The Comparison of Dexmedetomidine and Midazolam Used for Sedation of Patients Undergoing Upper Gastrointestinal Endoscopy: A Prospective Comparative Study

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Research Article

Keywords: Dexmedetomidine, Midazolam, sedation, and upper endoscopy.

Posted Date: November 27th, 2024

DOI: https://doi.org/10.21203/rs.3.rs-5405463/v1

Additional Declarations: No competing interests reported.

Abstract

Background: Endoscopic procedures are essential for diagnostic testing, examining, and treating a wide range of disorders like gastrointestinal tract blood loss, foreign object removal, and many other complicated procedures such as Endoscopic retrograde cholangiopancreatography. An endoscope is an irritating and painful procedure. during which patients should be anesthetized to avoid mobility, pain, coughing, gagging, and nausea. So, sufficient analgesia and sedation agents should be given and monitored with minimal side effects or complications. These agents can keep patients'response to pain and verbal stimuli without failing respiratory or cardiovascular function. The current study aims to compare and investigate the efficacy and safety of Midazolam versus Dexmedetomidine in terms of respiratory, hemodynamic, analgesia, sedation, patient satisfaction, endoscopist satisfaction, and adverse effects in patients undergoing upper endoscopy at An-Najah National University Hospital.

Methodology: A prospective observational study was performed on 68 patients (aged 18-60) undergoing upper endoscopy using theAmerican Society of Anesthesiologists (ASA) Physical Status Classification System (grades one and two). The study was conducted at An-Najah National University Hospital, Nablus-Palestine, between October 2021 and January 2022. All subjects received information about the purpose of the study, the study protocol, and the consent form was obtained from each subject.

Results: Regarding patient satisfaction, the Dexmedetomidine demonstrated much higher satisfaction, minor discomfort, and less anxiety than Midazolam with $P<0.05$. Regarding endoscopy specialists, the satisfaction, discomfort, gagging, retching, and technical difficulty showed that Dexmedetomidine outperformed the Midazolam with $P<0.05$. Dexmedetomidine patients recovered faster than Midazolam patients with $p <0.05$, Midazolam needs 2.4 ± 7.7 minutes to be sedated while Dexmedetomidine needs 9.5 ± 1.1 minutes , and this difference is significant since the $p <0.05$. Regarding side effects occurrence, Dexmedetomidine had fewer side effects than the Midazolam, but with no statistically significant difference. Regarding vital signs, there is no significant difference between Midazolam and Dexmedetomidine.

Conclusions: Dexmedetomidine outperformed Midazolam in recovery time, patient satisfaction, endoscopy specialist satisfaction, discomfort, anxiety, and retching; Dexmedetomidine appears to be a useful alternative to Midazolam for sedating patients during upper endoscopy because it is both safe and effective.

Background

In conscious sedation, patients can keep their response to pain and verbal stimuli without failing respiratory or cardiovascular function [1]. This type of sedation merges a benzodiazepine, and opioid and is commonly used in minor surgeries and endoscopy [2] [3]. Endoscopic procedures are essential for the treatment, diagnosis, and evaluation of many disorders like gastrointestinal tract bleeding, foreign body removal or in some complicated procedures like endoscopic retrograde cholangiopancreatography

(ERCP), which uses x-ray guidance to accurately treat and diagnose diseases inside the pancreas, bile ducts, liver, and gallbladder [4]. During the procedure, pain, anxiety, fear, and retching may let patients to be uncooperative, and it can induce harmful respiratory and cardiovascular effects [5]. The endoscope is an irritating and painful procedure performed without analgesia and sedation [6]. During endoscopy, patients should be anesthetized to avoid mobility, pain, coughing, gagging, and nausea. So, sufficient analgesia and sedation agents should be given and monitored [7]. It is necessary to guarantee that the client's protective reflexes are intact but immobile [8]. After this type of anesthesia, the patient can recover his reactions and return home on the same day, this benefits both the patient and the hospital so that the occupancy rate in hospitals is reduced and the hospital can receive more cases per day. Other advantages of this type of sedation over general anesthesia are the speed of recovery, ease of response of the patient to the nurse when he awakens and the increase in his level of satisfaction and comfort [9–11]. While using sedative drugs, the study aimed to do analgesia, amnesia, and quick patient recovery to the same level of consciousness before the procedure [12]. Midazolam is one of the benzodiazepines family with a short duration and rapid onset of action [13]. It triggers γ-aminobutyric acid receptors and causes central nervous system depression [14]. Midazolam was the most common sedative agent used in critical care units [15].

Dexmedetomidine is an antagonist and highly selective drug that works on alpha 2-adrenoceptor and has sedative, amnestic, sympatholytic, and analgesic properties [16]. Dexmedetomidine started to be used in the critical care unit in 1998, then in other medical applications [17]. Dexmedetomidine is a good surrogate to Midazolam in sedation [18]. With the increase in the use of Dexmedetomidine, many side effects appeared, such as bradycardia and hypotension [19]. Beneficent clinical applications of Dexmedetomidine sedation are found in endoscopic procedures and retrograde cholangiopancreatography [20]. In terms of the respiratory system, compared to Midazolam, Dexmedetomidine has been statistically shown to be more effective, it has a lower effect on oxygen saturation in the blood and more respiratory stability, as it leads to faster recovery, it is recommended to be used as an alternative, especially for people who suffer from respiratory problems [21] [22] [2]. Regarding the cardiovascular system, the most critical complication of Dexmedetomidine is bradycardia and hypotension [23]. However, other studies found no effect of hypotension or bradycardia. [21] [24]. The slow flow of the drug for ten minutes showed that the drug does not lead to a decrease in blood pressure, the correct preparation and administration of the drug give positive results regarding the safety of the circulatory system [25]. However, caution should be exercised while administering this drug to people with slow heartbeat problems or heart block [26]. And if the comparison between the two drugs was made from the perspective of anesthesia, Dexmedetomidine proved more effectiveness during endoscopy, as the degree of anesthesia that the patient reaches through Dexmedetomidine gives the patient the ability to respond to commands such as moving to the right or left [27–29]. In addition to the side effects that occur during anesthesia, complications during endoscopic operations were more minor when using Dexmedetomidine, the most important of which are respiratory failure and the need for pulmonary intubation, therefore, the benefits gained from Dexmedetomidine exceed that of Midazolam

during endoscopy [30]. The optimum technique to reduce pain and provide an adequate amount of sedation via endoscopy is still being debated and researched [13].

