamically supportive and less likely to cause hypotension, is associated with more emergence reactions and vomiting.

For this specific patient, hemodynamically stable, no cardiovascular instability thus, propofol offers quicker recovery and a smoother post-procedure course without increased clinically significant respiratory risk. Ketamine would be more appropriate in patients with hypotension or shock, but that is not the case here. Regardless of the agent chosen, appropriate monitoring and preparedness for adverse events remain essential.