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# The Effect of Anesthesia Induction with Midazolam and Propofol on Hemodynamics in Abdominal Hysterectomy Surgeries

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**ABSTRACT**
**Objective:** The primary task of anesthesiology is to control the patient's hemodynamic values, including blood pressure and heart rate, from pre-operative to post-operative. Many drugs are used alone or in combination for induction and maintenance of anesthesia. Various hemodynamic responses may develop to these drugs. In our study, we aimed to compare the effects of midazolam and propofol used alone in intravenous anesthesia induction on hemodynamics in patients undergoing abdominal hysterectomy. **Materials and Methods:** A total of 60 ASA I-II patients scheduled for abdominal hysterectomy were included in the study. During anesthesia induction, midazolam (0.2 mg/kg) was administered to Group M (n:30) and propofol 1% (2 mg/kg) was administered to Group P (n:30). Noninvasive systolic blood pressure, diastolic blood pressure, mean blood pressure and minute heart rate values were recorded. **Results:** Systolic blood pressure was significantly lower in group P than in M during intubation, skin incision, extubation and recovery. **Conclusion:** As a result, anesthesia induction with intravenous 0.2 mg/kg midazolam may cause higher systolic blood pressure values than 2 mg/kg propofol. It should not be overlooked that the hemodynamic response that will occur after the use of midazolam during anesthesia monitoring will vary depending on the anesthetic drugs and doses used together.
**Keywords:** General Anesthesia, Midazolam, Propofol, Hemodynamic.

# Abdominal Histerektomi Ameliyatlarında Midazolam ve Propofol ile Anestezi İndüksiyonunun Hemodinami Üzerine Etkisi

**ÖZ**
**Amaç:** Anesteziyolojinin birincil görevi, ameliyat öncesinden ameliyat sonrasına kadar hastanın kan basıncı ve kalp atış hızı dahil olmak üzere hemodinamik değerlerini kontrol etmektir. Anestezi indüksiyonu ve idamesi için birçok ilaç tek başına veya kombinasyon halinde kullanılır. Bu ilaçlara karşı çeşitli hemodinamik yanıtlar gelişebilmektedir. Çalışmamızda abdominal histerektomi yapılan hastalarda intravenöz anestezi indüksiyonunda tek başına kullanılan midazolam ve propofolün hemodinami üzerine etkilerini karşılaştırmayı amaçladık. **Gereç ve Yöntem:** Abdominal histerektomi planlanan toplam 60 ASA I-II hasta çalışmaya dahil edildi. Anestezi indüksiyonu sırasında Grup M'ye (n:30) midazolam (0.2 mg/kg) ve Grup P'ye (n:30) propofol %1 (2 mg/kg) uygulandı. Noninvaziv sistolik kan basıncı, diyastolik kan basıncı, ortalama kan basıncı ve dakika kalp atım hızı değerleri kaydedildi. **Bulgular:** Entübasyon, cilt insizyonu, ekstübasyon ve derlenme sırasında sistolik kan basıncı P grubunda M grubuna göre anlamlı olarak daha düşüktü. **Sonuç:** İntravenöz 0,2 mg/kg midazolam ile anestezi indüksiyonu 2 mg/kg propofolden daha yüksek sistolik kan basıncı değerlerine neden olabilir. Anestezi takibi sırasında midazolam kullanımı sonrası oluşacak hemodinamik yanıtın birlikte kullanılan anestezik ilaçlara ve dozlarına bağlı olarak değişeceği göz ardı edilmemelidir.
**Anahtar Kelimeler:** Genel Anestezi, Midazolam, Propofol, Hemodinami.

