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Clinical Pharmacist's knowledge of general anesthesia and drugs used to anesthetize patients with hypertension in Saudi Arabia, 2024

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ABSTRACT

Background: The integration of the pharmacist in the care pathway could optimize patient information regarding the correct use of analgesics, communication in the multi-professional team, community-hospital coordination, and patient adherence to the prescribed medications, so that patients become more engaged in their care.In addition to enforcing pharmaceutical safety regulations, pharmacists are required to play significant roles as members of various perioperative care teams. Their responsibilities also include optimizing drug therapy and other clinical interventions. However, it would be beneficial to include general perioperative management in pharmaceutical education since it is another essential function that operating room pharmacists perform. Enhancing the perioperative care that pharmacists offer can help to raise their level of clinical competency.

The study aimed: To assess the pharmacist's knowledge of general anesthesia and drugs used to anesthetize patients who suffer from hypertension.

Materials and Methods: A cross-sectional study was conducted in Makkah, Saudi Arabia. A self-designed questionnaire was distributed to 100 pharmacists.

Results: The study discovered that 36.0% of the pharmacists were aware that sodium nitroprusside is used to regulate blood pressure during the procedure, that over half of them had rudimentary knowledge of the medications used in anesthesia, and that their knowledge of the medications used to treat hypertension during surgery was lacking.

Conclusion: According to this study, a significant portion of the pharmacist participants' knowledge was inaccurate due to their weaknesses. These shortcomings could result from inadequate training or inadequate educational preparation prior to the pharmacists' employment in hospitals.

Keywords: Clinical Pharmacist's, knowledge, anesthesia and hypertension

INTRODUCTION

The importance of a multidisciplinary healthcare (MDH) approach in modern healthcare delivery, particularly surgery, cannot be overstated due to the enormous benefits and value it has added to patient care. Since the introduction of concepts of pharmaceutical care and drug therapy in surgical services in the 1980s, the concept of integrating pharmacists in surgical services has not been widely utilized[(1, 2)]. Nonetheless, pharmacists' primary responsibilities back then were medication distribution and regulatory compliance, but this has changed in recent years[(1)].

The Perioperative Clinical Pharmacist (CP) has advanced therapeutic knowledge and experience in order to ensure appropriate medication use and patient outcomes throughout the surgical procedure. They are also

responsible and accountable for correcting any medication-related issues that may arise during the preoperative, intraoperative, and postoperative phases for all surgical patients[3]. During the preoperative period, the CP ensures fluid status optimization, appropriate analgesia administration, antimicrobial prophylaxis, and venous thromboembolism prophylaxis[4]. At the intraoperative stage, the CP ensures that antimicrobial prophylaxis, fluid resuscitation, and anesthetic plans are re-dosed. Opioid doses are adjusted based on the patient's tolerance and adverse effects[5, 6]. During the postoperative period, the patient receives medication monitoring, withdrawal of strong opioids, and counseling[6].

Safe and reliable medication management during rapid sequence induction and intubation is made possible in large part by CP. Although the mechanisms influencing inadequate reporting among pharmacists are unknown, they can play a crucial role in monitoring and reporting adverse drug reactions (ADRs) [7]. A number of factors, including a lack of knowledge, ineffective pharmacovigilance programs, healthcare professionals' failure to report an adverse event, or their inability to identify a previously unidentified adverse event, may contribute to insufficient reporting. As drug specialists, pharmacists are supposed to be knowledgeable about the safety features of medications and notify health authorities of adverse drug reactions. However, several obstacles prevented the complete implementation of clinical pharmacy services[8].

Several obstacles included the incapability to preserve the service due to a deficiency of trained personnel, insufficient service promotions, and the fact that doctors and nurses had little experience working with pharmacists and had a cloudy understanding of their roles, which made it harder for them to cooperate, the poor quality of drug information services, the lack of dedication and confidence among the pharmacists, and conflicts of interest resulting from the lack of clarity regarding the scope of practice [8].

The risks of anesthesia are increased in patients with hypertension because they are more vulnerable to blood pressure changes brought on by anesthetic medications, vasopressors, and vasodilators. These alterations may lead to cerebral and myocardial ischemia. Anesthetics and muscle relaxants are frequently administered in large doses over a short period of time to produce anesthesia. The hemodynamic characteristics of these medications vary. Endotracheal intubation and laryngoscopy both significantly stimulate the sympathetic nervous system, which can raise heart rate and blood pressure [9]. Positive pressure ventilation is then started, which lowers venous return and may cause a patient's blood pressure to plummet[9].

Several subsequent investigations also highlighted the increased risk of anesthesia and surgery[10], and Estafanous (1989) [10] reported a mortality rate of 30.0% in patients with hypertension having surgery. Barbiturates lower blood pressure and cardiac output and induce dose-related myocardial depression [11]. On the other hand, benzodiazepines are more commonly employed as premedication to induce drowsiness and forgetfulness, and they are also sometimes utilized as an ingredient in inducing drugs. Small doses of this class of medications alone result in negligible alterations in blood pressure, heart rate, and cardiac contractility [12]. Utilizing them as potent sedatives and amnesic reduces the increase in blood pressure. Combining barbiturates with benzodiazepines can result in cardiac depression and hypotension [13].