There are numerous contraindications to using Midazolam, such as hypotension, acute angle-closure glaucoma, and deffrent types shocks [31]. Adjusting the dosage of the medication should be done with caution in the patients with liver and kidney disease, drug-dependent and alcohol-dependent individuals, pregnant women, comorbid psychiatric problems, and children, to avoid the accumulation of Midazolam active metabolites in severely ill and elderly patients, administration should be done with caution [32]. Patients with renal failure and those using opioids, clarithromycin, erythromycin, sertraline, diltiazem, alcohol, protease inhibitors, antipsychotics, phenobarbital, rifampin, phenytoin, and carbamazepine should be administered with caution, furthermore, grapefruit juice boosts drug activity by inhibiting the CYP450 enzyme, but St. plant lowers drug impact by activating the CYP450 enzyme [33]. Midazolam toxicity is uncommon but can occur when combined with central nervous system depressants such as tricyclic antidepressants, opioids, and alcohol. In elderly patients, intravenous administration increased the risk, particularly in patients with chronic obstructive pulmonary disease. Furthermore, the role of sedation in endoscopy is important to promote patient's participation throughout the process; however, there is less evidence on the effects of Dexmedetomidine in upper endoscopy [9–11].

We gathered information comparing Midazolam and Dexmedetomidine for upper endoscopy from databases like Google Scholar, Scopus, and PubMed, using keywords such as "Dexmedetomidine," "Midazolam," and "sedation". A review of studies that found Dexmedetomidine superior in analgesia, reliability, and patient and provider satisfaction, with both drugs showing similar safety profiles for respiratory and circulatory systems when dosed accurately [34]. In a meta-analysis of nine studies involving 657 patients, Dexmedetomidine was linked to fewer side effects, with no significant differences in oxygen saturation or mean arterial pressure between the drugs [21]. One protocol administered 0.3 mcg/kg Dexmedetomidine and 1 mcg/kg Fentanyl ten minutes before endoscopy, resulting in higher satisfaction and oxygen levels compared to the Midazolam group, which used a similar protocol [35]. Another study reported that Dexmedetomidine caused fewer side effects, like retching, and greater provider satisfaction compared to Midazolam, which used a 0.07 mg/kg dose with lidocaine throat spray [7]. In ERCP studies, Dexmedetomidine was preferred due to lower oxygen desaturation and faster recovery compared to Midazolam [36] [20, 37]. In patients aged 18–80, Dexmedetomidine protocols showed similar sedation levels as Midazolam but with fewer side effects like nausea, coughing, and gagging, as well as higher endoscopist satisfaction [38].

There has been minimal research on the use of Dexmedetomidine in endoscopy, both globally and within Palestine, despite its proven usefulness, efficacy, and safety across various medical applications [39]. This study aims to compare and evaluate the efficacy and safety of Midazolam versus Dexmedetomidine for patients undergoing upper endoscopy at An-Najah National University Hospital. The primary focus includes respiratory and hemodynamic stability, analgesia, sedation, patient satisfaction, endoscopist satisfaction, and adverse effects.

Primary Outcomes include changes in vital signs such as mean arterial pressure (MAP), oxygen saturation (SpO2), respiratory rate, and heart rate. Additional primary outcomes encompass the Ramsay Sedation Scale (RSS), time to achieve full sedation, recovery time, the need for additional doses of sedative or analgesic drugs, and any interventions required to manage side effects during the procedure.

Secondary Outcomes include patient and endoscopy specialist satisfaction. For patients, secondary outcomes focus on anxiety, gagging, discomfort, and overall satisfaction. For the endoscopy specialist, secondary outcomes assess technical difficulty, satisfaction with the patient's sedation level, as well as patient discomfort, retching, and gagging.

The purpose of this study is to identify a safer and more effective sedative for upper gastrointestinal endoscopy by comparing Midazolam and Dexmedetomidine. An ideal sedative would provide analgesia, amnesia, a rapid return to pre-treatment consciousness, and fewer adverse effects.

Methods

Study Design

This study follows a prospective, observational design aimed at comparing two sedation interventions for patients undergoing elective upper endoscopy. Two groups of patients were observed: one group received the sedative Dexmedetomidine, while the other was administered Midazolam. Both groups underwent a pre-test assessment to establish baseline data before the intervention. Post-intervention, outcomes were measured using a post-test assessment to evaluate the efficacy and safety of each sedative in achieving the desired sedation level, maintaining patient comfort, and minimizing complications. The same endoscopist performed all procedures to maintain consistency in technique, while the anesthesiologist, who was not involved in the research data analysis, conducted the sedation to reduce bias.

Study Setting and Site

The study was conducted in the Endoscopic Department at An-Najah National University Hospital, located in Nablus, Palestine. The department serves a range of patients undergoing diagnostic and therapeutic endoscopic procedures. All procedures followed standard protocols established by the hospital's endoscopy team and took place in a clinical environment with access to emergency equipment, ensuring patient safety throughout the study.

Study Population

The study population consisted of adult outpatients scheduled for elective upper endoscopy procedures at An-Najah National University Hospital. Inclusion criteria focused on patients aged 18 to 60 with American Society of Anesthesiologists (ASA) physical status classifications of I or II, indicating patients

with no or mild systemic disease. Data collection took place from October 2021 to January 2022. The study received ethical approval from the Institutional Review Board (IRB) at An-Najah National University and the Ethics Committee of An-Najah National University Hospital. All patients received a clear explanation of the study objectives, protocol, and potential risks and benefits. Written informed consent was obtained from each participant, and confidentiality, autonomy, and the right to withdraw were assured throughout the study.

Sampling and Sample Size Calculation

A sample size calculation was performed based on an expected difference in satisfaction and sedation efficacy between the two drugs, using a type I error (α) of 0.05 and a type II error (β) of 0.20 to ensure an 80% power to detect statistical significance. Based on prior studies, it was anticipated that patients receiving Dexmedetomidine would report a higher satisfaction rate (90%) compared to those receiving Midazolam (55%). Using an online sample size calculator for two-proportion testing, it was determined that each group required 34 participants, totaling 68 patients, after accounting for a potential 10% dropout rate.

