ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 02 | February - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A PROSPECTIVE, RANDOMIZED STUDY TO COMPARE KETAMINE VERSUS KETAMINE PROPOFOL MIXTURE AS AN INDUCTION ANAESTHETIC AGENT IN SHORT GYNECOLOGICAL SURGICAL PROCEDURE AT S.M.S MEDICAL COLLEGE AND ATTACHED GROUP OF HOSPITALS, JAIPUR DURING 2021-23.

Anaesthesiology

Dr. Pradeep Charan	Associate professor S.M.S Medical College & Attached Group of Hospitals, Jaipur.
Dr. Chandra Shekhar Tanwar*	P.G Student S.M.S Medical College, Jaipur. *Corresponding Author
Dr. Pawan Gupta	P.G Student S.M.S Medical College, Jaipur.
Dr. Jitendra Kumar Yadav	P.G Student S.M.S Medical College, Jaipur.

ABSTRACT

Objective: To evaluate efficacy and compare ketamine versus ketofol (1:2 ketamine/ propofol) as an induction anaesthetic agent in short gynecological surgical procedures. **Method:** A prospective, randomized, comparative study was designed Total 80 patients were selected with simple random technique by sealed envelope method Group A (Ketamine 1.5 mg/kg) Group B (Ketofol, ketamine0.75mg/kg +propofol 1.5 mg/kg). Primary aim of study was to assess and compare effects of ketamine and ketofol as an induction agent on hemodynamic parameters (SBP, DBP, MAP, HR, R/R, SPO2) from baseline at various time intervals. We recorded time to sleep (loss of verbal contact), Numeric pain rating scale (NRS) pain score after recovery from anaesthesia and the proportion of respiratory events and postoperative complications. **Results:** In regards of hemodynamic parameters at various time intervals the results were comparable to baseline for ketofol group P value was < 0.001 statistically highly significant and time to sleep was also significantly lower in ketofol group. In ketofol group higher number of patients required additional doses, apnea events were less in ketofol group although PONV events were higher in ketofol group and hallucinations were lower in ketofol group but not statistically significant. **Conclusion:** Hemodynamic parameters remained comparable to baseline in ketofol group, time to sleep and quality of anaesthesia was also superior in ketofol group, intraoperative respiratory complications that are very common with propofol were also reduced.

KEYWORDS

Ketofol, Ketamine, Propofol

INTRODUCTION

Ideal induction agent should provide proper amnesia, analgesia, preserving airway with stable hemodynamic parameters and minimal post-op complications. Induction of general anaesthesia is usually accomplished by intravenous or inhalational drug administration. (1)

Ketamine is an intravenous anaesthetic developed in 1960s from its precursor phencyclidine and its mode of action is through causing dissociative anaesthesia. Several advantages have been attributed to ketamine starting from its amnesic and analgesic effects, maintenance of muscle tone, protecting airway reflexes and spontaneous respiration. However, ketamine has many side effects that limited its frequent use as an anaesthetic. These side effects include nausea, vomiting, emergence hallucinations, elevation of blood pressure and heart rate due to its sympathomimetic effects and also it was presumed to increase intracranial pressure.(2)

Propofol, commonly dubbed as “milk of anaesthesia”, is one of the most popular intravenous anaesthetic agents in modern medicine. The mechanisms of action on the central nervous system are rather complex with interactions at various neurotransmitter receptors. Propofol has many pharmacological advantages over other anaesthetic agents such as rapid effect, short action, and fewer side effects like postoperative nausea.[3] It also has the advantages of functioning as an antiemetic, an anticonvulsant, and an amnestic agent. [4] Propofol also has limitations in patients with preoperative hypotension and it can cause hypotension and sudden bradycardia after induction, and it can cause suppression of respiratory drive.

Ketofol is mixture of Ketamine and Propofol. Ketofol has additive effect so that we can decrease the dose used from each drug and benefit from advantages regarding amnesia, analgesia, hypnosis and hemodynamically stability while reducing the side effects.[2]

The positive effects of each drug may indeed balance the other product downsides: sympathomimetic effects of ketamine could mitigate propofol-associated hypotension and respiratory depression, and propofol could limit the digestive and psychiatric side effects of ketamine.[5]

AIM AND OBJECTIVES

AIM

- The aim is comparison of ketamine versus ketamine propofol mixture (1:2 ketamine/ propofol) as an induction anaesthetic agent in short gynecological surgical procedures.

