

Paramedics practice of administering S-ketamine for analgesia following trauma in the prehospital setting.

Introduction.

Trauma is a common reason for activating emergency medical services (EMS) worldwide (Møller *et al.* 2015). Following physical trauma patients are often subjected to some level of pain or discomfort. The subsequent need for pain management and experienced severity and timing of pain can be a predictor for patient outcomes (Ahmadi *et al.* 2016). Pain management is a core skill across all levels of prehospital care, and paramedic administration of (S)-Ketamine (Ketamine) as an analgesic has been proven safe and effective (Jabourian *et al.* 2020). Educational standards and Clinical Practice Guidelines (CPG) for pain management are heterogeneous across EMS systems, and there is a relatively small body of literature concerned with Paramedic practice therefore it is not a well-defined concept (Williams *et al.* 2021). National regulation and education are contributors to this and in recent years calls for uniform education across continents have been made (Dúason *et al.* 2021). In this review, relevant databases were searched for articles regarding paramedics' practice of administering Ketamine for analgesia, following trauma in the prehospital setting.

Method.

Literature was identified by searching CINAHL (Medline, Academic search included), Embase, Pubmed, Scopus and Glucksman Library online. Boolean operators “AND” and “OR” were applied to combine search terms, and “NOT” defined exclusion criteria. After duplicate removal 38 unique articles were identified. Filters were applied to remove articles more than 10 years old, non-English language and non-published articles. Also, articles were excluded if they were based in a military or combat setting, traumatic pain was not well defined, physician-administered Ketamine or in-hospital setting was found. Screening for inclusion/exclusion criteria left 7 articles for inclusion. Supplemental free search of Google Scholar with applied filters and exclusion criteria as mentioned earlier found 4 articles meeting the inclusion criteria. A total of 11 unique articles were eligible for review.

Inclusion			
Population	Intervention	Outcome	Time
ems	ketamine	trauma*	pre-hospital
"emergency medical services paramedic* ambulance	esketamine	fall* injur* fracture* analgesi* pain	prehospital "pre hospital" "out of hospital"
Exclusion			
Population	Intervention	Outcome	Time
phycisian doctor		sedat* anesthe* intubat*	combat "battlefield" "emergency department"

Tabel 1- Search Terms

Results.

Quality of current literature.

The identified articles were mainly retrospective cohort studies (8/11), two cross-sectional studies and one mixed-methods study. One paper is disclosed as a non-scientific paper relying on self-reported audit data, although published by a peer-reviewed journal (Metcalf 2018). 8/11 articles have a single service or county study population, one paper has two counties as study groups and two articles are nationwide. Applying the GRADE (Guyatt *et al.* 2011) framework with paramedic practice as an outcome found an overall Very Low to Low quality of the current evidence (See appendix 1).

Author and Year	Study type	Country	Population	Inclusion period	(n)	GRADE
Mahmood <i>et al.</i> 2023	Retrospective Cohort	US	Two counties	10-2019 - 3/2021	14	Very Low
Häske <i>et al.</i> 2023	Observational Cross-sectional	Germany	Single service/county	6/2022 - 11/2022	119	Low
Goyal <i>et al.</i> 2022	Retrospective Cohort	US	Single service/county	01/2019-12/2020	1291	Moderate
Lourens <i>et al.</i> 2020	Retrospective Cohort	SA	Single service/county	2017	1	Very Low
Cowley <i>et al.</i> 2018	Retrospective Cohort	UK	Single service/county	3/2013 - 4/2017	449	Low
Matthews <i>et al.</i> 2017	Retrospective Cohort	SA	Single service/county	8/2013-7/2014	9	Very Low
Losvik <i>et al.</i> 2015	Retrospective Cohort	Iraq	Countrywide	01/1997-12/2006	713	Very low
Randal <i>et al.</i> 2022	Retrospective Cohort	US	Single service/county	6/2018-12/2019	79	Low
Metcalf <i>et al.</i> 2018	Retrospective Cohort	UK	Single service/county	7/2016-6/2017	69	NA
Buckland <i>et al.</i> 2018	Cross-sectional Survey	US	Countrywide	6/2015 - 11/2015	1086	Low
Johnston <i>et al.</i> 2023	Mixed-Methods	Canada	Single service/county	06/2020	ND	NA

Table 2: US - United States, SA - South Africa, UK - United Kingdom, (n) – Unique patients, ND – Non Disclosed, NA – Not Applicable.

Main themes.

