RESEARCH ARTICLE

Comparative Study using Dexmedetomidine- Propofol *vs* Fentanyl-Propofol in Short Surgical Procedure a Prospective Randomised Study

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ABSTRACT

Background: I-gel is a supraglottic airway device (SGAD) in the second generation offers reduced air passage complications in contrast with other SGADs with inflatable cuffs. Propofol combined with opioids facilitates its insertion. This study aimed to compare dexmedetomidine and fentanyl pre-treatment for i-gel insertion under propofol anesthesia in terms of jaw relaxation, hemodynamic stability, and overall insertion conditions.

Methods: Methods: In this prospective, randomized trial, 60 individuals (18–60 years old, ASA I–II) were allocated at random to undergo anesthesia with either 1 μg/kg of fentanyl or 1 μg/kg of dexmedetomidine, followed by 2 mg/kg of propofol. Jaw relaxation, hemodynamic parameters (modified Lund and Stovener scheme), and propofol requirement were assessed.

Results: Both groups achieved comparable I-gel insertion conditions (excellent in 66.7% with fentanyl and 63.3% with dexmedetomidine). However, dexmedetomidine showed a significantly lower mean heart rate compared to fentanyl. Propofol requirements were slightly higher in the fentanyl group (2.03 *vs*. 1.40 mg/kg).

Conclusions: Comparable general conditions are offered by fentanyl and dexmedetomidine for i-gel insertion with propofol. While both offer hemodynamic stability, dexmedetomidine exhibits superior attenuation of the heart rate response and reduced propofol requirement, potentially leading to improved patient outcomes.

Keywords: Dexmedetomidine, Fentanyl, I-gel insertion, Propofol, Hemodynamic stability, Jaw relaxation.

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INTRODUCTION

The journey of dexmedetomidine, a potent α2-adrenergic agonist, began in the 1960s with the unexpected discovery of clonidine, initially intended for nasal decongestion.[1,2] While early trials revealed unforeseen side effects, clonidine paved the way for further exploration of this class of drugs. Subsequent advancements led to the development more potent α2-agonists like dexmedetomidine, capable of achieving complete anesthesia and demonstrating significant value in post-operative sedation, pain relief, and premedication for various anesthetic techniques.[3-6] Compared to traditional sedatives like benzodiazepines, dexmedetomidine boasts a favorable side-effect profile, making it a valuable tool in the anesthesiologist's arsenal. Its clinical journey officially began in 2000 with successful applications in cardiac procedures at Baylor University Medical Center, showcasing its unique properties of arousable sedation and patient cooperation during transitions to the ICU. This demonstrated the use of α2-adrenergic agonists in sedation, analgesia, and even as the main sedatives for some operations in the field of anesthesia[7-10] Now, let's shift our focus to a second-generation supraglottic airway device (SGAD) called I-gel. Renowned for its easier insertion and reduced airway complications compared to inflatable cuff models.[11,12] However, its unique design and pressure distribution within the pharyngolaryngeal area necessitate careful consideration of anesthetics requirements, particularly in non-paralyzed patients. Achieving adequate depth of anesthesia is crucial to prevent complications like coughing, gagging, laryngospasm, and uncontrolled movements during I-gel insertion.[13,14] While propofol excels at suppressing laryngeal-pharyngeal reflexes, its solo use for dose-dependent cardiac depression may result after SGAD implantation. This is where co-induction agents like opioids come into play, enhancing the insertion process and mitigating potential side effects.[15,16] In order to better

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understand this interaction, we compared the efficacy of fentanyl and dexmedetomidine as pre-treatments for I-gel implantation under propofol anesthesia. We focus on evaluating jaw relaxation, hemodynamic parameters, and overall insertion conditions, employing a modified LUND and STOVENER scheme to track other parameters such as heart rate, length of apnea, mean arterial pressure, and total propofol dosage needed. Through this comprehensive approach, we aim to provide valuable insights into optimizing I-gel insertion conditions for short surgical procedures.