OBJECTIVES

Primary:

- To assess and compare the effects of ketamine and ketofol as an induction agent on hemodynamic parameters (SBP, DBP, MAP, HR, R/R and SPO_2) from the baseline at various time intervals.

Secondary:

1. To assess and compare the difference in the meantime to sleep (loss of verbal contact) between both the study groups.
2. To assess and compare the difference in mean Numeric pain rating scale (NRS) pain score after recovery from effect of anaesthesia between both the study groups.
3. To assess and compare the difference in proportion of respiratory events and postoperative complications between both the study groups.

MATERIAL AND METHOD

PERMISSION: Permission from institutional ethics committee was obtained.

STUDY LOCATION: The study was conducted in gynaecological OT's at Pandit Deendayal Upadhyay hospital, gangauri bazar and Zanana hospital chandpol attached to S.M.S. Medical College and Group of Hospitals, Jaipur.

STUDY PERIOD: Data collection was started after approval from research review board and institutional ethical committee of S.M.S Medical College Jaipur till desired sample size to be achieved.

STUDY DESIGN: Hospital based prospective, randomized, comparative study.

STUDY UNIVERSE: Cases undergoing short elective surgical gynaecological procedures under general anaesthesia (Duration ≤ 30 minutes).

SAMPLING TECHNIQUE: Simple random technique by sealed envelope method was used to allocate cases in two groups. A total of 80 envelopes was made, each envelope mentioning study group. One of

my colleagues picked an envelope. Patient was allocated to group mentioned on the envelope.

SAMPLE SIZE: At 95% confidence interval with 80% power the sample size of 40 for each group is calculated to verify expected minimum differences of 8.4 mmHg (+/- 12.2mmHg) in variance of Mean blood pressure in patients of both groups at 5 minutes post induction as per seed article. [6]

Study Groups

The study was conducted in following two groups of patients. Each group consisted of 40 patients (n = 40/group).

Group A: Patients received Injection Ketamine (1.5mg/kg) I.V. diluted in 20 ml N.S. over 30 seconds.

Group B: Patients received Injection Ketofol (mixture of Injection Ketamine 0.75mg/kg plus Injection Propofol 1.5mg/kg i.v) diluted in single 20 ml syringe with N.S over 30 seconds.

Procedure

After approval from the ethics committee of the institute and registration of the trial in CTRI with registration number CTRI/2022/10/046679 study was started. This study included total 80 patients who were randomized into 2 equal groups by Simple random technique. Sealed envelope method was used to allocate cases in two groups.

Each group had 40 patients Group A (ketamine group) and Group B (Ketofol group). Standard monitors were applied with BIS monitoring. Patients were premedicated, preoxygenation was done, Group-A patients received injection Ketamine 1.5 mg/kg diluted in 20ml saline i.v bolus in 30 seconds and Group-B patients received mixture of injection Ketamine 0.75mg/kg and injection Propofol 1.5mg/kg (1:2) diluted in 20 ml single syringe in 30 seconds.

Hemodynamic parameters were noted at 1,3,5,10,15,30 minutes after induction. The need of another dose of ketamine or ketofol to maintain BIS in the range of 40-60 and adverse event in the form of apnea, airway obstruction, or any respiratory complication and spasm was be recorded.

After the surgery patient shifted to recovery room and observed for any side effects till one hour postoperatively, NRS was recorded at 1 hour after surgery and further follow up was done in postoperative ward till 8 hours of surgery for any side effects.

RESULTS

Table 1 Is Showing That There Are No Differences In Demographic Data Of Both Groups As Regards Patient's Age, Asa Grade, Weight And Mallampatti Score.

Table 1: Demographic data (data expressed in mean± SD)

Parameter	Group	
	Ketamine (N= 40)	Ketofol (N= 40)
Mallampatti score 1/2/3	24/13/3	24/14/2
Age (Years)	44.20 ± 8.78	40.73 ± 9.21
Weight (kg)	54.78 ± 4.76	53.40 ± 4.60
ASA grade I/II	33/7	30/10

Time To Sleep

Patients in ketamine group showed higher values compare to patients in ketofol group which were statistically significant. Mean time of ketamine group was 60.68 seconds and ketofol, group was 45.58 seconds.

Table 2: Comparison Of Time To Sleep (sec) Among Study Groups.