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## INTRODUCTION

In anesthesia applications, many drugs are used alone or in combination during the induction phase. The maintenance phase can also be provided with anesthetic drugs administered as intravenous infusion, other than inhalation agents. Various hemodynamic responses may develop to intravenous anesthetic drugs used in anesthesia applications. The primary task of anesthesiology is to control the patient's hemodynamic values, including blood pressure and heart rate, from pre-operative to post-operative. An ideal intravenous anesthetic agent is expected to provide rapid and reliable anesthesia induction and recovery, have minimal effects on vital functions, have no effects such as reactions or pain at the injection site, be in a stable solution, and preferably have a solution in water (Kayhan, 2004). Propofol is a short-acting, intravenous sedative-hypnotic used for induction of anesthesia. It provides quick and comfortable induction, which usually occurs within 40 seconds (arm-brain circulation time) following the start of the injection. It causes pain in up to 58% of cases when given from the back of the hand. It is depressant for the cardiovascular system (CVS), lowers blood pressure and cardiac output depending on the dose, and slightly reduces heart rate. In clinical studies, intravenously administered midazolam has been shown to be an adequate agent for induction of general anesthesia (Reves et al., 1985). It can be safely used in general anesthesia induction at a dose of 0.25 mg/kg to 0.35 mg/kg, although there is inter-subject variability (Kyeong et al, 1993). Midazolam is a benzodiazepine derivative with a short duration of action (Conway et al., 2016). The general anesthetic effect begins after intravenous injection (30-100 seconds). Its effects in CVS are minimal and it does not cause pain or irritation during injection. However, midazolam alone is rarely used for anesthesia induction. There are no sufficient studies in the literature comparing the effects of propofol and midazolam used alone in anesthesia induction on hemodynamics. In our study, the effects of midazolam and propofol used during induction on intraoperative hemodynamics in patients undergoing abdominal hysterectomy were compared.

## MATERIALS AND METHODS

### Study type

Prospective observational study

### Study group

Between January 2008 and January 2009, routine preoperative anesthesia visits were made to 60 patients with American Society of Anesthesiologists (ASA) score I-II, ages 35-60, who were scheduled for abdominal hysterectomy, and informed consent was obtained about the study.

### Procedures

No premedication was applied to the patients. The patients were divided into two equal groups: those given midazolam during induction (Group M) and those given propofol (Group P). During anesthesia induction, midazolam (0.2 mg/kg) was administered to Group M (n:30) and propofol 1% (2 mg/kg) was administered to Group P (n:30). After standard monitoring was performed on the volunteer patients in both groups, vascular access was established with a 20 G branule. Infusion of 0.9% NaCl solution was started at a constant rate in all patients and infusion was continued throughout the surgery according to the 4-2-1 rule. In the operating room, non-invasive systolic blood pressure, diastolic blood pressure, mean blood pressure, minute heart rate values were recorded at the beginning of anesthesia induction (T1), after intubation (T2), during skin incision (T3), extubation (T4) and in the recovery room at the fifth minute of extubation (T5). During induction of anesthesia, 0.2 mg/kg midazolam, 2 mcg/kg fentanyl, and 0.2 mg/kg cisatracurium were given intravenously to patients in Group M. Patients in Group P received 2 mcg/kg propofol 1%, 2 mcg/kg fentanyl, and 0.2 mg/kg cisatracurium intravenously. After 3 minutes of mask oxygenation, patients were orotracheally intubated. Following orotracheal intubation in both groups, anesthesia was maintained with a mixture of 4-6% desflurane, 50% oxygen and 50% nitrogen oxide. Patients were administered intravenous (0.05-01mcg/kg) fentanyl and (0.02mg/kg) cisatracurium at 45-minute intervals as additional doses. All patients were administered 100 mg tramadol when skin closure stitching was applied. During the surgical skin closure suture stage, the nitrogen protoxide flow was stopped, and a fifty percent air-oxygen mixture was switched to. At the end of skin closure, desflurane was discontinued and air-oxygen flow was continued. Decurarization was achieved by administering 1 mg atropine and 2 mg neostigmine to patients who started spontaneous breathing, and then extubation was performed. Patients who had an eye-opening response with verbal stimulation and had adequate spontaneous respiration were sent to the recovery room. Patients whose Aldrete score reached 9 points in the recovery room were sent to the ward.

### Statistical analysis

In this study, statistical analyzes were performed with the NCSS 2007 package program. In addition to descriptive statistical methods (mean, standard deviation) in the evaluation of the data, repeated analysis of variance was used for repeated measurements of multiple groups, Newman Keuls multiple comparison test was used for subgroup comparisons, independent t test was used for comparison of paired groups, and chi-square test was used for comparisons of qualitative data. The results were evaluated at the significance level of $p<0.05$.