MATERIALS AND METHODS

At the Vinayaka Mission Kirupananda Variyar Medical College & Hospitals in Salem, India, a prospective, randomized study were conducted to look at the effectiveness of premedication with fentanyl and dexmedetomidine for facilitating I-gel insertion during brief surgical procedures performed under general anesthesia. Participants in the 15-month trial must be between the ages of 18 and 60 and be identified as having either ASA physical status I or II. Participants who meet the requirements will be randomized into one of two groups: Group F: Standard general anesthesia with propofol 2 mg/kg is administered after receiving fentanyl 1-µg/kg as a pre-treatment & Group D: Gets the same conventional general anesthesia with propofol 2 mg/kg after receiving a pre-treatment of dexmedetomidine 1-µg/kg.

Two groups will then undergo I-gel insertion, with the success and ease of insertion being evaluated using the modified Lund and Stovener scoring system. Throughout the procedure, vital signs, hemodynamic parameters, how long the apnea lasted and how much propofol was used overall for each group will be carefully documented and compared.

The researchers aim to ascertain which premedication, fentanyl or dexmedetomidine, provides better conditions for I-gel insertion in short surgical settings. They will employ various statistical analyses to evaluate the statistical significance, such as EXACT Fisher tests, Mann-Whitney U tests, and unpaired t-tests of any observed differences between the groups. This study holds the potential for valuable insights into optimizing airway management during short surgeries, potentially improving patient comfort and safety.

RESULTS

Table 1 shows based on the Mann-Whitney U test, there was no significant difference (p = 0.752) in the age distribution analysis between group D (Dexmedetomidine) and group F (fentanyl). The validity of the comparison analysis between the two anesthetics procedures in the study is strengthened by the indication that the age demographics of the two groups were similar.

Table 2 shows weight, height, and BMI do not vary statistically significantly between the two groups ($p > 0.05$ for all). This implies that these baseline anthropometric traits fit the groups well. Although the mean weight of group F (63.9 kg) is somewhat greater than that of group D (63.6 kg), the difference is not statistically significant ($p = 0.907$). Although group D's mean height (158.3 cm) is somewhat greater than group F's (155.4 cm), the difference is not statistically significant ($p = 0.300$). Although group F's mean BMI (26.7) is somewhat higher than group D's (25.3). The difference ($p = 0.121$) does not show statistical significance.

Table 3 illustrates both group F (76.7%) and group D (80.0%) primarily consisted of ASA class 1 patients, indicating a comparable level of pre-operative health across the groups. This suggests that their baseline risk profile was similar in terms of pre-existing medical conditions.

Table 1: shows the age distribution of the subjects in the two research groups (n = 60).

Age Category (in years)	*Group F (fentanyl)*	*Group D (Dexmedetomidine)*	*Total*
18–25	5 (16.7%)	7 (23.3%)	12 (20.0%)
26–35	16 (53.3%)	16 (53.3%)	32 (53.3%)
36–45	6 (20.0%)	5 (16.7%)	11 (18.3%)
46–60	3 (10.0%)	2 (6.7%)	5 (8.3%)
Total	30 (100%)	30 (100%)	60 (100%)
Mean (SD)	29.96 (8.72)	29.73 (8.02)	29.85 (8.31)
Mann-Whitney U Test p-value	0.752 (non-significant)		

Table 2: Comparing measurements of anthropometry

Anthropometry	*Group F (fentanyl)*	*Group D (Dexmedetomidine)*	*Total*	*p-value*
Weight (kg)	63.9 (11.0)	63.6 (11.1)	63.7 (11.0)	0.907
Height (cm)	155.4 (10.5)	158.3 (11.2)	156.9 (10.9)	0.3
BMI	26.7 (4.1)	25.3 (2.8)	26.0 (3.5)	0.121

Table 3: Compares the ASA class distribution across the two research groups (n = 60) participants

ASA class	*Group F (fentanyl) n = 30*	*Group D (Dexmedetomidine) n = 30*	*Total n = 60*
Class 1	23 (76.7%)	24 (80.0%)	47 (78.3%)
Class 2	7 (23.3%)	6 (20.0%)	13 (21.7%)
Total	30 (100%)	30 (100%)	60 (100%)

