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Prospective observational comparison of propofol–ketamine, propofol–fentanyl, propofol–dexmedetomidine combinations on intraoperative hemodynamics, post-operative recovery in upper abdominal surgery

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Abstract:
Balanced general anesthesia optimization remains challenging as propofol adjuvants (dexmedetomidine, fentanyl, ketamine) uniquely affect intraoperative hemodynamics and post-operative recovery profiles. Therefore, it is of interest to compare the propofol-dexmedetomidine (PD), propofol-fentanyl (PF) and propofol-ketamine (PK) in 114 ASA I-II patients (18-65 years) undergoing elective upper abdominal surgery. PD provided superior hemodynamic stability (reduced HR/BP versus PK/PF; $p<0.05$), while PF achieved fastest recovery; PK minimized post-operative analgesic needs across VAS assessments. Oxygen saturation and $EtCO_2$ remained comparable ($p>0.05$), through PD showed deeper sedation (Modified Ramsay) versus PF's rapid Aldrete recovery. Thus, data shows the adjuvant-specific profiles—PD for stability, PF for recovery speed, PK for analgesia, enabling clinical goal-directed anesthetic selection.

Keywords: Dexmedetomidine, fentanyl, hemodynamics, ketamine, propofol, recovery

Background:
Optimal analgesia, stable hemodynamics during surgery, a speedy recovery with few side effects, a smooth and quick induction—these are the goals of general anesthesia. The idea of balanced general anesthesia is to use a number of different drugs in a coordinated and synergistic fashion to accomplish various goals, such as numbing the pain, hypnosis, relaxing the muscles and reducing the reflex reactions **[1, 2]**. Significant sympathetic activation is linked to laryngoscopy and endotracheal intubation, which may cause unwanted hemodynamic reactions including hypertension and tachycardia. The quick onset and excellent recovery profile of induction drugs like propofol make them frequently employed. However, the dose-dependent depression of circulatory and respiratory systems might occur at larger doses needed to attenuate these effects **[3]**. Many adjuvant medications are often used in conjunction with propofol to circumvent these restrictions. Despite their ability to reduce the stress response to airway manipulation, opioids like fentanyl have the potential to cause respiratory depression and postpone recovery **[4]**. Ketamine's sympathomimetic characteristics mean it may assist keep the heart stable and give excellent pain relief, but it also comes with the risk of psychomimetic symptoms and a protracted recovery time **[5]**. Sedation and analgesia are provided by dexmedetomidine, a selective α2-adrenergic agonist, with little respiratory depression. Nevertheless, bradycardia and hypotension, particularly at larger dosages, may be linked with its usage **[6, 7].** Propofol-dexmedetomidine provided better attenuation of intraoperative hemodynamic responses than propofol-fentanyl during supraumbilical surgery, although recovery was modestly delayed with dexmedetomidine **[8]**. Different propofol medication combinations have a different pharmacodynamic profile, which means they might affect intraoperative hemodynamics, post-operative analgesic needs and recovery traits. There is a lack of comparative examination of routinely used propofol-based combinations under typical clinical practice situations, despite the fact that several researches have examined these combinations either alone or in selective comparisons **[9]**. Therefore, it is of interest to evaluate the patients undergoing upper abdominal surgeries under general anesthesia to be studied and to compare the effects of propofol-ketamine, propofol-fentanyl and propofol-dexmedetomidine combinations on intraoperative hemodynamic parameters and post-operative recovery profiles.

Materials and Methods:
Following Institutional Ethics Committee permission, this prospective observational comparative research was carried out at the Department of Anaesthesiology at a tertiary care teaching hospital in Central India. All participants were asked to sign an informed consent form before they could be included in the research. The research comprised 114 patients slated for elective upper abdominal procedures under general anesthesia, ranging in age from 18 to 60 years old and belonging to ASA physical status I and II. We did not include patients who had a history of systemic disease, were expecting a baby, were nursing, had a body mass index (BMI) more than 29.9 kg/m^2, refused to participate, or were pregnant or lactating.