### Ethical considerations

For this observational study, permission was obtained from the ethics committee of Istanbul Training and Research Hospital (Tarih 02.05.2008; Karar sırano:22, no: 5/8).

## RESULTS

No statistically significant difference was observed between the age and weight averages and ASA score distributions of the groups (Table 1). The duration of abdominal hysterectomy surgeries was similar in both groups respects. Groups; They were similar in terms of extubation times, recovery times, and Aldrete score.

While no significant difference was observed between the groups in terms of initial systolic blood pressure averages, the 5th minute systolic blood pressure averages of intubation, skin incision, extubation, and recovery were significantly lower in group P than in M (Table 2).

**Table 1. Group M and Group P, age, weight averages and ASA score distributions.**

| | | Group M | Group P | P* |
|---|---|---|---|---|
| **Age (year)** | | 47.53±5.56 | 45±7.33 | 0.137 |
| **Weight (kg)** | | 70.83±7.76 | 74.27±8.27 | 0.103 |
| **ASA score** | **I** | 15 (%50) | 19 (%63.3) | 0.297 |
| | **II** | 15 (%50) | 11 (%36.7) | |

ASA: American Society of Anesthesiologists, *P<0.05 is significant.

**Table 2. Group M and Group P, systolic blood pressure averages.**

| Systolic blood pressure (mmHg) | Group M | Group P | P |
|---|---|---|---|
| **T1** | 138.10±18.25 | 131.70±15.03 | 0.143 |
| **T2** | 155.87±19.08 | 135.47±23.32 | **0.0001*** |
| **T3** | 124.70±13.41 | 118.30±15.41 | **0.048*** |
| **T4** | 147.57±13.19 | 132.93±13.23 | **0.0001*** |
| **T5** | 134.33±14.14 | 124.90±13.45 | **0.010*** |

| Newman Keuls Multiple Comparison Test | Group M | Group P |
|---|---|---|
| **Induction / Intubation** | **0.001*** | 0.259 |
| **Induction / Incision** | **0.001*** | **0.001*** |
| **Induction / Extubation** | **0.008*** | 0.621 |
| **Induction / Recovery** | 0.222 | **0.006*** |

T1: anesthesia induction, T2: after intubation, T3: during skin incision, T4: extubation, T5: fifth minute of extubation. *P<0.05 is significant.

In Group M, the mean systolic blood pressure after intubation and extubation was significantly higher than the initial value, while the value after skin incision was lower. In Group P, incision and recovery systolic blood pressure averages showed a significant decrease compared to the baseline value (Table 2) (Figure1).

While no significant difference was observed between the mean diastolic blood pressure values of groups M and group P at baseline, during incision and extubation, and also during recovery, a significant decrease was observed in the mean diastolic blood pressure values measured immediately after intubation in group P.The average of diastolic blood pressure values measured during intubation and extubation in both groups was observed to be significantly higher than the baseline (Table 3) (Figure 2) (P<0.05). While no significant difference was observed between the averages of intubation, incision and recovery mean blood pressure, measurements of the groups, the extubation mean blood pressure, averages of group P showed a significant decrease (Table 3) (Figure 3) (P<0.05).