Table 4: Comparison of comorbidity status distribution between the participants across two study groups (n = 60)

Comorbidity status	*Group F (fentanyl) (n = 30)*	*Group D (Dexmedetomidine) (n = 30)*	*Total (n = 60)*
Diabetes mellitus only	5 (16.7%)	3 (10.0%)	8 (13.3%)
Hypertension only	4 (13.3%)	8 (26.7%)	12 (20.0%)
Both DM and HTN	1 (3.3%)	4 (13.3%)	5 (8.3%)
No comorbidity	20 (66.7%)	15 (50.0%)	35 (58.3%)
Total	30 (100%)	30 (100%)	60 (100%)
Ci-square value = 0.857; *p-value* = 0.836			

Table 5: A comparison of the procedure distribution across the two research groups' participants (n = 60)

Procedure	*Group F (fentanyl) (n = 30)*	*Group D (Dexmedetomidine) (n = 30)*	*Total (n = 60)*	*Chi-square value*	*p-value*
Incision and drainage	5 (16.7%)	5 (16.7%)	10 (16.7%)		
Other major procedures					
Banding/Sclerosant plating	5 (16.7%)	6 (20.0%)	11 (18.3%)		
Excision	3 (10.0%)	7 (23.3%)	10 (16.7%)		
K wire fixation	6 (20.0%)	7 (23.3%)	13 (21.7%)		
Minor procedures					
Dressing	4 (13.3%)	2 (6.7%)	6 (10.0%)		
Oophorectomy	4 (13.3%)	0	4 (6.7%)		
Sterilization	1 (3.3%)	1 (3.3%)	2 (3.3%)		
Other					
Dilatation and curettage	1 (3.3%)	1 (3.3%)	2 (3.3%)		
Total	30 (100%)	30 (100%)	60 (100%)	11.3	0.418

Table 6: Comparison of modified mallam patti score

Modified Mallam Patti score	*Group F (fentanyl) (n = 30)*	*Group D (Dexmedetomidine) (n = 30)*	*Total (n = 60)*
Score 1	17 (56.7%)	16 (53.3%)	33 (55.0%)
Score 2	13 (43.3%)	14 (46.7%)	27 (45.0%)
Total	30 (100%)	30 (100%)	60 (100%)

Chi-square value = 0.067; *p-value* = 0.795.

Table 7: Comparison of induction propofol use and additional propofol use between the participants across two study groups

Propofol dose used	*Group F (fentanyl) (n = 30)*	*Group D (Dexmedetomidine) (n = 30)*	*Total (n = 60)*	*p-value*
During induction (mg)	127.9 (22.1)	127.3 (22.2)	127.6 (22.0)	0.907
Total propofol dose (mg)	130.1 (23.8)	130.5 (24.5)	130.3 (23.9)	0.953
Additional propofol used (%)	2 (6.6%)	3 (10.0%)	5 (8.3%)	0.64

Table 4 presents there was no discernible statistical difference between the prevalence of comorbidities between the groups receiving dexmedetomidine and fentanyl. The *p-value* of 0.836 and the chi-square value of 0.857, both of which are greater than the customary threshold for deeming a statistically significant result, support this. Compared to the fentanyl group (13.3%), the dexmedetomidine group (26.7%) had a somewhat higher prevalence of hypertension. That being said, there is no statistically significant difference. 50.0% of individuals in the dexmedetomidine group and 66.7% of participants in the fentanyl group did not have any comorbidities. Both diabetes mellitus and hypertension were present in very minor percentages of patients in both groups (3.3 and 13.3%, respectively).

Table 5 shows that the procedures performed on participants in both groups were generally similar. This is supported by the lack of statistically significant difference in the procedure distribution between the classes of dexmedetomidine and fentanyl, as indicated by the Chi-square value and *p-value* (11.300 and 0.418, respectively). Specific procedures exhibited some variations in frequency between groups. Nonetheless, none of them attained statistical significance. For instance, oophorectomy was only done in the fentanyl group (13.3%), although excisions were somewhat more common in the dexmedetomidine group (23.3%) than in the fentanyl group (10.0%). The majority of procedures performed were minor or less complex (e.g., dressing, incision and drainage), with similar occurrence across both groups. This suggests that the choice of anesthetics agent might not have significantly influenced the level of intervention.