A formula was used to determine the sample size:

$n = 2[Z(1-\alpha/2) + Z(1-\beta)]^2 \times \sigma^2/d^2$

The minimum number of patients needed for each group was determined to be 34 based on prior research that assumed a standard deviation (σ) of 10 units and a minimum clinically meaningful difference (d) of 8 units in mean arterial pressure. The study was conducted with a confidence level of 95% and power of 80%. We enrolled 38 patients in each group, for a total of 114 patients, after accounting for a 10% dropout rate.

The three groups of patients were determined by the anesthetic regimen that was provided in accordance with standard clinical practice:

[1] Group PK: Patients receiving propofol in combination with ketamine
[2] Group PF: Patients receiving propofol in combination with fentanyl
[3] Group PD: Patients receiving propofol in combination with dexmedetomidine

Electrocardiography, non-invasive blood pressure, pulse oximetry and end-tidal carbon dioxide monitoring were among the normal intraoperative monitoring that all patients got. They also had conventional pre-anesthetic examinations. As per the established procedure of the institution, anesthetic management was performed. One of the three adjuvant medications was administered to patients in addition to propofol for induction and maintenance of anesthesia. At baseline, during induction, every 5 minutes up to 60 minutes and every 10 minutes thereafter until the end of surgery, hemodynamic parameters such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP) were recorded. At the same times, we also measured end-tidal carbon dioxide ($EtCO_2$) and oxygen saturation (SpO_2). The Modified Aldrete score was used to evaluate post-operative recovery both immediately after extubation and 10 minutes later. We used the Modified Ramsay Sedation Scale to measure sedation levels. The VAS was used to measure pain severity after surgery. Additionally, we documented the frequency of postoperative problems and the time it took for the patient to be given their first rescue analgesic. Since this was an observational study, the researchers had no say on the anesthetic method and there was no blinding or randomization. Consistency in perioperative treatment was sought in order to reduce the influence of any confounding variables.

Statistical analysis:

The data was input into excel and analyzed using SPSS version 20, a statistical package for social sciences. Mean ± standard deviation (SD) was used to represent quantitative data, whilst frequency and percentage were used to describe categorical variables. We used one-way analysis of variance (ANOVA) and, if necessary, post-hoc tests to compare continuous variables between groups. The chi-square test was used for the analysis of categorical variables. Statistical significance was determined by a p-value less than 0.05.

Results:

The research comprised 114 patients in total, with 38 individuals in each of the three groups (PK, PF and PD). There were no statistically significant variations ($p > 0.05$) in the demographic parameters of the three groups, which included age, gender distribution, weight, ASA physical status and length of operation **(Table 1).** Intraoperative hemodynamic measurements, such as heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP) and mean arterial pressure (MAP), showed statistically significant differences between the groups ($p < 0.001$). The propofol-dexmedetomidine (PD) group had substantially reduced heart rate and blood pressure readings when compared to the propofol-ketamine (PK) and propofol-fentanyl (PF) groups, according to the results of the pairwise comparison ($p < 0.001$). When comparing the PK and PF groups, we did not find any statistically significant changes in HR ($p = 0.990$), SBP ($p = 0.461$), DBP ($p = 0.179$), or MAP ($p = 0.213$) **(Figure 1, 2 and Table 2).** During the course of the operation, there were no discernible variations in oxygen saturation (SpO_k) or end-tidal carbon dioxide ($EtCO_k$) across the three groups ($p > 0.05$). There were substantial intergroup differences ($p < 0.05$) in sedation ratings as measured by the Modified Ramsay Sedation Scale. There was no statistically significant difference in sedation levels between the PK and PF groups, however the PD group showed significantly higher values than the other two **(Table 3)**. At 10 minutes after extubation, there was no statistically significant difference in postoperative recovery as measured by the Modified Aldrete score ($p = 0.230$), although there was a significant difference immediately after extubation ($p = 0.049$) **(Table 4)**. There was a substantial difference in the time it took for each group to get their first rescue analgesic (ANOVA, $p < 0.0001$). The time it took for patients in the PK group to no longer need rescue analgesia was much longer than that of the PF group and it was the shortest in the PD group **(Table 5, Figure 3).** There was no statistically significant difference between the PF and PD groups with regard to the occurrence of postoperative complications ($p > 0.05$). Statistical analysis revealed no significant difference ($p = 0.40$) in postoperative pain levels as measured by the visual analogue scale (VAS).