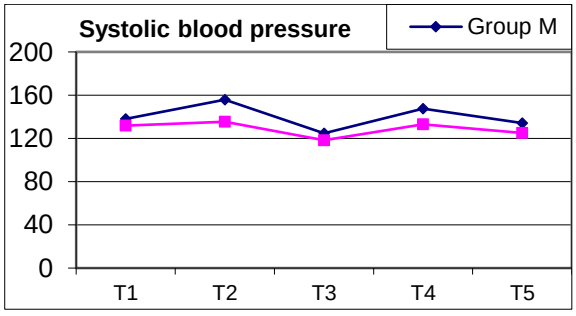


**Figure1: Average values of systolic blood pressure.**

**Table 3: Group M and P, diastolic and mean blood pressure average, mean minute heart rate.**

| Diastolic blood pressure (mmHg) | Group M | Group P | P |
|---|---|---|---|
| **T1** | 76.03±8.27 | 73.57±8.98 | 0.077 |
| **T2** | 88.63±10.52 | 81.40±16.16 | **0.044*** |
| **T3** | 73.67±11.21 | 68.63±12.49 | 0.106 |
| **T4** | 83.83±12.58 | 78.13±11.44 | 0.071 |
| **T5** | 75.17±13.17 | 72.37±10.8 | 0.372 |
| **Mean blood pressure (mmHg)** | | | |
| **T1** | 95.97±8.9 | 91.97±8.67 | 0.079 |
| **T2** | 107.40±21.58 | 98.57±16.08 | 0.077 |
| **T3** | 87.53±18.3 | 85.53±12.18 | 0.620 |
| **T4** | 103.70±9.46 | 96.60±9.92 | **0.006*** |
| **T5** | 94.23±11.22 | 89.97±11.19 | 0.146 |
| **Minute heart rate (beats/minute)** | | | |
| **T1** | 81.73±10.18 | 86.13±7.12 | 0.057 |
| **T2** | 89.33±9.92 | 94.40±11.13 | 0.068 |
| **T3** | 78.70±13.18 | 78.63±9.55 | 0.982 |
| **T4** | 97.23±14.05 | 89.17±10.48 | **0.014*** |
| **T5** | 87.03±11.6 | 83.60±9.07 | 0.207 |

T1: anesthesia induction, T2: after intubation, T3: during skin incision, T4: extubation, T5: fifth minute of extubation. *P<0.05 is significant.

While there was no difference in the averages of intubation, incision, and recovery minute heart rate measurements between the groups, the group P extubation minute heart rate averages showed a significant decrease. While intubation and extubation minute heart rate averages in Group M were significantly higher than the baseline values, in Group P, only intubation measurements showed a significant increase compared to the baseline. In addition, the mean values of minute heart rate numbers measured during the incision in group P were significantly lower than the initial values (Table 3) (P<0.05).

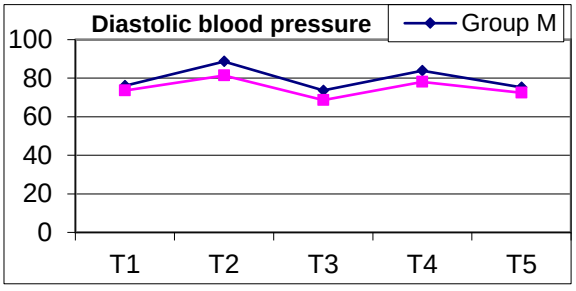


**Figure 2: Average values of diastolic blood pressure**

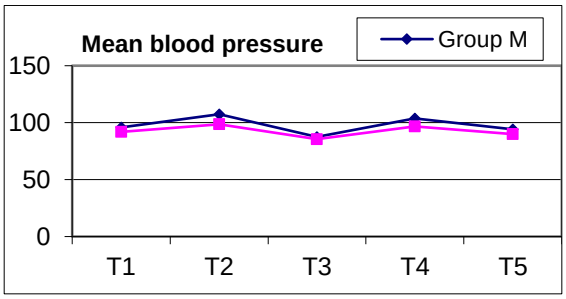


**Figure 3: Average values of mean blood pressure**

## DISCUSSION

In our study, it was observed that midazolam did not prevent the hemodynamic response after induction, and intravenous 0.2 mg/kg midazolam caused higher systolic blood pressure values than 2 mg/kg 1% propofol. Neither drug alone provided hemodynamic stability. Similarly, Bosna et al. (Bosna et al., 2002) reported in their study aiming to compare the hemodynamic effects of midazolam and propofol that hemodynamic stability could not be maintained in both groups. The addition of midazolam during induction of anesthesia has been reported to attenuate intubation-induced increases in blood pressure and minute heart rate, cardiac autonomic system responses, and serum epinephrine and norepinephrine concentrations (Nishiyama et al.,2002). Midazolam helps maintain hemodynamic stability by reducing