Educational level and confidence:

About half of the articles (4/11) describes paramedics administering Ketamine for analgesia has a bachelor's degree or an equivalent qualification (Respectively: 2 United Kingdom, 1 South Africa, 1 Canada), four articles disclose US paramedic training without further specification (ND), one describes BSc and local specialist training (Metcalf 2018) and one reports critical care paramedics (CCP) holding a post graduate certificate or equivalent qualification (Cowley *et al.* 2018). Two articles report local training only and one does not disclose. Three of eight articles report on further local training focused on Ketamine administration.

Among a sample of paramedics from across the USA, 53% reported receiving education in Ketamine doing initial training and 42% reported education through personal efforts or initiative. 33%? Reported continuous training in Ketamine administration through local training.

In the same study group 94% of paramedics reported they felt confident about administering Ketamine as an analgesic even though almost half of the participants had administered Ketamine <10 times (48%) (Buckland *et al.* 2018). In a small sample of Canadian Primary Care Paramedic confidence in

administering IN Ketamine following a local training program, was found to be high (Johnston *et al.* 2023).

One paper measured the prevalence of consultant calls from paramedics in one UK county regarding Ketamine administration to 54% (Cowley *et al.* 2018) and in another UK article 26% of paramedics had called for senior medical advice (Metcalf 2018). One qualitative study states that study group paramedics report a high degree of confidence in support from local management regarding Ketamine administration (Johnston *et al.* 2023).

CPG and dosing:

In 8/11 articles, the study population had CPGs determining administration route, individual dosing, and max total volume. 2 of 8 articles did not evaluate the volume of medicine and CPGs were not disclosed in one paper. Only one article found a strict single dose regime and repeated doses were possible in 5 of 8 CPGs. Dosing ranged from 0,1-0,3 mg/kg IV/IN bolus, and one CPG stated Ketamine was to be given as a 5-10 min IV drip (Randall *et al.* 2022). In two articles a 5 or 10 mg IV bolus is recommended for the ease of the practitioner. One article described paramedics regularly exceeding max total volume allowed in pediatric patients (Goyal *et al.* 2023). One CPG states 1 mg Midazolam is to be given with any dose of Ketamine (Häske *et al.* 2023), and two CPGs describe a benzodiazepine can be administered if the patients present with agitation after Ketamine administration (Losvik *et al.* 2015; Häske *et al.* 2023). One CPG also describes the administration of 1mg Atropin IV if transport or retrieval times were prolonged to mitigate cholinergic response (Losvik *et al.* 2015). Ketamine is described as both a mono- and multimodal treatment in similar study groups (Matthews *et al.* 2017; Lourens *et al.* 2020). Two articles report mean total dose given as 28mg, interquartile range 20-40mg (Cowley *et al.* 2018), and 30mg ranging from 5-90mg (Metcalf 2018).

Patient demographics and injury severity:

7/11 articles account for all age groups, two evaluate pediatric patients, one adult patients only and one senior patients only (<65 years). 7/11 articles describe a greater likelihood of receiving Ketamine if the patient has single trauma to extremities or other visible injuries e.g. luxation of hip or shoulder. This is comparable between patients with single dose and multiple doses administered.

In a study group of geriatric patients, a higher ISS (0-10) were reported in the Ketamine group vs non-Ketamine group (9/10 vs 5/10). The same author found that patients receiving Ketamine as an analgesic were more likely to be transferred from a local hospital to a specialist hospital 10% vs 2,5%. Length of stay in the emergency department for patients in the same Ketamine group were shorter than the non-ketamine group, suggesting that patients are more severely injured and in need of rapid transfer (Randall *et al.* 2022). In an all-ages study group 97% of patients receiving Ketamine reports an initial pain as unbearable with a median pain score (NRS 1-10) of 10 (Häske *et al.* 2023).

Author and year	Level of education	Patient age (years)	CPG	Predictor
Mahmood <i>et al.</i> 2023	ND	7 to12	0,2mg/kg IV, max 50mg	Visible (luxation)
Häske <i>et al.</i> 2023	ND		0,125mg/kg IV, repeated. 1mg Midazolam IV, repeated once if needed.	Severe pain
Goyal <i>et al.</i> 2022	ND	<18	0,25mg/kg IV	
Lourens <i>et al.</i> 2020	Local	All		
Cowley <i>et al.</i> 2018	Bsc + PGC	>12	0,1mg/kg IV (40-70kg 5mg, >70kg 10mg)	Lower limp and poly trauma
Matthews <i>et al.</i> 2017	Bsc	All		Lower limb
Losvik <i>et al.</i> 2015	Local 3x150 hours	Adults	0,2mg/kg IV, Diazepam 5mg IVif agitated. If prolonged transport 1 mg Atropin IV.	ISS higher
Randal <i>et al.</i> 2022	ND	All	0,3mg/kg IV, max 30mg in a 5 min drip	ISS higher
Metcalf <i>et al.</i> 2018	Bsc	All	10 mg dose IV, if Morphine administered 5mg. Max 0,5mg/kg or <50 kg 20mg, <80 kg 40mg, >80 kg 60mg.	Visible limb injury
Buckland <i>et al.</i> 2018	ND	All		
Johnston <i>et al.</i> 2023	BSc	All	IN only	

Table 3: US - United States, SA - South Africa, UK - United Kingdom, AAS – Associate of Applied Science, ND – Not disclosed, BSc – Bachelor of Science, PGC – Post Graduate Certificate, CPG – Clinical Practice Guideline, ISS – Injury Severity Score.