Table 1: Baseline demographic and clinical characteristics of the study population

Variables		Group PK (n=38)	Group PF (n=38)	Group PD (n=38)	P- Value
Age (years) (Mean±SD)		36.55±8.494	40.96±10.309	35.24±13.435	0.42
Gender	Male	22 (31.9%)	20 (29.0%)	27 (39.1%)	0.80
	Female	16 (35.6%)	18 (40.0%)	11 (24.4%)	
Weight (kg) (Mean±SD)		53.00±8.161	60.14±10.061	54.71±10.099	0.12
ASA grade	I	32 (33.3%)	34 (35.4%)	30 (31.3%)	0.43
	II	06 (33.3%)	04 (22.2%)	08 (44.4%)	

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Duration of surgery (minutes)	63.16±18.760	68.49±18.566	62.63±17.658	0.52

Table 2: Intergroup comparison of intraoperative hemodynamic parameters

Intergroup difference	**P- value**		
	Group PK vs. Group PF	Group PK vs. Group PD	Group PF vs. Group PD
Heart rate (HR)	0.990	<0.001*	<0.001*
Systolic Blood pressure (SBP)	0.461	<0.001*	<0.001*
Diastolic Blood pressure (DBP)	0.179	<0.001*	<0.001*
Mean Arterial pressure (MAP)	0.213	<0.001*	<0.001*
Oxygen Saturation (SpO_2)	0.221	0.640	0.064
End-tidal Carbon dioxide ($EtCO_2$)	0.685	0.946	0.636

Statistically significant

Table 3: Intergroup comparison of postoperative sedation scores (Modified Ramsay Scale)

Intergroup difference in Modified Ramsay Sedation score		**P- value**
Group PK	Group PF	0.200
Group PK	Group PD	0.022*
Group PF	Group PD	0.012*

Statistically significant

Table 4: Comparison of recovery profile and postoperative outcomes among study groups

Parameters		**Pearson Chi square test**	
		Value	P-value
Modified Aldrete's Recovery Score at different time interval	Immediately post-extubation	15.9	0.049*
	10 minutes post-extubation	14.6	0.230
Post-operative complication		18.1	0.08
VAS score		3.6	0.40

Statistically significant

Table 5: Comparison of time to first rescue analgesia among study groups

Groups	**Mean (mins)**	**Standard deviation**	**ANOVA test**	
			F value	P-value
PK	26.05	11.692	9.3	<0.0001*
PF	32.11	8.748		
PD	21.32	11.951		