the stress response during induction of anesthesia. It may suppress physiologic responses during induction of anesthesia (Jeon et al., 2018). In their fifty percent effective dose (ED50) study, (Mcclune et al., 1992) reported that the doses of midazolam and propofol required to eliminate the eye-opening response to voice command were 0.26 and 1.25 mg/kg, respectively. It has been reported that the same drug doses for midazolam and slightly higher doses for propofol are required for face mask tolerance, and both drugs require similarly higher doses to eliminate the eyelash reflex. In our study, midazolam was used at 0.2 mg/kg, considering that it was given together with fentanyl were used in both groups for anesthesia induction, and after induction, intubation and surgical incision, decreases in hemodynamic parameters were detected in both groups. They reported that propofol-fentanyl and midazolam-fentanyl combinations were similar to each other in terms of hemodynamic stability (Arda et al., 2000). In our study, fentanyl was used in lower doses as 2 microgram/kg and midazolam as 0.2 mg/kg. Midazolam and propofol can be used together, but there is no clarity about the effects of the doses to be applied on hemodynamics. It has been reported that hemodynamic values after induction of anesthesia are lower when propofol and midazolam are used together (midazolam 0.03, 0.06 or 0.12 mg/kg, respectively, followed by propofol 0.3, 0.6 or 0.9 mg/kg administered 2 minutes later) than when used alone (McClune et al., 1992). It has been shown to be synergistic when used within the commonly accepted dosage range. There is a 44% reduction in the ED50 of each agent individually. If 0.13 mg/kg midazolam is used in anesthesia applications, a 52% decrease in propofol dose is required (Short & Chuı, 1991). Another study used midazolam-propofol-alfentanil, evaluating the drugs individually and in combination in 400 patients; Although all responses to two-drug combinations are synergistic, the three-drug combination has been reported to result in a response less than that expected from the effects of the individual agents and their two-drug interactions (Short et al., 1992). We think that the lower hemodynamic responses with propofol compared to midazolam in our study are due to the dose we used. In a study in which general anesthesia induction with propofol was performed by adding 0.03 mg/kg and 0.06 mg/kg intravenous midazolam, it was reported that a significant decrease in systolic blood pressure, diastolic and mean blood pressure was prevented immediately after induction. The authors reported decreased postoperative anxiety score, decreased cortisol response to surgery, and decreased propofol requirement for induction (Mihali et al., 2022). Two specific hypotheses were tested by heart rate variability analysis of heart rate and arterial blood pressure changes during conscious sedation with propofol and midazolam. According to this study, propofol induces a decrease in heart rate and blood pressure by inducing the dominance of parasympathetic activity, while midazolam induces an increase in heart rate and a decrease in blood pressure by inducing the dominance of sympathetic activity (Win et al., 2005). In our study, we think that the lower hemodynamic responses with propofol compared to midazolam may be due to suppression of parasympathetic activity. Propofol's ability to reduce blood pressure during induction of anesthesia has been reported as a 25-40% decrease in systolic blood pressure when administered at an induction dose of 2-2.5 mg/kg, regardless of any cardiovascular disease. It shows that it is a result of the direct negative inotropic effects of propofol as well as its direct effects on arterial and venous vascular tone (Pagel & Warltier, 1993). Additionally, in studies comparing the 2% and 1% formulation of propofol in use reported that the formulations were similar in terms of hemodynamic responses to intubation (Öztürk, 2007; Servin et al., 1997).

## CONCLUSION

As a result, anesthesia induction with intravenous 0.2 mg/kg midazolam may cause higher systolic blood pressure values than 2 mg/kg propofol. It should not be overlooked that the hemodynamic response that will occur after the use of midazolam during anesthesia monitoring will vary depending on the anesthetic drugs and doses used together.

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**Conflict of Interest**

The authors declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

**Author Contributions**

**Plan, design:** S.U.; **Material, methods and data collection:** S.U.; **Data analysis and comments:** S.U., E.N.T.; **Writing and corrections:** S.U., E.N.T.

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None

**Ethical considerations**

For this observational study, permission was obtained from the ethics committee of Istanbul Training and Research Hospital (Tarih 02.05.2008; Karar sırano:22, no: 5/8).

## REFERENCES

Arda, N. B., Ulufer, S. G., Tezal, D., Özbakış, Ç., & Hancı, A. (2000). Effects of Propofol-Fentanyl and Midazolam-Fentanyl Combinations and TIVA on Hemodynamics and Recovery. *The Medical Bulletin of Sisli Etfal Hospital, 34*(3): 20-23.