Group	N	Mean ± SD	Median (Range)
Ketamine	40	60.68 ± 24.01	56.5 (25 – 100)
Ketofol	40	45.85 ± 15.79	45.5 (16 – 75)
t test = 3.263; at 78 degrees of freedom; p = 0.002 (S)			

Hemodynamic Parameters

Hemodynamic were recorded for both the groups and it was found that in regards of Heart Rate, SBP, DBP, MAP, RPP at 3 minutes and 5 minutes after induction p value was <0.001 and the difference between the groups was highly statistically significant. In regards of Spo_2 at 5 and 10 minutes after induction the difference was statistically significant p value <0.001 and in regards of R/R at 1 minute after induction difference was highly statistically significant.

Table 3: Comparison Of Intra Op Heart Rate (/min) Among Study Groups

Time	Ketamine	Ketofol	P value
Baseline	92.08 ± 6.04	92.85 ± 5.8	0.560
Pre induction	93.53 ± 7.29	95.15 ± 5.65	0.268
1 min	107.3 ± 7.51	102.15 ± 5.65	0.001 (S)
3 min	106.8 ± 11.79	94 ± 7.77	<0.001 (S)
5 min	103.93 ± 7	91.45 ± 5.92	<0.001 (S)
10 min	97.63 ± 11.32	90.53 ± 7.38	0.002 (S)
15 min	95.55 ± 10.84	92.98 ± 8.94	0.250
30 min	94.75 ± 10.6	92 ± 9.91	0.234
t-test for both samples, (S) denotes statistically significant P value			

Table 4: Comparison Of Intra Op Sbp (mmhg) Among Study Groups

Time	Ketamine	Ketofol	P value
Baseline	115.4 ± 7.86	116.85 ± 7.21	0.393
Pre induction	118.18 ± 7.21	116.95 ± 8.18	0.480
1 min	124.75 ± 11.58	121.75 ± 8.52	0.191
3 min	130.33 ± 9.32	118.55 ± 5	<0.001 (S)
5 min	131.58 ± 10.54	119.08 ± 9.26	<0.001 (S)
10 min	127.55 ± 9.66	124.58 ± 6.9	0.117
15 min	124.4 ± 10.3	123.43 ± 6.63	0.616
30 min	121.7 ± 10.46	119.8 ± 6.13	0.312
t-test for both samples, (S) denotes statistically significant P value			

Table 5: Comparison Of Intra Op Dbp (mmhg) Among Study Groups

Time	Ketamine	Ketofol	P value
Baseline	76.95 ± 5.26	78 ± 4.79	0.354
Pre induction	78.78 ± 4.86	77.85 ± 5.43	0.425
1 min	82.98 ± 8.74	81.33 ± 7.99	0.381
3 min	86.95 ± 6.12	79.13 ± 3.47	<0.001 (S)
5 min	87.73 ± 7	79.43 ± 6.19	<0.001 (S)
10 min	85.03 ± 6.46	83.08 ± 4.53	0.122
15 min	82.98 ± 6.9	82.33 ± 4.5	0.619
30 min	81.18 ± 6.96	79.78 ± 4.1	0.276
t-test for both samples, (S) denotes statistically significant P value			

Table 6: Comparison of Intra op MAP (mmHg) among study groups

Time	Ketamine	Ketofol	P value
Baseline	89.7 ± 6.12	90.9 ± 5.61	0.363
Pre induction	91.9 ± 5.61	90.98 ± 6.33	0.491
1 min	96.9 ± 9.58	94.8 ± 7.93	0.286
3 min	101.43 ± 7.18	92.2 ± 3.9	<0.001 (S)
5 min	102.43 ± 8.21	92.6 ± 7.25	<0.001 (S)
10 min	99.18 ± 7.5	96.88 ± 5.28	0.117
15 min	96.73 ± 8.1	96 ± 5.15	0.634
30 min	94.73 ± 8.1	93.15 ± 4.75	0.292
t-test for both samples, (S) denotes statistically significant P value			

Table 7: Comparison Of Intra Op Spo2 (% Among Study Groups)

Time	Ketamine	Ketofol	P value
Baseline	99.23 ± 0.8	99.08 ± 0.89	0.430
Pre induction	99 ± 0.82	99.15 ± 0.77	0.400
1 min	98.9 ± 0.81	99.25 ± 0.81	0.069
3 min	98.85 ± 0.8	99.1 ± 0.88	0.161
5 min	98.8 ± 0.82	97.03 ± 2.17	<0.001 (S)
10 min	98.8 ± 0.76	96.55 ± 2.21	<0.001 (S)
15 min	98.88 ± 0.82	99.03 ± 0.80	0.411
30 min	98.98 ± 0.77	99.0 ± 0.78	0.886
t-test for both samples, (S) denotes statistically significant P value			