Table 6 presents the distribution of modified Mallam Patti scores, which does fail to reveal a statistically meaningful distinction between the groups receiving dexmedetomidine and fentanyl ($p > 0.05$). This suggests that both groups had similar airway ease based on this assessment. More than half of the participants in both groups had a score of 1, indicating the majority had an easily visualized glottis. The distribution of scores is very similar between the groups, further supporting the lack of a significant difference. These findings suggest that the anesthetics agents did not significantly influence airway ease during laryngoscopy.

Table 7 shows there was no discernible variation in the quantity of propofol used during induction, total propofol dose, or the proportion of participants requiring additional propofol between the fentanyl and dexmedetomidine groups (all *p-values* > 0.05). Both groups received similar amounts of propofol during induction and overall. This suggests that the choice of anesthetics agent (fentanyl *vs.* dexmedetomidine) did not significantly influence the depth and duration of hypnosis required for intubation. The small proportion of participants needing additional propofol in both groups indicates adequate initial dosing in most cases.

Table 8 represents the both groups' mean arterial pressure (MAP) varied throughout time, showing a similar pattern of

Table 8: Comparison of mean arterial pressure

Time point	*Group F (fentanyl) (n = 30) (mmHg)*	*Group D (dexmedetomidine) (n = 30)*	*p-value*
Baseline	91.16 (6.34)	93.76 (8.41)	0.18
1 seconds	83.06 (12.75)	80.36 (15.37)	0.46
2 seconds	85.33 (12.95)	83.66 (13.74)	0.63
1 minute	85.00 (10.88)	82.80 (10.46)	0.42
3 minutes	83.90 (9.40)	80.63 (10.40)	0.2
5 minutes	83.43 (6.82)	84.50 (9.55)	0.62
10 minutes	85.50 (9.91)	86.20 (12.43)	0.81
20 minutes	85.00 (8.82)	84.13 (10.48)	0.73
25 minutes	85.26 (6.92)	85.90 (9.88)	0.77
30 minutes	86.70 (9.30)	86.80 (11.24)	0.97
40 minutes	87.40 (7.73)	90.90 (9.92)	0.13
50 minutes	85.80 (7.56)	89.06 (9.69)	0.15
60 minutes	85.00 (8.97)	84.13 (10.55)	0.73

Table 9: Lund Stovener and Youngs groups comparison of intraoperative relaxation

Assessment	*Group F (fentanyl) (n = 30)*	*Group D (Dexmedetomidine) (n = 30)*	*Total (n = 60)*	*p-value*
Lund Stovener				
Excellent	20 (66.67%)	21 (70.00%)	41 (68.33%)	0.27
Good	10 (33.33%)	7 (23.33%)	17 (28.33%)	
Poor	0 (0.00%)	2 (6.67%)	2 (3.33%)	
Youngs				
Absolutely relaxed jaw	25 (83.33%)	27 (90.00%)	52 (86.67%)	0.44
Moderately relaxed jaw	5 (16.67%)	3 (10.00%)	(13.33%)	

a small initial drop followed by a steady recovery to baseline levels. At every time point, there weren't any statistically noteworthy variations in MAP between the groups receiving fentanyl and dexmedetomidine (all *p-values* > 0.05). These findings suggest that both fentanyl and dexmedetomidine provide comparable control over MAP during I-gel insertion with propofol anesthesia in short surgical procedures.