Bosna, G., Yalçıntuna, İ. B., & Aydın, N. (2002). Comparison of the hemodynamic effects of midazolam and propofol in the induction of general anesthesia. *Haydarpaşa*

*Numune Training and Research Hospital Medical Journal*, *42*(2): 19-22.

Conway, A., Rolley, J., Sutherland, J. R., & Cochrane Emergency and Critical Care Group. (2016). Cochrane Database of Systematic Reviews: CD009491. https://doi.org/10.1002/14651858.CD009491.pub2.

Jeon, S., Lee, H. J., Do, W., Kim, H. K., Kwon, J. Y., Hwang, B. Y., & Yun, J. (2018). Randomized controlled trial assessing the effectiveness of midazolam premedication as an anxiolytic, analgesic, sedative, and hemodynamic stabilizer. Medicine(Baltimore);*97*(35):e12187. https://doi.org/10.1097/MD.0000000000012187.

Kayhan Z (2004). *Clinical Anesthesia* (3rd Edition) Logos Publishing.

Kyeong, T. M., Myeong, H. L., Yong, I. K., & Jong, R. K. (1993). Induction Dose of Midazolam for General Anesthesia. *Korean Journal of Anesthesiology*; *26*(2):233-242. https://doi.org/10.4097/kjae.1993.26.2.233.

Mcclune, S., Mckay, A. C., Wright, M.C., Patterson, C.C., & Clarke R.S.J. (1992). Synergistic Interaction Between Midazolam And Propofol. *British Journal of Anaesthesia*; *69*:240-245.

Mihalj, M., Karlović, Z., Vladić-Spaić, D., Matić, B., Mikulić, I., Mikulić, V., & Golubović V. (2022). Effects of midazolam co-induction to general anesthesia: A randomized clinical trial. *Medicine (Baltimore); 101*(45): e31400. https://doi: 10.1097/MD.0000000000031400

Nishiyama,T., Misawa, K., Yokoyama, T., & Hanaoka, K. (2002). Effects of combining midazolam and barbiturate on the response to tracheal intubation: changes in autonomic nervous system. *Journal of Clinical Anesthesia*;*14*(5):344–8. https://doi.org/10.1016/s0952-8180(02)00370-7.

Öztürk, Ç. E. (2007). Comparison of 1% and 2% propofol formulations used in induction in terms of injection pain and hemodynamic response to intubation. [Specialization in Medicine Thesis, Osmangazi University Faculty of Medicine, Eskişehir]. http://openaccess.ogu.edu.tr:8080/xmlui/bitstream/handle/11684/2033.

Pagel, P.S., & Warltier, D.C. (1993). Negative inotropic effects of propofol as evaluated by the regional preload recruitable stroke work relationship in chronically instrumented dogs. *Anesthesiology* ;*78*:100-8. https://doi.org/10.1097/00000542-199301000-00015.

Reves, J. G., Fragen, R.J., Vinik, H. R., & Greenblatt D. J. (1985). Midazolam pharmacology and uses. ; *Anesthesiology*, *62*(3): 310-24.

Servin, F. S., Desmonts, J. M., Melloni, C., & Martinelli, G. (1997). A comparison of 2% and 1% formulations of propofol for the induction and maintenance of anaesthesia in surgery of moderate duration. *Anaesthesia*;*52*(12):1216-21. https://doi.org/10.1111/j.1365-2044.1997.222-az0357.x.

Short, T. G., & Chuı, P. T. (1991). Propofol And Midazolam Act Synergistically In Combination. *British Journal of Anaesthesia*; *67*: 539-545.

Short, T. G., Plummer, J. L., & Chui P.T. (1992). Hypnotic and anaesthetic interactions between midazolam, propofol and alfentanil. *British Journal of Anaesthesia*;*69*(2):162-7. https://doi.org/10.1093/bja/69.2.162.

Win, N.N., Fukayama, H., Kohase, H., & Umino, M. (2005). The different effects of intravenous propofol and midazolam sedation on hemodynamic and heart rate variability. *Anesthesia and Analgesia;101*(1):97-102. https://doi.org/10.1213/01.ane.0000156204.89879.5c