Table 8: Comparison Of Intra Op Respiratory Rate/min Among Study Groups

Time	Ketamine	Ketofol	P value
Baseline	16.1 ± 1.34	16.18 ± 1.26	0.797
Pre induction	16.3 ± 1.36	16.45 ± 1.34	0.621
1 min	15.83 ± 1.36	13.08 ± 2.09	<0.001 (S)
3 min	15.93 ± 1.4	15.73 ± 2.09	0.616
5 min	15.9 ± 1.28	15.13 ± 2.19	0.056
10 min	15.83 ± 1.57	15.1 ± 1.78	0.122
15 min	15.8 ± 1.38	15.03 ± 2.89	0.139
30 min	15.75 ± 1.45	15.08 ± 2.07	0.095
t-test for both samples, (S) denotes statistically significant P value			

Table 9: Comparison Of Rate Pressure Product Among Study Groups

Time	Ketamine	Ketofol	P value
Baseline	10.61 ± 0.81	10.85 ± 0.91	0.222
Pre induction	11.05 ± 1.01	11.13 ± 0.98	0.723
1 min	13.42 ± 1.8	12.45 ± 1.24	0.006 (S)
3 min	13.92 ± 1.84	11.15 ± 1.07	<0.001 (S)
5 min	13.68 ± 1.5	10.92 ± 1.4	<0.001 (S)
10 min	12.47 ± 1.84	11.29 ± 1.19	0.001 (S)
15 min	11.95 ± 2.06	11.47 ± 1.21	0.207
30 min	11.59 ± 1.96	11.01 ± 1.25	0.124
t-test for both samples, (S) denotes statistically significant P value			

NRS At 1 Hour

There was no statistical difference between two groups regarding NRS for pain after 1 hour of induction.

Table 10: Comparison Of Nrs At 1 Hour Among Study Groups

Group	N	Mean ± SD	Median (Range)
Ketamine	40	2.03 ± 2.39	1 (0 – 8)
Ketofol	40	1.60 ± 1.81	1 (0 – 5)
t test = 0.897; at 78 degree of freedom; p = 0.373			

Additional Doses

- There was significant difference in between groups in regards additional doses need where the patients who required additional doses of ketamine and ketofol were 7 and 17, respectively.

Table 11: Distribution Of Study Subjects According To Additional Dose.

Additional dose	Ketamine	Ketofol	Total			
	N	%	N	%	N	%
No	33	82.5	23	57.5	56	70
Yes	7	17.5	17	42.5	24	30
Total	40	100	40	100	80	100
Chi-square = 4.821 with 1 degree of freedom; P = 0.028 (S)						

Apnea / Obstruction/ Spasm

- There was significant difference in regards of number of apnea events in between groups, the number of patients who experienced apnea in ketamine group were 5 in comparison of 12 patients in ketofol group, the number of airway obstruction and spasm were zero in both groups.

Table 12: Distribution Of Study Subjects According To Intra Op Complications

	Ketamine		Ketofol		P value
	N	%	N	%	
Apnea	5	12.5	12	30	0.034 (S)
Obstruction	0	0	0	0	-
Spasm	0	0	0	0	-
Chi-square test, P value for apnea- 0.034					

Post Operative Complications

There was no significant difference in both groups in regards of post operative complications like post operative nausea vomiting and hallucination.

Table 13: Distribution Of Study Subjects According To Post Op Complications

	Ketamine		Ketofol		P value
	N	%	N	%	
PONV	1	2.5	5	6.2	0.203
Hallucination	7	17.5	6	15	1.000
Chi square test was performed for the % of PONV and Hallucinations p values were respectively 0.203 and 1.000.					

DISCUSSION

Our present study included 80 female patients between the age group 18 to 60 years ASA grade I and II divided into 2 groups. Group A ketamine group and Group B ketofol group going under surgical gynecological procedures of short duration 30 minutes or less than 30 minutes at obstetric hospitals of S.M.S medical college and group of hospitals.

In our study there was no difference among patients in regard of patient's age, ASA grade, weight and mallampatti score. In our study in regards of Heart rate, Systolic blood pressure, mean arterial pressure in ketofol group was more comparable to baseline in compare of ketamine group.