Data Collection Tools and Procedure

Data was systematically gathered using three structured tools to ensure a comprehensive and reliable approach (Appendix B). First, a Sociodemographic Data Sheet was used to document each patient's initials, case number, age, gender, height, weight, BMI, substance use history, education level, and the reason for undergoing endoscopy (such as dysphagia, esophageal reflux, or dyspepsia). This information provided essential background on each participant, supporting the analysis of how these factors might influence sedation and recovery.
In addition, a Sedation and Recovery Times record was maintained for each patient, capturing the time needed to achieve full sedation (defined as a Ramsay Sedation Scale [RSS] score of ≤ 4), the time to reach recovery (RSS score of 2), and the overall duration of the endoscopic procedure. Post-procedure recovery was tracked at specified intervals of 15, 30, and 45 minutes to ensure a thorough assessment of each sedative's effectiveness and safety.

Finally, a Follow-up Observation Sheet was designed to monitor sedation depth and the physiological responses of each patient at key time points throughout the procedure. Observations were recorded before sedation (baseline), immediately before endoscopy initiation (aiming for RSS 3–4), five minutes into the endoscopy or upon any significant changes, and one hour post-endoscopy to identify any delayed adverse effects. This sheet documented vital signs and side effects such as bradycardia, tachycardia, hypotension, hypertension, respiratory issues, and any signs of patient discomfort, allowing a continuous assessment of patient safety.

The datasheet's validity was ensured through a review process involving a panel of experts that included two anesthesiologists, an academic with specialization in nurse anesthesia, an anesthesia nurse, and a statistician. Their input helped ensure the tool's alignment with both clinical and research standards.

Data Collection Process

The data collection process spanned three main phases: pre-procedure, during the procedure, and post-procedure.

Pre-Procedure: Each patient was briefed on the study objectives and procedure, after which they signed a consent form (Appendix A). Baseline data, including vital signs and American Society of Anesthesiologists (ASA) classification, were recorded to establish a starting point for comparison. To ensure safety, an emergency resuscitation cart was prepared. Each patient was also advised to have a responsible adult accompany them home, as the effects of sedation could temporarily impair alertness.

During the Procedure: Patients were positioned in the left lateral position, with continuous monitoring of blood pressure, pulse oximetry, and heart rate throughout the procedure. Sedation was administered according to the group assignment: In the Dexmedetomidine group, each patient received 0.3 mcg/kg of Dexmedetomidine combined with 1 mcg/kg of Fentanyl intravenously, ten minutes before the procedure, followed by a continuous Dexmedetomidine infusion. In the Midazolam group, each patient received 0.05 mg/kg of Midazolam and 1 mcg/kg of Fentanyl intravenously, with additional doses of Midazolam administered every 2–5 minutes as needed to achieve the desired sedation level. The Ramsay Sedation Scale (RSS) was used to assess sedation depth during the procedure, aiming for an RSS score between 3 and 4.

Post-Procedure: Following the endoscopy, patients were closely monitored until they achieved a full recovery, indicated by an RSS score of 2. Discharge readiness was assessed using the Post-Anesthesia Recovery Scoring System (PARS). Patients were informed of possible post-procedure effects, such as mild throat soreness, and advised to avoid activities requiring full alertness until they were fully recovered.

Ethical Considerations

This study was conducted with IRB approval from An-Najah National University and in compliance with the Declaration of Helsinki. All participants received information about the study's objectives, methods, and potential risks. Written consent was obtained, and participants retained the right to withdraw at any stage. Patient confidentiality was protected, and all data was securely stored and anonymized during analysis. Participants were informed that sedation was used for their comfort and that an experienced endoscopist and anesthesiologist would monitor the procedure to ensure safety.

Data Analysis

Data analysis was performed using SPSS software version 20. Continuous variables were summarized as means and standard deviations, while categorical data were presented as counts and percentages. Statistical tests, such as the t-test for continuous variables and chi-square for categorical variables, were conducted to assess differences between the two groups. Statistical significance was set at $p < 0.05$.

Result

This study aimed to compare the Midazolam and Dexmedetomidine used for upper endoscopy performed under sedation, The primary outcome: vital signs changes, including mean arterial pressure, oxygen saturation, respiration rate, and heart rate of the patients and Ramsay sedation scale (RSS), time to full sedation, time to full recovery, an additive dose of any sedative or analgesic drug and if using of any drug to treat any side effect during the procedure. Secondary outcomes included: patient and endoscopy specialist satisfaction and adverse effects, regarding patient: anxiety, gagging, discomfort, and satisfaction, regarding endoscopy specialist: technical difficulty, satisfaction with the patient's sedation level, patient discomfort, patient retching, and patient gagging.

Demographic Data of patients in Midazolam and Dexmedetomidine groups

The study recruited 68 patients, who were randomly assigned to receive either Midazolam or Dexmedetomidine (n = 34/group). Demographic and clinical data of the patients are shown in Table 1. There were no statistically significant differences between groups in sex distribution, age, BMI, smoking distribution and education level. While there was a significant difference in endoscopy duration between the two groups, Dexmedetomidine required 11.0 ± 1.9 minutes and Midazolam required 9.9 ± 1.5 minutes, $p = 0.008$.

Table 1
Demographic Data of patients in Midazolam group and Dexmedetomidine group. Data is reported as Mean Standard deviation (SD) unless otherwise stated.

Variable	Midazolam group (n = 34)	Dexmedetomidine group (n = 34)	p
Age, year*	39.8 ± 13.0	40.8 ± 11.4	0.744
Sex, Male%/Female%	47.05%/52.95%	52.95% /47.05%/	0.809
Body mass index, kg/m2*	28.1 ± 6.0	28.4 ± 4.8	0.429
Duration of endoscopy, min*	9.9 ± 1.5	11.0 ± 1.9	**0.008**
Smoking%	35.29%	20.58%	0.280
Education level, n			
grammar school%	2.94%	0%	0.543
high school%	29.4%	20.59%	0.475
College%	38.23%	35.29%	0.841
graduate school%	29.4%	41.17%	0.542
*Mean ± SD			

Indications for endoscopy in Midazolam and Dexmedetomidine groups

When it came to endoscopic indications, there was a significant difference between the groups. When it came to dysphagia: 12/34 (35.3%) patients in the Midazolam group and 17/34 (50%) patients in the Dexmedetomidine group, p = 0.032. There were also significant differences between the groups in terms of esophageal reflux, with 17/34 (50%) patients in the Midazolam group and 7/34 (20.5) patients in the Dexmedetomidine group, respectively, p = 0.035. As well as significant differences in Dyspepsia across the groups 5/34 (14.7%) patients in the Midazolam group and 10/34 (29.4%) patients in the Dexmedetomidine group, p = 0.031.(Table 2).