Statistically significant

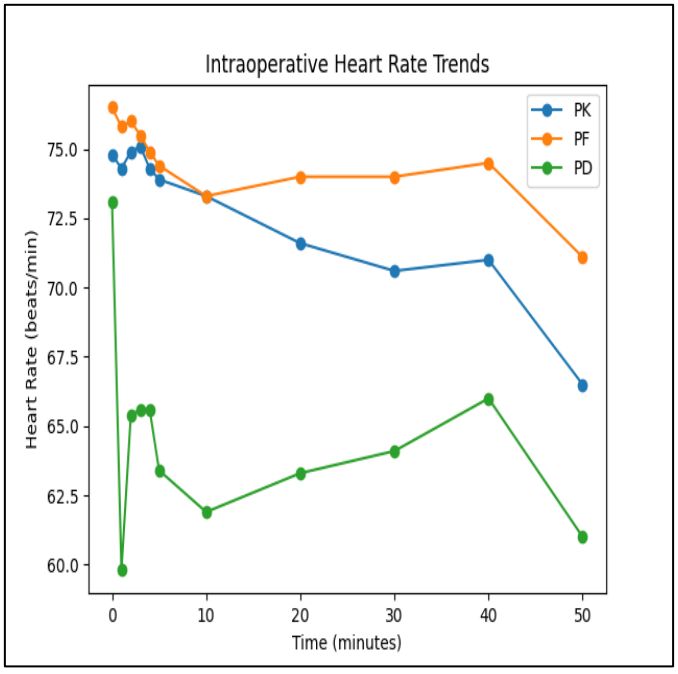

Figure 1: Comparison of intraoperative heart rate trends among study groups

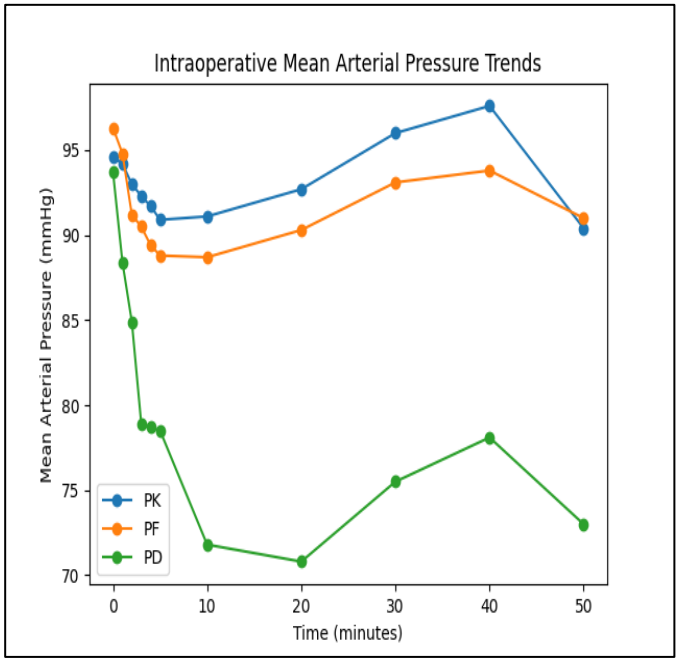

Figure 2: Comparison of mean arterial pressure trends among study groups

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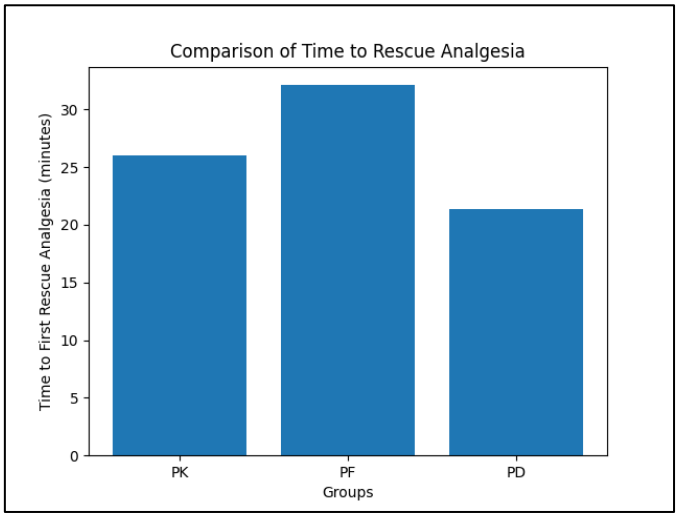

Figure 3: Comparison of time to first rescue analgesia among study groups

Discussion:

This prospective observational study compared three popular propofol-based combinations with regard to intraoperative hemodynamic parameters and post-operative recovery characteristics in patients having upper abdominal surgeries under general anesthesia. The combinations were propofol-ketamine, propofol-fentanyl and propofol-dexmedetomidine. Consistent with the hypothesis that the research groups were homogenous and that confounding factors were not at work, the demographic features of the three groups were similar. Earlier research by Joshi *et al.* **[10]** and Bajwa *et al.* **[11]** also showed similar results. The propofol-dexmedetomidine group showed a considerable improvement in hemodynamic measures, such as blood pressure and heart rate, when compared to the propofol-ketamine and propofol-fentanyl groups. This may be accounted for by the pharmacological activity of dexmedetomidine, which causes a reduction in norepinephrine release and a weakening of stress reactions by exerting sympatholytic effects through central α2-adrenergic receptor agonism **[12, 13].** Studies conducted by Tanriverdi *et al.* **[14]** and Bajwa *et al.* **[11]** also found that dexmedetomidine enhanced intraoperative hemodynamic stability. The propofol-ketamine group, on the other hand, had hemodynamic characteristics that were more stable. The sympathomimetic actions of ketamine prevent the heart from collapsing as a result of propofol's myocardial depressive effects. The sympathomimetic action of ketamine was attributed by Joshi *et al.* **[10]** to the fact that the propofol-ketamine group saw a smaller decrease in heart rate compared to the propofol-fentanyl group. In terms of hemodynamic stability, the dexmedetomidine group fared better than the propofol-fentanyl group. Due to its lack of intrinsic sympathomimetic activity, fentanyl may cause a higher drop in blood pressure, even while it effectively reduces the hemodynamic response to intubation and laryngoscopy. Findings demonstrating a reduction in heart rate and blood pressure with propofol-fentanyl combinations were reported by Ghomeishi *et al.* **[15]** and Mayer *et al.* **[16].** There were no notable variations in oxygen saturation (SpO_k) and end-tidal carbon dioxide ($EtCO_k$) between the three groups in this investigation, suggesting that all three medication combinations preserved sufficient respiratory function. According to Mi *et al.* **[17],** similar results were also found. The groups given propofol with fentanyl recovered more quickly than the groups given propofol with ketamine or dexmedetomidine, according to recovery characteristics. This could be because of fentanyl's pharmacokinetic features, which include its short half-life and fast redistribution when administered in regulated amounts. Fentanyl-based combinations were associated with faster recovery than dexmedetomidine-based regimens **[18-20].** The group given propofol with dexmedetomidine had much better sedation ratings. The sedative effects of dexmedetomidine, which induce a condition similar to sleep, are known to be mediated via the locus cerulean, thus this makes sense. In addition, research by Kakarla *et al.* **[9]** and Tosun *et al.* **[7]** has shown that dexmedetomidine produces more sedation. The propofol-ketamine group showed a longer time before rescue analgesia was needed after surgery, which is consistent with the analgesic effects of ketamine, which are mediated by NMDA receptor antagonism. Shirisha *et al.* similarly reported a significant reduction in heart rate and blood pressure with propofol-dexmedetomidine compared with propofol-ketamine and propofol-fentanyl, supporting its favorable hemodynamic profile **[21]**. Although there was no statistically significant difference between the groups, the propofol-fentanyl group had a greater incidence of post-operative problems than the propofol-dexmedetomidine group. All three medicine combinations seem to be safe when given under the right circumstances of supervision. In sum, the results of this research provide further evidence that different propofol-based combinations have different beneficial effects on patients' health. The combination of propofol and dexmedetomidine improves hemodynamic stability, whereas propofol and ketamine give greater analgesia after surgery and propofol and fentanyl have been linked to a quicker recovery. Thus, each patient's anesthetic regimen should be tailor-made according to their specific needs and medical history. There are several restrictions on this research. Results may not be applicable to a broader population due to the study's small sample size and fact that it was conducted at just one location. The findings may not be applicable to groups at greater risk since only individuals with ASA physical status I or II were included. The absence of blinding and randomization in this observational research raises concerns about the possibility of selection and observer bias. Furthermore, spectral index monitoring or any other objective method for gauging anesthetic depth was not used. Additionally, we did not evaluate patients' levels of satisfaction or their long-term post-operative results. This research compares three popular propofol-based anesthetic combinations in a controlled setting during surgery. The results are more applicable to real-world situations because of the prospective design and the incorporation of many clinically relevant outcome measures. These measurements include hemodynamic parameters, recovery profile, sedation needs and analgesic

requirements. There was less variation among the groups because to the similar anesthetic treatments and uniform monitoring. The results of this research should be confirmed by conducting further large-scale, multicentric randomized controlled trials. Patients with higher ASA grades should be included in future research and objective monitoring methods like the spectral index should be used to determine the depth of anesthesia. Additional insights into the best choice of anesthetic combinations might be gained by evaluating long-term results, patient satisfaction and cost-effectiveness. This study's results provide credence to the idea that different clinical goals might inform the selection of propofol-based anesthetic combinations. When hemodynamic stability is critical, propofol-dexmedetomidine may be the way to go, while propofol-ketamine could be the way to go for patients who need more pain relief after surgery. When you want to get well quickly, propofol-fentanyl can be a good choice. Perioperative results may be better if anesthetic regimes were chosen individually according to patient characteristics and surgical needs.

Conclusion:

Propofol-dexmedetomidine and propofol-ketamine provided greater intraoperative hemodynamic stability than propofol-fentanyl during upper abdominal procedures under general anesthesia. Propofol-ketamine offered better analgesia, whereas propofol-fentanyl enabled faster post-operative recovery. These findings support individualized selection of propofol adjuvants according to hemodynamic, analgesic and recovery requirements.

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