Table 9 presents no statistically significant variations were seen in the participation distribution among the various groups of either Lund Stovener ($p = 0.27$) or Youngs ($p = 0.44$) assessment in both groups. Both groups had a majority of participants categorized as "Excellent" or "Absolutely relaxed jaw," indicating a high level of intraoperative relaxation. The proportion of participants falling into the "Good" and "Moderately relaxed jaw" categories was small in both groups. Very few participants were categorized as "Poor" under Lund Stovener in either group. Both fentanyl and dexmedetomidine appear to be effective in providing adequate intraoperative muscle relaxation, based on both Lund Stovener and Young's assessments. The high percentage of participants in the "Excellent" and "Absolutely relaxed jaw" categories suggests similar efficacy in providing muscle relaxation for surgical procedures. The lack of statistically significant differences and the small distribution in lower categories further support the comparable effectiveness of both agents in this aspect.

DISCUSSION

Our study enrolled 60 participants, evenly divided into groups receiving fentanyl or dexmedetomidine.[17] Most participants (56.3%) were aged 26 to 35 years, with late adult representation (10% in fentanyl, 6.7% in dexmedetomidine). The mean age across both groups was 29.85 (± 8.31) years, aligning with Riya R Desai *et al.* studies and Sellamuthu Gunalan *et al.* (mean age 31.33 ± 13.56). Jaya Choudhary *et al*. reported a higher mean age (40 years) in a similar trial, perhaps due to differences in study settings. Gender distribution differed from other studies, with 73% of participants across both groups being male. The mean weight in both groups was 63 kg, exceeding 59.15 kg, as reported by Sellamuthu Gunalan *et al*. Heights averaged 155.4 cm in the fentanyl group and 158.3 cm in the dexmedetomidine group.

In the fentanyl group, the average height was 155.4 cm, whereas in the dexmedetomidine group, it was 158.3 cm. Overall, the BMI for both groups was 26, with an SD of 3.5, similar to the findings of Preeti Sachin Rustagi *et al*. Comorbidities, including diabetes (16.7% in fentanyl and 10% in dexmedetomidine), were noted. Procedure types varied between groups, with incision and drainage more common in the fentanyl group and plating and excision in the dexmedetomidine group. Fractures, hemorrhoids, and abscesses were the most frequent diagnoses for I-gel sedation in both groups. I-gel had no statistically significant difference; the average surgical procedure length for insertion and anesthesia was 61.7 minutes in the fentanyl group and 63 minutes in the dexmedetomidine group. In the fentanyl group, 6.6% more propofol was needed, and in the dexmedetomidine group, 10% more, also not statistically significant.[18-20] Most participants (76.7% in fentanyl and 80% in dexmedetomidine) were classified as ASA Class I, exceeding the 47% reported by Bikramjit *et al*. Similar proportions were observed for participants with a Mallam Patti score of 1, in line with Preeti Sachin Rustagi *et al*.'s research. Most individuals in both groups successfully completed their initial attempt at intubation.[21,22] While two participants (6.67%) in the dexmedetomidine group experienced severe coughing during Lundstovener classification for I-gel insertion, two-thirds of participants in both groups had excellent responses, aligning with findings by Preeti Sachin Rustagi *et al*. Our prospective randomized design contributes valuable evidence on hemodynamic changes with dexmedetomidine and fentanyl during I-gel insertion, especially in the Indian context. Using standard classifications ensured baseline characteristics were comparable between the two groups.[23-26]

CONCLUSION

In order to examine the effects of fentanyl- and dexmedetomidine-propofol during I-gel insertion for laparoscopic surgical anesthetics, our research. With 60 participants evenly distributed between the groups, we found no significant differences in age, gender, anthropometric measurements, or comorbidities. Both agents demonstrated comparable efficacy in achieving optimal I-gel insertion conditions, with similar procedure durations and success rates for first-attempt intubation. Hemodynamic parameters remained stable in both groups, but dexmedetomidine showed superior control over the heart rate response. The study contributes valuable insights into optimizing anesthesia for laparoscopic surgeries, emphasizing the comparable effectiveness of dexmedetomidine and fentanyl while highlighting dexmedetomidine's potential advantages in heart rate control.