Table 2
Indications for endoscopy in Midazolam and Dexmedetomidine groups

Variable	Midazolam group (n = 34)	Dexmedetomidine group (n = 34)	p
Dysphagia%	35.29%	50%	**0.032**
Esophageal reflux symptoms%	50%	20.59%	**0.035**
Dyspepsia%	14.70%	29.41%	**0.031**
Data presented as n(%)			

Pre-procedural expected patient satisfaction

Expected patient satisfaction before receiving Midazolam or Dexmedetomidine is not significantly different between the two groups for Satisfaction and discomfort ($p > .05$), but there is a significant difference between groups for gagging and anxiety. Mean gagging for Midazolam is lower than Dexmedetomidine 1.0 ± 1.1versus 1.6 ± 1.1, $p = 0.020$), and mean anxiety for Midazolam is higher than Dexmedetomidine, 2.6 ± 0.9 versus 2.1 ± 1.4, $p = 0.018$ (Table 3).

Table 3
Pre-procedural expected patient satisfaction, discomfort, gagging and anxiety score. Data presents as mean (± SD)

Variable	Midazolam group (n = 34)	Dexmedetomidine group (n = 34)	p
Expected Satisfaction	7.7 ± 1.2	7.1 ± 1.9	0.228
Expected Discomfort	1.7 ± 1.6	2.1 ± 1.8	0.515
Expected gagging	1.0 ± 1.1	1.6 ± 1.1	**0.020**
Anxiety Score	2.6 ± 0.9	2.1 ± 1.4	**0.018**

Post-procedural patient satisfaction

Table 6 shows the patient satisfaction after receiving Midazolam or Dexmedetomidine. Except for the gagging score, there are significant variations between the two groups in terms of satisfaction, discomfort, and anxiety (Table 4). There was a significant difference in satisfaction between the Dexmedetomidine group (9.1 ± 1.0) and the Midazolam group (8.06 ± 0.9), $p = 0.001$. There was a significant difference in discomfort between the Dexmedetomidine group (0.7 ± 0.9) and the Midazolam group (1.7 ± 1.1), $p = 0.001$. There was a substantial difference in anxiety between the Dexmedetomidine

group 0.5 ± 0.8 and the Midazolam group 1.8 ± 1.4, p = 0.001. When compared to the Midazolam group, the Dexmedetomidine group demonstrated much higher satisfaction, less discomfort, and less anxiety.

Table 4
Post-procedural patient satisfaction, discomfort, gagging and anxiety score. Data presents as mean (± SD)

Variable	Midazolam group (n = 34)	Dexmedetomidine group (n = 34)	p
Satisfaction (0–10 score)	8.06 ± 0.9	9.1 ± 1.0	**0.001**
Discomfort (0–10 score)	1.7 ± 1.1	0.7 ± 0.9	**0.001**
Gagging (0–10 score)	0.7 ± 0.9	0.6 ± 1.5	0.077
Anxiety (0–10 score)	1.8 ± 1.4	0.5 ± 0.8	**0.001**

Endoscopy specialist satisfaction

Patients receiving Dexmedetomidine had significantly better endoscopic specialist satisfaction than those receiving Midazolam (8.7 ± 1.6 versus 8.2 ± 1.0); P = 0.001. Respectively. Patients taking Dexmedetomidine had significantly less discomfort than those receiving Midazolam (1.0 ± 1.4versus 1.8 ± 0.9); p = 0.037. Patients taking Dexmedetomidine had considerably less gagging than those receiving Midazolam (0.8 ± 1.3versus 1.0 ± 0.8; p = 0.036).

Also Patients taking Dexmedetomidine had considerably less retching than those receiving Midazolam (0.5 ± 1.1 versus 0.6 ± 0.6; P0.013) (Table 5). There was a significant difference in technical difficulty between the Dexmedetomidine and Midazolam groups, with the Dexmedetomidine group scoring 1.1 ± 1.1vs the Midazolam group scoring 1.6 ± 0.8, p = 0.035. In all facets of endoscopic specialist, the Dexmedetomidine group outperformed the Midazolam group (Table 5).

Table 5
Endoscopy specialist satisfaction, discomfort, gagging, retching, and technical difficulty. Data reported as Mean (± SD)

Variable	Midazolam group (n = 34)	Dexmedetomidine group (n = 34)	p
Satisfaction	8.2 ± 1.0	8.7 ± 1.6	0.001
Discomfort	1.8 ± 0.9	1.0 ± 1.4	0.037
gagging	1.0 ± 0.8	0.8 ± 1.3	0.036
Retching	0.6 ± 0.6	0.5 ± 1.1	0.013
Technical difficulty	1.6 ± 0.8	1.1 ± 1.1	0.035

Recovery data in Midazolam and Dexmedetomidine groups

For average recovery, Dexmedetomidine patients were recovered faster than Midazolam patients, Midazolam patients need 48.8 ± 6.0 min to recover while the Dexmedetomidine patients need 18.0 ± 5.2 min and this difference significant since the $p < .05$, Midazolam need 2.4 ± 7.7 min to sedate while the Dexmedetomidine need 9.5 ± 1.1 min and this difference significant since the $p < .05$ (Table 5).

Table 6
Recovery data in Midazolam and Dexmedetomidine groups.

Variable	Midazolam group (n = 34)	Dexmedetomidine group (n = 34)	p
Time min RSS 3–4	2.4 ± 7.7	9.5 ± 1.1	**0.001**
Time min RSS = 2	48.8 ± 6.0	18.0 ± 5.2	**0.001**
Patients fully recovered, n (%)			
15 Min	0	17 (50%)	**0.001**
30 Min	0	17 (50%)	**0.001**
45 Min	34 (100%)	0	**0.001**
Data presented as Mean (± SD) and as n (%)			

Adverse effect

Regarding side effect, Table 7 represent the most side effect after receiving Midazolam or Dexmedetomidine, While assessing the following side effects, which are: hypertension, hypotension, tachycardia, bradycardia, hypoxia, tachypnea, bradypnea, apnea, coughing, vomiting, retching, nausea, allergies, and abnormal body movements. The most frequent side effect was hypertension for both groups. It was found that the occurrence of side effects in the Dexmedetomidine group was less than in the Midazolam group but it was not significant.