Paulo Sérgio Lucas da Silva, et al.[7] also observed same results as our study in regards of hemodynamic stability of the patients intraoperatively and without delay in recovery and without post operative emergence hallucination or confusion and nausea and vomiting. They used 1:1 doses of ketamine and propofol in their study.

Mehdi, et al.[8] used Propofol and Ketamine in different infusion regimes in group 1 they used, 2:1 (propofol 9mg/ml and ketamine 4.5 mg/ml) and in group 2, 4:1 (propofol 9 mg/ml and ketamine 2.25 mg/ml). They also observed the same results with propofol and ketamine combination in combination of 2:1 in regards of hemodynamic parameters.

Arora[4] studied ketofol in emergency department as procedural and sedation anaesthesia using 1:1 mixture of ketamine and propofol they recorded only 2.6% cases of transient hypoxia and no patient developed post operative nausea and vomiting these findings can be explained by the low doses of the propofol used which was 0.75 mg/kg. In our current study ketofol group took significantly less time to sleep provide by the time for loss of verbal contact then ketamine group. Aboeldahab, et al.[2] also experienced same kind of results that ketofol group showed less time to sleep in regards of loss of verbal contact.

Our study showed significant statistical difference between ketamine group and ketofol group in regards of additional doses. Total 7 patients required additional doses in ketamine group and 17 patients required additional doses in ketofol group. Similar results were found by Erden,et al.[9] In there study they used ketofol is 2 different regimes 1:1 and 1:2, and found out that for patient in group 2 required more additional doses of propofol as rescue and over sedated patients were also higher in group 2.

In another study Singh, et al.[10] studies efficacy and safety of propofol and combination of propofol and ketamine in children's undergoing spinal anaesthesia they concluded the combination propofol and ketamine required a smaller number of additional bolus doses in comparison of propofol group.

In this study we used Numeric rating scale for pain assessment 1 hour post operatively and there was no statistically difference between the two groups. According to this data higher doses of ketamine does not significantly improve the post operative analgesia.

Similar outcome was observed by Chahyun Oh, et al.[11] They studied procedural sedation in patients undergoing loop electrosurgical excision procedures inducing with propofol and combination of ketamine and propofol (ketofol) study was conducted between three groups group Overall patient satisfaction and surgeons satisfaction was evaluated and it was found that increasing the dose of ketamine showed no additional benefits between k1 and k 2 group K1 group was found superior and between propofol and ketofol, ketofol was more effective.

In our study 5 patients from group ketamine and 12 patients from group propofol went into apnea and it was statistically significant but no patient experienced spasm and obstruction of the airway. Ghojazadeh M, et al.[12] did a review and meta-analysis for using ketamine and propofol in emergency department total number of cases were 1250, of which 635 were treated with propofol and 615 were treated with propofol plus ketamine for sedation in there study incidence of apnea, assisted ventilation, and desaturation for the propofol-treated group was 1.47, 1.57, 2.64, and 1.09 times more than the group treated with propofol plus ketamine, respectively.

Singh, et al.[10] also observed the similar results in there study where in group 1 propofol group four patients had respiratory depression and 3 patients airway obstruction compared to group 2 ketofol group only one patient of respiratory depression and obstruction.

In our study 1 patient in ketamine group and 5 patients in ketofol group experience post operative nausea and vomiting which was not statistically significant. Singh R, et al.[10] also studied the post op nausea and vomiting after procedural sedation in children's undergoing spinal anaesthesia they also found out that none of the patient experienced nausea and vomiting.

Andolfatto G, Willman E [13] did a case series in adult for procedural

sedation and analgesia in adults they studied 728 patients for orthopedic procedures. They used single syringe ketofol (ketamine and propofol) was 0.7 mg/kg each (range = 0.2 to 2.7 mg/kg, IQR = 0.5–0.9 mg/kg) they found out that post operatively 1 patient had vomiting episodes. Paulo Sérgio Lucas da Silva, et al. [7] also found out similar results where they used ketofol for children's in hematological procedures that no patient had episodes of vomiting post operatively.

We observed post operative episodes of hallucinations in ketamine group 7 patients and in ketofol group 6 patients had episodes of hallucinations which was not statistically significant. Hafez, A. A. A. [6] also observed same observations where in ketamine group they had 7 patients experienced hallucinations and in ketofol group 5 patients which were not statistically significant.

Shah, et al. [14] had same observations that in regards of hallucination they found out no difference between ketamine and ketamine propofol combination (1:1). In another study Hashemi, et al. [15] studied the side effects and efficacy of two different combinations of ketamine and propofol 9 1:1) and (2:1) they observed that with increase in ketamine doses there was increase in psychomimetic effects hence it was concluded that smaller doses of ketamine in ketofol minimizes side effects and it also shorten the recovery time.