Discussion.

Paramedic practice regarding administration of Ketamine is heterogeneous worldwide though recommended doses seems to be more uniform. Comparing paramedic and physician practices in providing prehospital pain management has suggested that paramedics can be more reluctant to administer more potent analgesics (Kiavialaitis *et al.* 2020). When injuries are more visible the odds for physician to administer a potent analgesic are increased, and the findings in this study suggests the same trend for paramedic-administered Ketamine (Metcalf 2018). In the same article the author also mentions that the most injured and critical patients might have a fall in GCS and therefore were not provided analgesia by a paramedic following local CPG where patients must have a GCS of 15 to be eligible for Ketamine. In the UK and South African settings HEMS or MICU units can be deployed for the most critical calls and a physician on scene can possibly alter paramedics practice. Anecdotal evidence of adverse events and unpleasant experiences following Ketamine administration are well known among EMS personnel (Buckland *et al.* 2018), but current literature suggests that the actual number of adverse events is low and with minor severity (Cowley *et al.* 2018; Jabourian *et al.* 2020; Häske *et al.* 2023).

Actual doses given by paramedics can be higher than recommended and its suggested that being a multipurpose medication and a fairly new addition to paramedics practice as an analgesic, there can be some confusion regarding dosing and administration routes (Goyal *et al.* 2023). Proper education, follow up training and access to supervision has shown to be an effective measures in supporting paramedics (Johnston *et al.* 2023).

Limitations.

An obvious limitation of this paper is the quality of evidence in the body of included articles. It was not possible to identify articles with a study design or methodology that directly evaluate paramedic practice. Also, this paper have only been semi-structured in regards of the review process and only one reviewer have been involved.

Conclusion.

The findings of this review can contribute to the current body of literature regarding paramedic practice. The topic is not well defined and regarding administration of Ketamine for analgesia, current practices are heterogenous worldwide. The findings suggest that ongoing education and confidence in support from administrators are important to support paramedics administration of Ketamine. Further research is needed to understand paramedics practices regarding Ketamine administration.

Appendix 1:

	GRADE										RELEVANT FINDINGS	
	Study type score	Lower					Publication bias	Large effect	Dose response	Higher		QOE
		Risk of bias	Inconsistency	Indirectness	Imprecision	All plausible confounding						
Mahmood <i>et al.</i> 2023	Low	--									Very Low	Dissociation 14.3%. Addresses potential selection bias. Paramedics are unexperienced with Ketamine
Häske <i>et al.</i> 2023	Low	-					+				Low	General satisfaction with treatment. Small sample size. >80y reported more side effects
Goyal <i>et al.</i> 2022	Low						+				Moderate	ALS and phycisians. Few pt's with pain score. 68/2401 recieved single dose 3/4. 14% recieved 2.5x recommended dose
Lourens <i>et al.</i> 2020	Low	--									Very Low	analgesia. 54.1% call to consultant. Median dose 30mg. Trauma patients 5-90mg total.
Cowley <i>et al.</i> 2018	Low	-					+				Low	Patients needing higher doses or sedation most likely handed over to HEMS.
Matthews <i>et al.</i> 2017	Low		-								Very Low	Few administrations. 58% singel dose. 67% only analgesic.
Losvik <i>et al.</i> 2015	Low	-									Very Low	Prolonged transport time when given Ketamine
Randal <i>et al.</i> 2022	Low	-							+		Low	Patients transferred in Ketamine group 10% vs 2.5%. LOS in ED in Ketamine group 385 min vs 528 min. Dissociation only seen after first dose.
Metcalf <i>et al.</i> 2018	NA	--									NA	Potentially HART paramedics are sent to an intermediate group of patients. Severely ill/injured patients may be rushed to the hospital or HEMS are dispatched alongside paramedics.
Buckland <i>et al.</i> 2018	Low	-							+		Low	1/3 of NRP's can administer Ketamine by CPG. 95% feel comfortable, even though anecdotal evidence claims adverse events are normal.
Johnston <i>et al.</i> 2023	Low						+				NA	

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