Table 7
Adverse effects in Midazolam and Dexmedetomidine groups

Variable	Midazolam group (n = 34)	Dexmedetomidine group (n = 34)	p-value
Bradycardia%	8.82%	0%	0.076
Hypertension%	17.64%	17.64%	0.493
Coughing%	8.82%	2.94%	0.303
Tachycardia%	5.88%	0%	0.151
Nausea%	2.94%	0%	0.314

Vital signs of the patients in both Midazolam and Dexmedetomidine groups

Regarding vital signs, there is no significant difference between the Midazolam group and the Dexmedetomidine group, except for respiratory rate, Dexmedetomidine group has less rate compared to the Midazolam group 16.7 ± 1.9, 18.6 ± 4.7 respectively, p = 0.028. Table 8, Table 9, Table 10, Table 11 and Table 12 showed the measurement for all vital signs at four points for two groups Midazolam and Dexmedetomidine, as a result, there are no significant differences for all points (MAP, HR, and SpO2), while there significant difference at point 3 and 4 in respiratory rate sign. Dexmedetomidine group has less rate compared to the Midazolam group.

Tabe 8 Vital signs of the patients in both Midazolam and Dexmedetomidine groups

Variable	Midazolam group (n = 34)	Dexmedetomidine group (n = 34)	p
Mean Arterial Pressure	90.7 ± 6.3	91.4 ± 8.5	0.713
Heart Rate	80.7 ± 11.5	77.4 ± 11.6	0.238
oxygen saturation	97.7 ± 1.3	97.8 ± 2.5	0.861
Respiratory Rate	18.6 ± 4.7	16.7 ± 1.9	**0.028**
Data displayed as Mean (± SD)			

Tabe 9 MAP in both Midazolam and Dexmedetomidine groups

Variable	Midazolam group (n = 34)	Dexmedetomidine group (n = 34)	p
Point 1	92.7 ± 11.4	92.7 ± 10.5	0.896
Point 2	91.3 ± 7.8	95.9 ± 13.8	0.311
Point 3	89.7 ± 10.2	90.2 ± 8.7	0.777
Point 4	88.7 ± 9.6	88.4 ± 11.3	0.658
Data displayed as Mean (± SD)			

Tabe 10 HR in both Midazolam and Dexmedetomidine groups

Variable	Midazolam group (n = 34)	Dexmedetomidine group (n = 34)	p
Point 1	80.91 ± 16.58	80.18 ± 13.52	0.654
Point 2	81.03 ± 13.20	77.977 ± 15.64	0.353
Point 3	80.82 ± 14.24	75.74 ± 13.75	0.049
Point 4	78.8 ± 12.13	74.79 ± 11.41	0.163
Data displayed as Mean (± SD)			

Tabe 11 SpO2 in both Midazolam and Dexmedetomidine groups

Variable	Midazolam group (n = 34)	Dexmedetomidine group (n = 34)	p
Point 1	97.65 ± 1.64	98.65 ± 2.56	0.063
Point 2	97.59 ± 1.74	97.50 ± 2.50	0.970
Point 3	97.24 ± 1.89	97.09 ± 2.77	0.975
Point 4	97.29 ± 1.60	96.97 ± 3.43	0.797

Tabe 12 RR in both Midazolam and Dexmedetomidine groups			
Variable	Midazolam group (n = 34)	Dexmedetomidine group (n = 34)	p
Point 1	17.74 ± 0.71	16.53 ± 2.56	0.063
Point 2	17.59 ± 0.92	17.00 ± 2.53	0.970
Point 3	17.38 ± 0.98	15.82 ± 2.40	**0.004**
Point 4	20.38 ± 0.84	16.06 ± 2.55	**0.001**
Data displayed as Mean (± SD)			

Discussion

The result of the current study proved the efficacy and safety of using Dexmedetomidine and its superiority to Midazolam in many aspects, such as patient satisfaction, endoscopy specialists' satisfaction, stability of vital signs, and the lack of side effects, as well as the speed of recovery after procedure, which reduces the patient's stay in the hospital and increases the occupancy rate of the department to provide places for patients in a way faster. The importance of this research stems from the large number of side effects expected from the drug Midazolam, these findings are consistent with those of other research that have been published which were shown that the concomitant use of Midazolam with analgesia drugs increases the risk of respiratory and circulatory failure in patients [40] Bartolomé et al., 2007) [41, 42], its toxicity, its conflict with many drugs, and the many caveats with many pathological conditions [32, 33] Add to that the length of the patient's stay in recovery departments, which reduces the possibility of receiving other cases [36, 37]. As a result, there was a need to look for a safe and effective alternative to meet the endoscopic anesthetic need.

During this research, Midazolam and Dexmedetomidine were compared in upper endoscopy only, and the drug Fentanyl was used as analgesia, as many researches [35, 37]. But in other research, Remifentanil was used as an analgesia [36], another used topical lidocaine [7], Others, on the other hand, did not utilize analgesics and instead focused on treating pain with the effects that each of the two medications has on patients [20, 38].

The ratio of males to females in this study was randomly 1:1, While in other studies, the percentage of males was more than female, percentage was as follows 62% [38], 55% [35] and 52% [36]. On the contrary, the percentage of males was lower in other studies, and their percentage was as follows 44% [7], 46% [20] and 45% [37].

There are significant difference between two groups for all binoculars of patient satisfactions except gagging score, Dexmedetomidine group showed higher satisfaction, less discomfort and less anxiety compared to Midazolam group.In Demiraran and his colleges research, both gropes showed satisfactory and similar results in terms of anxiety, discomfort and gagging, as well as patient satisfaction [7]. In

another study for the gagging assessment, more occurrence were observed in the Midazolam group than in the Dexmedetomidine group [38]. And in a systematic review study for 12articles including 883 patients, the superiority and merit of Dexmedetomidine over Midazolam was shown in patient satisfaction [34]. Also in a meta-analysis for 9 eligible randomized controlled trials included 657 patients, the superiority of Dexmedetomidine was shown in patient satisfaction aspect over Midazolam [21]. In a retrospective randomized study for 60 adult patients, the satisfaction in the Dexmedetomidine group was higher, [35]. The results in terms of patient satisfaction were preferable to the Dexmedetomidine group in a Prospective, randomized, single-blinded preliminary trial including 198 patients [36].Finally, the satisfaction of patients was the highest in the Dexmedetomidine group in a randomized controlled trial for 60 patients [37].