CONCLUSION

On the bases of our results and previous studies we can conclude that with Ketofol as an induction agent hemodynamic parameters remained comparable to baseline, time to sleep and quality of anaesthesia was also superior in ketofol group.

REFERENCES

1. Butterworth, F.J. & Macey, C.D (2018) Wasnick D.J. Morgan and Mikhail's clinical anesthesiology (6th ed). McGraw- Hill Education.
2. Aboeldahab, H., Samir, R., Hosny, H., & Omar, A. (2011). Comparative study between propof, ketamine and their combination (ketofol) as an induction agent. *Egyptian Journal of Anaesthesia*, *27*(3), 145-150.
3. Chidambaran, V., Costandi, A., & D'Mello, A. (2015). Propofol: a review of its role in pediatric anesthesia and sedation. *CNS drugs*, *29*(7), 543-563.
4. Arora, S. (2008). Combining ketamine and propofol ("ketofol") for emergency department procedural sedation and analgesia: a review. *Western Journal of Emergency Medicine*, *9*(1), 20.
5. Lemoel, F., Contenti, J., Giolito, D., Boiffier, M., Rapp, J., Istria, J., Fournier, M., Ageron, F. X., & Levraut, J. (2017, December). Adverse events with ketamine versus ketofol for procedural sedation on adults: A Double-blind, randomized controlled trial. Academic Emergency Medicine, 24(12), 1441–1449.
6. Hafez, A. A. A. (2020). Ketamine Alone versus Ketamine Propofol Mixture as an Induction Anesthetic Agent a Comparative Study.
7. da Silva, P. S. L., de Aguiar, V. E., Waisberg, D. R., Passos, R. M. A., & Park, M. V. F. (2011). Use of ketofol for procedural sedation and analgesia in children with hematological diseases. *Pediatrics International*, *53*(1), 62-67.
8. Sanatkar, M., Abianeh, S. H., Ghazizadeh, S., Rahmati, J., Ghanbarzadeh, K., Fathi, H. R., ... & Shahriyari, A. (2015). The comparison of infusion of two different sedation regimens with propofol and ketamine combination during plastic and reconstructive surgery. *Aesthetic plastic surgery*, *39*(1), 141-146.
9. Erden, I. A., Pamuk, A. G., Akinci, S. B., Koseoglu, A., & Aypar, U. (2009). Comparison of two ketamine-propofol dosing regimens for sedation during interventional radiology procedures. *Minerva anestesiologica*, *76*(4), 260-265.
10. Singh, R., Batra, Y. K., Bharti, N., & Panda, N. B. (2010). Comparison of propofol versus propofol-ketamine combination for sedation during spinal anesthesia in children: Randomized clinical trial of efficacy and safety. *Pediatric Anesthesia*, *20*(5), 439-444.
11. Standing, J. F., Tibboel, D., Korpela, R., & Olkkola, K. T. (2011). Diclofenac pharmacokinetic meta-analysis and dose recommendations for surgical pain in children aged 1–12 years. *Pediatric Anesthesia*, *21*(3), 316-324.
12. Ghojazadeh, M., Sanaie, S., Paknezhad, S. P., Faghih, S. S., & Soleimanpour, H. (2019). Using ketamine and propofol for procedural sedation of adults in the emergency department: a systematic review and meta-analysis. *Advanced Pharmaceutical Bulletin*, *9*(1), 5.
13. Andolfatto, G., & Willman, E. (2011). A Prospective Case Series of Single-syringe Ketamine–Propofol (Ketofol) for Emergency Department Procedural Sedation and Analgesia in Adults. *Academic Emergency Medicine*, *18*(3), 237-245.
14. Shah, A., Mosdossy, G., McLeod, S., Lehnhardt, K., Peddle, M., & Rieder, M. (2011). A blinded, randomized controlled trial to evaluate ketamine/propofol versus ketamine alone for procedural sedation in children. *Annals of emergency medicine*, *57*(5), 425-433.
15. Hashemi, A., Ayatolahi, V., Ghilian, R., Ghadami, Y. A., Fadavi, N., Yadegari, Y., Shahri, T., Mir, A. M., Askari, N. A., & Pour, M. S. Ketofol for bone marrow aspiration and lumbar puncture in children with ALL.