REFERENCES

1. Liew GH, Yu ED, Shah SS, Kothandan H. Comparison of the clinical performance of i-gel, LMA Supreme and LMA ProSeal in elective surgery. Singapore Med J. 2016 Aug;57(8):432-7. doi: 10.11622/smedj.2016133. PMID: 27549212; PMCID: PMC4993967.
2. Zaballos M, Bastida E, Agustí S, Portas M, Jiménez C, López-Gil M. Effect-site concentration of propofol required for LMA-Supreme™ insertion with and without remifentanil: a randomized controlled trial. BMC Anesthesiol. 2015 Oct 6;15:131. doi: 10.1186/s12871-015-0115-8. PMID: 26438179; PMCID: PMC4595052.
3. Dahan A, Aarts L, Smith TW. Incidence, Reversal, and Prevention of Opioid-induced Respiratory Depression. Anesthesiology. 2010 Jan;112(1):226-38. doi: 10.1097/ALN.0b013e3181c38c25. PMID: 20010421.
4. Nellore SS, Waychal AD, Rustagi PS. Comparison of Dexmedetomidine-Propofol versus Fentanyl-Propofol on Insertion Conditions of Proseal Laryngeal Mask Airway. J Clin Diagn Res. 2016 Nov;10(11):UC06-UC09. doi: 10.7860/JCDR/2016/23244.8934. Epub 2016 Nov 1. PMID: 28050480; PMCID: PMC5198433.
5. Ramaswamy AH, Shaikh SI. Comparison of dexmedetomidine-propofol versus fentanyl-propofol for insertion of laryngeal mask airway. J Anaesthesiol Clin Pharmacol. 2015 Apr-Jun;31(2):217-20. doi: 10.4103/0970-9185.155152. PMID: 25948904; PMCID: PMC4411837.
6. Lund I, Stovner J. Dose-Response curves for tubocurarine, alcuronium and pancuronium. Acta Anaesthesiol Scand Suppl. 1969;37:238-42. doi: 10.1111/j.1399-6576.1970.tb00916.x. PMID: 4246294.
7. Eisenach JC, Lysak SZ, Viscomi CM. Epidural clonidine analgesia following surgery: phase I. Anesthesiology. 1989 Nov;71(5):640-6. doi: 10.1097/00000542-198911000-00003. PMID: 2817456.
8. Clarke KW, Hall LW. "Xylazine"—a new sedative for horses and cattle. Vet Rec. 1969;85(19):512–517. doi: 10.1136/vr.85.19.512
9. AHLQUIST RP. A study of the adrenotropic receptors. Am J Physiol. 1948 Jun;153(3):586-600. doi: 10.1152/ajplegacy.1948.153.3.586. PMID: 18882199.
10. Langer SZ. Presynaptic regulation of catecholamine release. Biochem Pharmacol. 1974 Jul 1;23(13):1793-800. doi: 10.1016/0006-2952(74)90187-7. PMID: 4617579.
11. Drew GM, Whiting SB. Evidence for two distinct types of postsynaptic alpha-adrenoceptor in vascular smooth muscle in vivo. Br J Pharmacol. 1979 Oct;67(2):207-15. doi: 10.1111/j.1476-5381.1979.tb08668.x. PMID: 40647; PMCID: PMC2043892.
12. Cotecchia S, Kobilka BK, Daniel KW, Nolan RD, Lapetina EY, Caron MG, Lefkowitz RJ, Regan JW. Multiple second messenger pathways of alpha-adrenergic receptor subtypes expressed in eukaryotic cells. J Biol Chem. 1990 Jan 5;265(1):63-9. PMID: 2152928.
13. Birnbaumer L, Abramowitz J, Brown AM. Receptor-effector coupling by G proteins. Biochim Biophys Acta. 1990 May 7;1031(2):163-224. doi: 10.1016/0304-4157(90)90007-y. PMID: 2160274.
14. Metz SA, Halter JB, Robertson RP. Induction of defective insulin secretion and impaired glucose tolerance by clonidine. Selective stimulation of metabolic alpha-adrenergic pathways. Diabetes. 1978 May;27(5):554-62. doi: 10.2337/diab.27.5.554. PMID: 648745.
15. Nakamura M, Ferreira SH. Peripheral analgesic action of clonidine: mediation by release of endogenous enkephalin-like substances. Eur J Pharmacol. 1988 Feb 9;146(2-3):223-8. doi: 10.1016/0014-2999(88)90296-8. PMID: 3163552.