The endoscopy specialist rating for all satisfaction aspects was significant difference between two groups, for patient satisfaction significantly higher in the patients receiving Dexmedetomidine than those receiving Midazolam (87.8 ± 1.6 versus 8.2 ± 1.0; P = 0.001). Retching was significantly lower in patients receiving Dexmedetomidine compared with those receiving Midazolam (0.5 ± 1.1 versus 0.6 ± 0.6; P < 0.001). Dexmedetomidine group showed better than Midazolam group in all Visual analog scale (VAS) score. This was in line with many studies that support the superiority of Dexmedetmomidine over Midazolam in the context of specialist satisfaction, and this was demonstrated by Barends and colleagues in the Systemic Review Study, which was conducted in 2017 [34]. In another study, the endoscopy was performed by the same specialist, and the scale was weighed in favor of Dexmedetomidine in the context of the specialists' satisfaction, where several criteria were considered, which are the patient's discomfort from the specialist's point of view, satisfaction with the patient's sedation, technical problems, gagging and retching [7]. In another study, to examine the specialists' satisfaction with using criteria from one to four, where one is poor, followed by Fair, then Good, and then Excellent, the superiority of Dexmedetemomidine over the other drug was shown through this scope [37]. In another study, a tool with two options, either satisfied or very satisfied, was used to assess the specialist's satisfaction, and the results showed similar results to the previous one with the superiority of Dexmedetomidine [38]. In the research conducted by Zhiqiang Lu and his colleagues in a study that included 198 patients, it was found that the specialist's satisfaction in the Dexmedetomidine group is not different from his satisfaction in the Midazolam group. A scale of one to six was used to assess their satisfaction, with six being very satisfactory [36].

For average recovery, Dexmedetomidine patients were recovered faster than Midazolam patients, Midazolam patients need 48.8 ± 6.0 min to recover while the Dexmedetomidine patients need 18.0 ± 5.2 min and this difference significant since the p < .05, Midazolam need 2.4 ± 7.7 min to sedate while the Dexmedetomidine need 9.5 ± 1.1 min and this difference significant since the p < .05. One of the studies that used a mechanism to assess the time required to recover from sedation, as the time was calculated from the moment the procedure ended until reaching modified ramsay sedation score 2, it showed that the duration of recovery in the Dexmedetomidine group is shorter than in the Midzolam group, but the difference does not constitute a statistical difference [36]. Further research showed that ninety percent of the Dexmedetomidine group achieved a Modified Aldrete score of nine or more within five minutes of

completing the procedure, while seventeen percent of the Midazolam group showed the same result after the same period and the difference was statistically different [37].

Regarding to vital signs, there are no significant difference between Midazolam group and Dexmedetomidine group, except respiratory rate, Dexmedetomidine group has less rate compared to Midazolam group 16.7 ± 1.9, 18.6 ± 4.7 respectively. In a review of a group of studies examining the safety of Dexmedetomidine on the respiratory system compared to Midazolam, it was found that twenty cases of hypoxemia occurred in the Dexmedetomidine group compared to twenty-four cases. So that this research included an analysis of evidence for seven hundred and sixty-seven cases, and this difference was not statistically significant, while both showed safety in terms of affecting the circulatory system in the same research, so that during the analysis of the data, the striking results were those that were mentioned in eight studies, where there was a drop in blood pressure for ten patients in the Dexmedetomidine group compared to seven patients in the Midazolam group and this difference is not statistically different, and two of the studies that were analyzed showed the emergence of some cases of high blood pressure in the Midazolam group(Barends et al., 2017).In analyzing the results of five studies with no significant heterogeneity in data, it was found that there is no difference between the two drugs in the effect on the concentration of oxygen in the blood, the results of six studies with no significant heterogeneity in datashowed that there was no difference in the effect between the two drugs on the mean arterial pressure [21]. In the research conducted by Wei Wu and his colleagues the preference for the Dexmedetomidine group in terms of the mean arterial pressure reading was lower in the Midazolam group, the blood oxygen concentration was more high in the Dexmedetomidine group [35]. In another studythe results showed the following that blood oxygen saturation, mean arterial pressure, heart rate and respiratory rate were similar in the two groups [7]. While the Midazolam group showed a higher incidence of decreased blood oxygen concentration than the other group [36]. The results in terms of safety, there were low incidence of cases of low blood oxygen concentration in the Dexmedetomidine group, and also in the Dexmedetomidine group the median of the Midazolam dose used was lower; In addition to this, the systolic blood pressure reading and heart rate decreased in the Dexmedetomidine group, but no complications that led to heart failure or irregular heartbeats [20]. Further research showed that in the Dexmedetomidine group, there was a decrease in heart rate, while there was no significant difference in the reading of blood pressure and respiratory rate [37]. In the research conducted by Kilic and his colleagues the results showed a lower heart rate in the Dexmedetomidine group, in terms of respiratory rate and MAP the results were similar [38].

While assessing the following side effects, which are: hypertension, hypotension, tachycardia, bradycardia, hypoxia, tachypnea, bradypnea, apnea, coughing, vomiting, retching, nausea, allergies and abnormal body movements. The most important and most frequent side effect was hypertension for both groups.Eighteen times side effects occurred in the Midazolam group, and they were in the following numbers in each symptom: three in bradycardia, six in hypertension, three in coughing, three in hypoxia, two in tachycardia, one in nausea. Compared to the Dexmedetomidine group, in which five times side effects occurred, four of which were in hypertension and one in coughing. It was found that the occurrence of side effects in the Dexmedetomidine group was less than in the Midazolamgroup.In

another study, as for the side effects, only four studies dealt with this matter, and they looked at the following side effects, which are: nausea and vomiting, respiratory depression, dysphoria, dizziness, reflux, pain and abdominal distention, It was found that the occurrence of side effects in the Dexmedetomidine group was less than in the Midazolam group [21]. But in another study the results showed that there are no clinically significant complications in the two groups, and that the use of Dexmedetomidine is safe and effective in upper endoscopy [35]. While the preferential results of Dexmedetomidine were shown in several aspects, namely, fewer side effects compared to Midazolam, less retching, and a significant increase in specialist satisfaction [7]. In another study Dexmedetomidine showed less nausea reaction than in the Midazolam group during endoscopy [36]. Inatomi and his colleagues conclude that, it is no complications that led to heart failure or irregular heartbeats [20]. In gaging assessment Sethi conclude that the appearance of the gag reaction was more in the Midazolam group than in the Dexmedetomidine group [37]. Finally Killic and his colleagues conclude that regarding to side effects, nausea, vomiting, and coughing were observed in the Midazolam group, with none in the Dexmedetomidine group [38].

