Remimazolam for procedural sedation: a future sedative potential in the emergency department?

Procedural sedation (PS) is a frequently performed clinical practice in the ED[1] aiming to facilitate a state that allows patients to tolerate uncomfortable procedures.[2] The ideal agent for PS in the ED should provide anxiolysis, analgesia and amnesia in a rapid and predictable manner, with minimal adverse events and a rapid recovery phase.[3] Remimazolam (RMZ) is a novel benzodiazepine with rapid conversion into an inactive metabolite, making it ultra-short acting. Compared with other intravenous sedative agents, it is less likely to cause cardiovascular or respiratory depression and in case of an adverse event, it can be antagonised using flumazenil.[4] This beneficial risk profile suggests safe use of RMZ in the ED. Previous studies have described the success of RMZ for PS during endoscopic procedures[5]; however, there is no literature on the use of RMZ in the ED.

The aim of the current study was to gain knowledge on the efficacy and safety of RMZ for PS in the ED. Therefore, we conducted an observational prospective multicentre study in patients aged 18 years or older requiring PS in the ED at Canisius Wilhelmina Hospital or Radboudumc in Nijmegen, the Netherlands. There was no competing interest, and no funding was received. Patients were enrolled from August 2022 to December 2022, and verbal informed consent was obtained prior to the procedure. Patients with an allergy to benzodiazepines or a body mass index >40 were excluded from the study. Following our national guidelines,[6] the initial dose of RMZ depends on the desired effect, specifically 7.5 mg for sedation and 5 mg for anxiolysis or sedation in special patient groups (age >65 years, American Society of Anesthesiologists >3 and body weight <50 kg). Top-up doses of 2.5 mg, up to a maximum of 5, were administered if the desired sedation level was not achieved after 2 min. In expected painful procedures, RMZ was combined with analgesia (fentanyl or esketamine). The primary outcome was the success of sedation, defined as successful completion of the procedure with no requirement for a rescue sedative. Secondary outcomes were starting dose of RMZ, the depth of sedation classified by the Richmond Agitation-Sedation Scale (RASS), number of top-up doses needed, achievement of amnesia (based on patients' self-report), time to recovery (RASS 1) and adverse events.

Table 1 Demographic data

Patient characteristics	Number (%) or median (IQR)
Total number of patients	26 (100)
Age (years)	66 (53–72)
ASA classification	
ASA I	5 (19)
ASA II	16 (62)
ASA III	5 (19)
Type of procedure	
Hip reduction	8 (31)
Closed fracture reduction	8 (31)
Electrical cardioversion	4 (16)
Shoulder reduction	2 (8)
Incision and drainage	2 (8)
Ureteral stent removing	1 (4)
Urgent endoscopy	1 (4)
Combined analgesia	
Fentanyl	14 (54)
Esketamine	2 (8)

ASA, American Society of Anesthesiologists.

Table 2 Primary and secondary outcomes

Primary outcome	Number (%) or median (IQR)
Success rate of sedation	21 (81)
Successful completion of the procedure	26 (100)
Requirement for a rescue sedative (propofol)	5 (19)
Secondary outcome	
Starting dose of remimazolam	
5 mg	11 (42)
7.5 mg	11 (42)
10 mg	4 (15)
Maximum sedation depth (RASS)	−4 (−4 to −4)
Top-up doses	1.4 (0.0–2.0)
Achieved amnesia	26 (100)
Time to recovery (min)	15 (5–29)
Adverse events	
Manual airway manoeuvre*	8 (31)
Hypotension	0 (0)
Bradycardia	0 (0)
Fever	1 (4)
Prolonged sedation requiring flumazenil	0 (0)

*Head tilt-chin lift or jaw-thrust manoeuvre.
RASS, Richmond Agitation-Sedation Scale.

There were 26 patients who underwent sedation with RMZ with a median age of 66 years (IQR 53–72) (table 1). Hip reduction and closed fracture reduction accounted for over half of procedures. Initial dose ranged from 5 to 10 mg (table 2). All procedures were successfully competed; however, in five cases, additional propofol was required, indicating a success rate of sedation with RMZ alone of 81%. All patients had amnesia for the procedure and a median of 1.4 top-up doses (IQR 0–2) were needed for the desired sedation level. Adverse events included airway obstruction requiring manual airway manoeuvres (8 cases, 31%). Median recovery time was 15 min (IQR 5–29). None of the patients developed hypotension or other serious complications.

This small case series shows that RMZ facilitates successful procedural sedation in patients in the ED. Specifically, RMZ exhibited high sedative efficacy, with all patients experiencing amnesia for the event, a fast recovery and no incidence of clinically relevant adverse events. However, limitations of our study include a small sample size, no comparison with traditional sedative drugs and the administration of a higher starting dose of RMZ based on physicians' experience. Therefore, high-quality randomised controlled trials with large samples and comparison with other sedatives are needed in the future to investigate the potential of RMZ.

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