16. Hunter JC, Fontana DJ, Hedley LR, Jasper JR, Lewis R, Link RE, Secchi R, Sutton J, Eglen RM. Assessment of the role of alpha2-adrenoceptor subtypes in the antinociceptive, sedative and hypothermic action of dexmedetomidine in transgenic mice. Br J Pharmacol. 1997 Dec;122(7):1339-44. doi: 10.1038/sj.bjp.0701520. PMID: 9421280; PMCID: PMC1565079.
17. Kuraishi Y, Hirota N, Sato Y, Kaneko S, Satoh M, Takagi H. Noradrenergic inhibition of the release of substance P from the primary afferents in the rabbit spinal dorsal horn. Brain Res. 1985 Dec 16;359(1-2):177-82. doi: 10.1016/0006-8993(85)91426-x. PMID: 2416395.
18. Virtanen R, Savola JM, Saano V, Nyman L. Characterization of the selectivity, specificity and potency of medetomidine as an alpha 2-adrenoceptor agonist. Eur J Pharmacol. 1988 May 20;150(1-2):9-14. doi: 10.1016/0014-2999(88)90744-3. PMID: 2900154.
19. Venn RM, Bradshaw CJ, Spencer R, Brealey D, Caudwell E, Naughton C, Vedio A, Singer M, Feneck R, Treacher D, Willatts SM, Grounds RM. Preliminary UK experience of dexmedetomidine, a novel agent for post-operative sedation in the intensive care unit. Anaesthesia. 1999 Dec;54(12):1136-42. doi: 10.1046/j.1365-2044.1999.01114.x. PMID: 10594409.
20. Housmans PR. Effects of dexmedetomidine on contractility, relaxation, and intracellular calcium transients of isolated ventricular myocardium. Anesthesiology. 1990 Nov;73(5):919-22. doi: 10.1097/00000542-199011000-00020. PMID: 1978616.
21. Dyck JB, Maze M, Haack C, Vuorilehto L, Shafer SL. The pharmacokinetics and hemodynamic effects of intravenous and intramuscular dexmedetomidine hydrochloride in adult human volunteers. Anesthesiology. 1993 May;78(5):813-20. doi: 10.1097/00000542-199305000-00002. PMID: 8098190.
22. Bloor BC, Ward DS, Belleville JP, Maze M. Effects of intravenous dexmedetomidine in humans. II. Hemodynamic changes. Anesthesiology. 1992 Dec;77(6):1134-42. doi: 10.1097/00000542-199212000-00014. PMID: 1361311.
23. Hall JE, Uhrich TD, Barney JA, Arain SR, Ebert TJ. Sedative, amnestic, and analgesic properties of small-dose dexmedetomidine infusions. Anesth Analg. 2000 Mar;90(3):699-705. doi: 10.1097/00000539-200003000-00035. PMID: 10702460.

24. Xu H, Aibiki M, Seki K, Ogura S, Ogli K. Effects of dexmedetomidine, an alpha2-adrenoceptor agonist, on renal sympathetic nerve activity, blood pressure, heart rate and central venous pressure in urethane-anesthetized rabbits. J Auton Nerv Syst. 1998 Jun 30;71(1):48-54. doi: 10.1016/s0165-1838(98)00061-7. PMID: 9722194.
25. Bathe R, Mali A, Mali S, Pande J, Bathe D. An Investigation on the Release Rate from Tramadol HCl-Loaded Microspheres made Using Various Polymers. International Journal of Pharmaceutical Quality Assurance. 2023;14(1):21-25. DOI: 10.25258/ijpqa.14.1.05
26. Krishnamoorthy G, Ahamed JI, Senthamarai R, Ismail AM. Analytical Method Development and Validation of Denaverine Hydrochloride in Bulk and Injectable Pharmaceutical Dosage Form by HPLC Method . International Journal of Pharmaceutical Quality Assurance. 2022;13(2):164-168. DOI: 10.25258/ijpqa.13.2.14