Conclusion

Dexmedetomidine proved to be a superior option over Midazolam for sedation during upper endoscopy, offering faster recovery, increased patient and specialist satisfaction, and reduced discomfort, anxiety, and retching. As a safe and effective alternative, Dexmedetomidine has shown significant advantages in terms of complication rates and quicker recovery, suggesting it as the preferred sedative in this context. However, the novelty of Dexmedetomidine in hospital settings and limited research on its benefits highlight the need for further studies to confirm these findings and explore its potential across other medical procedures. Such research could strengthen the evidence for its use, supporting Dexmedetomidine as a valuable option for procedural sedation

Abbreviations

ASA	American Society of Anesthesiologists
CYP	Cytochromes P
ERCP	Endoscopic retrograde cholangiopancreatography
G	Gauge
GABA	Gamma aminobutyric acid
hr	Hour
ICP	intracranial pressure
ICU	intensive care unit
IRB	institutional review board
IV	Intravenous
kg	kilogram
L	Litter
MAP	Mean arterial pressure
MAS	Modified Aldrete Score
mcg	Microgramme
min	Minute
PT	Prothrombin time
PTT	Partial thromboplastin time
RSS	Ramsay Sedation Scale
SD	Standard deviation
SPO2	Oxygen saturation
VAS	Visual analog scale

Declarations

Acknowledgements

The authors would like to thank An-Najah National University (www.najah.edu) for the technical support provided to publish the present manuscript

Author contributions

I.G. and A.A. conceptualized the study and prepared the main manuscript text. W.S. developed the anesthesia protocol. Data collection was conducted by Q.A., S.K., R.N., M.A., and A.A. All authors reviewed and approved the final manuscript.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Declarations

Ethics approval and consent to participate

The study received ethical approval from the Institutional Review Board (IRB) at An-Najah National University and the Ethics Committee of An-Najah National University Hospital. All patients received a clear explanation of the study objectives, protocol, and potential risks and benefits.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Clinical trial registration

This research did not involve a clinical trial; no clinical trial registration is applicable.

Consent for publication

Written informed consent was obtained from each participant, and confidentiality, autonomy, and the right to withdraw were assured throughout the study.

Competing interests

The authors declare no competing interests.

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References

1. Waring JP, Baron TH, Hirota WK, Goldstein JL, Jacobson BC, Leighton JA, Mallery JS, Faigel DO: **Guidelines for conscious sedation and monitoring during gastrointestinal endoscopy**. *Gastrointestinal endoscopy* 2003, **58**(3):317-322.
2. Huang Z, Chen Y-s, Yang Z-l, Liu J-y: **Dexmedetomidine versus midazolam for the sedation of patients with non-invasive ventilation failure**. *Internal medicine* 2012, **51**(17):2299-2305.

3. Ozel AM, Oncü K, Yazgan Y, Guerbuez AK, Demirtuerk L: **Comparison of the effects of intravenous midazolam alone and in combination with meperidine on hemodynamic and respiratory responses and on patient compliance during upper gastrointestinal endoscopy: a randomized, double-blind trial**. *The Turkish journal of gastroenterology: the official journal of Turkish Society of Gastroenterology* 2008, **19**(1):8-13.
4. Sethi A, Chen YK, Austin GL, Brown WR, Brauer BC, Fukami NN, Khan AH, Shah RJ: **ERCP with cholangiopancreatoscopy may be associated with higher rates of complications than ERCP alone: a single-center experience**. *Gastrointestinal endoscopy* 2011, **73**(2):251-256.
5. Eger EI, White PF, Bogetz MS: **Clinical and economic factors important to anaesthetic choice for day-case surgery**. *Pharmacoeconomics* 2000, **17**(3):245-262.
6. Riphaus A, Stergiou N, Wehrmann T: **Sedation with propofol for routine ERCP in high-risk octogenarians: a randomized, controlled study**. *Official journal of the American College of Gastroenterology| ACG* 2005, **100**(9):1957-1963.
7. Demiraran Y, Korkut E, Tamer A, Yorulmaz I, Kocaman B, Sezen G, Akcan Y: **The comparison of dexmedetomidine and midazolam used for sedation of patients during upper endoscopy: A prospective, randomized study**. *Canadian journal of gastroenterology* 2007, **21**(1):25-29.
8. □□□, □□□, □□□, □□□, □□□, □□□, □□□, □□□, □□□, □□□: **2021 Korean Society of Gastrointestinal Endoscopy clinical practice guidelines for endoscopic sedation**. *The Korean Journal of Gastroenterology* 2022, **79**(4):141-155.
9. Schweickert WD, Kress JP: **Strategies to optimize analgesia and sedation**. *Critical Care* 2008, **12**(3):1-10.
10. Moon S-H: **Sedation regimens for gastrointestinal endoscopy**. *Clinical endoscopy* 2014, **47**(2):135.
11. Kim KH: **Safe sedation and hypnosis using dexmedetomidine for minimally invasive spine surgery in a prone position**. *The Korean journal of pain* 2014, **27**(4):313.
12. Wang D, Chen C, Chen J, Xu Y, Wang L, Zhu Z, Deng D, Chen J, Long A, Tang D: **The use of propofol as a sedative agent in gastrointestinal endoscopy: a meta-analysis**. *PloS one* 2013, **8**(1):e53311.
13. Triantafillidis JK, Merikas E, Nikolakis D, Papalois AE: **Sedation in gastrointestinal endoscopy: current issues**. *World Journal of Gastroenterology: WJG* 2013, **19**(4):463.
14. Yilmaz E, Hough KA, Gebhart GF, Williams BA, Gold MS: **Mechanisms underlying midazolam-induced peripheral nerve block and neurotoxicity**. *Regional Anesthesia & Pain Medicine* 2014, **39**(6):525-533.
15. Chawla R, Myatra SN, Ramakrishnan N, Todi S, Kansal S, Dash SK: **Current practices of mobilization, analgesia, relaxants and sedation in Indian ICUs: A survey conducted by the Indian Society of Critical Care Medicine**. *Indian Journal of Critical Care Medicine: Peer-Reviewed, Official Publication of Indian Society of Critical Care Medicine* 2014, **18**(9):575.
16. Bajwa S, Kulshrestha A: **Dexmedetomidine: an adjuvant making large inroads into clinical practice**. *Annals of medical and health sciences research* 2013, **3**(4):475-483.
17. Takrouri MS, Seraj MA, Channa AB, el-Dawlatly AA, Thallage A, Riad W, Khalaf M: **Dexmedetomidine in intensive care unit: a study of hemodynamic changes**. *Middle East journal of*

anaesthesiology 2002, **16**(6):587-595.

18. Ihmsen H, Saari T: **Dexmedetomidin**. *Der Anaesthesist* 2012, **61**(12):1059-1066.
19. Bharati S, Pal A, Biswas C, Biswas R: **Incidence of cardiac arrest increases with the indiscriminate use of dexmedetomidine: a case series and review of published case reports**. *Acta Anaesthesiologica Taiwanica* 2011, **49**(4):165-167.
20. Inatomi O, Imai T, Fujimoto T, Takahashi K, Yokota Y, Yamashita N, Hasegawa H, Nishida A, Bamba S, Sugimoto M: **Dexmedetomidine is safe and reduces the additional dose of midazolam for sedation during endoscopic retrograde cholangiopancreatography in very elderly patients**. *BMC gastroenterology* 2018, **18**(1):1-6.
21. Zhang F, Sun HR, Zheng ZB, Liao R, Liu J: **Dexmedetomidine versus midazolam for sedation during endoscopy: a meta-analysis**. *Experimental and Therapeutic Medicine* 2016, **11**(6):2519-2524.
22. Tellor BR, Arnold HM, Micek ST, Kollef MH: **Occurrence and predictors of dexmedetomidine infusion intolerance and failure**. *Hospital practice* 2012, **40**(1):186-192.
23. Jalowiecki P, Rudner R, Gonciarz M, Kawecki P, Petelenz M, Dziurdzik P: **Sole use of dexmedetomidine has limited utility for conscious sedation during outpatient colonoscopy**. *The Journal of the American Society of Anesthesiologists* 2005, **103**(2):269-273.
24. Yu C, Li S, Deng F, Yao Y, Qian L: **Comparison of dexmedetomidine/fentanyl with midazolam/fentanyl combination for sedation and analgesia during tooth extraction**. *International Journal of Oral and Maxillofacial Surgery* 2014, **43**(9):1148-1153.
25. Cheung CW, Ying CLA, Chiu WK, Wong GT, Ng KFJ, Irwin MG: **A comparison of dexmedetomidine and midazolam for sedation in third molar surgery**. *Anaesthesia* 2007, **62**(11):1132-1138.
26. Arain SR, Ebert TJ: **The efficacy, side effects, and recovery characteristics of dexmedetomidine versus propofol when used for intraoperative sedation**. *Anesthesia & Analgesia* 2002, **95**(2):461-466.
27. Snapir A, Posti J, Kentala E, Koskenvuo J, Sundell J, Tuunanen H, Hakala K, Scheinin H, Knuuti J, Scheinin M: **Effects of low and high plasma concentrations of dexmedetomidine on myocardial perfusion and cardiac function in healthy male subjects**. *The Journal of the American Society of Anesthesiologists* 2006, **105**(5):902-910.
28. Gerlach AT, Dasta J, Armen S, Smith J, Steinberg S, Martin L, Cook C: **TITRATION PROTOCOL REDUCES HYPOTENSION DURING DEXMEDETOMIDINE INFUSION IN CRITICALLY ILL SURGICAL PATIENTS.: 534**. *Critical Care Medicine* 2006, **34**(12):A148.
29. Wijeysundera DN, Bender JS, Beattie WS: **Alpha-2 adrenergic agonists for the prevention of cardiac complications among patients undergoing surgery**. *Cochrane database of systematic reviews* 2009(4).
30. Coull JT, Jones ME, Egan TD, Frith CD, Maze M: **Attentional effects of noradrenaline vary with arousal level: selective activation of thalamic pulvinar in humans**. *Neuroimage* 2004, **22**(1):315-322.
31. Suri Y: **Evaluation of midazolam and diazepam for pre-operative sedation**. *Medical Journal Armed Forces India* 2000, **56**(4):287-292.

32. Verbeeck RK: **Pharmacokinetics and dosage adjustment in patients with hepatic dysfunction**. *European journal of clinical pharmacology* 2008, **64**(12):1147-1161.
33. Bushra R, Aslam N, Khan AY: **Food-drug interactions**. *Oman medical journal* 2011, **26**(2):77.
34. Barends CR, Absalom A, van Minnen B, Vissink A, Visser A: **Dexmedetomidine versus midazolam in procedural sedation. A systematic review of efficacy and safety**. *PloS one* 2017, **12**(1):e0169525.
35. Wu W, Chen Q, Zhang L-c, Chen W-h: **Dexmedetomidine versus midazolam for sedation in upper gastrointestinal endoscopy**. *Journal of International Medical Research* 2014, **42**(2):516-522.
36. Lu Z, Li W, Chen H, Qian Y: **Efficacy of a Dexmedetomidine–Remifentanil Combination Compared with a Midazolam–Remifentanil Combination for Conscious Sedation During Therapeutic Endoscopic Retrograde Cholangio-Pancreatography: A Prospective, Randomized, Single-Blinded Preliminary Trial**. *Digestive Diseases and Sciences* 2018, **63**(6):1633-1640.
37. Sethi P, Mohammed S, Bhatia PK, Gupta N: **Dexmedetomidine versus midazolam for conscious sedation in endoscopic retrograde cholangiopancreatography: An open-label randomised controlled trial**. *Indian journal of anaesthesia* 2014, **58**(1):18.
38. Kilic N, Sahin S, Aksu H, Yavascaoglu B, Gurbet A, Turker G, Kadioglu AG: **Conscious sedation for endoscopic retrograde cholangiopancreatography: dexmedetomidine versus midazolam**. *The Eurasian journal of medicine* 2011, **43**(1):13.
39. Samson S, George SK, Vinoth B, Khan MS, Akila B: **Comparison of dexmedetomidine, midazolam, and propofol as an optimal sedative for upper gastrointestinal endoscopy: A randomized controlled trial**. *Journal of Digestive Endoscopy* 2014, **5**(02):051-057.
40. Vermeeren A: **Residual effects of hypnotics**. *CNS drugs* 2004, **18**(5):297-328.
41. Korttila K, Aromaa U: **Venous complications after intravenous injection of diazepam, flunitrazepam, thiopentone and etomidate**. *Acta anaesthesiologica scandinavica* 1980, **24**(3):227-230.
42. McElhatton PR: **The effects of benzodiazepine use during pregnancy and lactation**. *Reproductive Toxicology* 1994, **8**(6):461-475.

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