Fentanyl and sufentanil, two new, powerful opioids, do not depress the heart and only slightly alter blood pressure. Catecholamine production in response to sympathetic stimulation is suppressed by high dosages of opioids. Prolonged postoperative respiratory depression that necessitates mechanical ventilation is not caused by high dosages of opioids. Excessive inhalational agent concentrations result in hypotension and blood pressure liability[10]. They do not inhibit endotracheal intubation or sympathetic reactions to stimulation, such as tachycardia and hypertension. These substances are useful in reducing excessive blood pressure and myocardial oxygen demand, and they can be used in small amounts during surgery. In addition to lowering venous return and muscular tone, muscle relaxants can lower blood pressure. The effects of non-depolarizing muscle relaxants are enhanced by preoperative ganglion blockers [10].

The effects of different muscle relaxants on blood pressure and heart rate vary. Pancuronium raises blood pressure and heart rate, while d-tubocurarine lowers blood pressure and raises heart rate. The circulatory effects of relaxants like atracurium and vecuronium alone are minimal. On the other hand, atracurium causes the release of histamine at high quantities [14]. There is no perfect agent that stabilizes hemodynamics or at least does not interfere with patient hemodynamics and interact with other medicines, as this synopsis of the hemodynamic effects of anesthetic agents makes evident [15]. The best way to reduce hemodynamic abnormalities in hypertensive individuals may be to combine large doses of opioids with the right muscle relaxants [16].

The most common medication for managing hypertensive crises, nitroprusside, is used as a peripheral vasodilator to regulate blood pressure during surgery. It is a peripheral vascular dilator that affects the artery and vein smooth muscles. It lowers blood pressure in a matter of seconds, but ongoing observation is required[10]. Typically, a continuous infusion pump administers it, adjusting the dosages based on the blood pressure response. Nitroprusside can now be automatically administered by computerized blood pressure controllers. Nitroprusside is a more powerful vasodilator than nitroglycerin, which is less effective as an arteriolar[14].

It is a vasodilator that acts quickly, taking only a few seconds to start working. In order to reduce blood pressure, large amounts of nitroglycerin are typically needed. Because of its unique vasodilator activity, it is the recommended vasodilator when myocardial ischemia is present. Labetalol is a blocking agent of α- and β-

adrenergic receptors. With little alteration in cardiac output, it slows the heart rate and reduces systemic vascular resistance[10]. Its benefits include lowering myocardial oxygen consumption and preventing tachycardia or selective redistribution of coronary blood flow in patients with coronary artery disease. When labetalol is administered intravenously, the β-blocking activity predominates over the α-blocking activity, which can lower cardiac output[10, 14].

By combining these two categories, peripheral vasodilators can significantly lower SVR while beta-blockers can avoid or lessen reflex tachycardia. Because of this combination, β-blockers can be used at lower doses to reduce their impact on cardiac contractility. These combinations are effectively employed in hypotensive anesthesia procedures. Continuous IV infusion should be gradually stopped once immediate blood pressure control has been obtained while long-term antihypertensive medication is started. [10]. Therefore, this study aimed to assess the knowledge of pharmacists working in hospitals about the anesthetics and their side effects in reducing the side effects of these drugs on hypertensive patients.

MATERIALS AND METHODS

A cross-sectional study was conducted in Makkah, Saudi Arabiafrom January to May 2024 to obtain exact and reliable data. The self- designed questionnaire included structured questions to identify the knowledge of the pharmacists about anesthetic drugs and their side effects in hypertensive patients. Ethical approval has been obtained from the University with oral agreement from all the participants.The study consists of 100 CPs working in hospitals and includes 24 questions divided into four parts. The first section is demographic data (five questions), the second section is general information about general anesthesia and diseases that are affected by it (five questions), and the third section is hypertension and its, relationship to anesthesia (seven questions).Statistical analysis: Data presented as frequency and percentage. The Chi-square test was used to analyze the data and the correlation between the knowledge of the CP about general anesthesia and hypertension was determined.

RESULTS

Table (1) shows that 20.0% of the study participants were males, while 80.0% of the study participants were females. Most of the participants (n=55, 55.0%) with the range of 20-30 years old, then with 31-40 years old with 36.0%. CPs with Bachelor of Pharmacy is found to be 65.0% and high diploma 05.0%. Most of the participants have experienced between one and five years (35.0%), while more than 10 years' experience 27.0%.

Table 1: Distribution of the study participants (N= 100)

Data	**Frequency**	**%**
Gender		
Male	20	20
Female	80	80
Age		
20-30	55	55
31-40	36	36
41-50	06	06
> 50	03	03
Educational level		
Bachelor of Pharmacy	65	65
Master of Pharmacy	06	06
Pharm.D	12	12
Diploma of Pharmacy	05	05
Others	12	12
Years of experience		
One year orless	19	19
One to five years	35	35
Five to ten years	27	27
More than ten years	19	19

Table (2) shows that 39.0% of the study participants say that general anesthesia is loss of sensation, 19.0% of the sample study say that general anesthesia is an outing to sleep, while 22.0% of the study participants say that general anesthesia is loss of responses, and 20.0% of the study participants do not know what general anesthesia is. The Chi-square test revealed 10.640 ($p<0.05$) which gives a significant difference between participants in

terms of general anesthesia. It can be seen that the highest percentage of general anesthesia is for loss of sensation.

Table 2: Knowledge of general anesthesia

Signs of anesthesia	**n**	**%**	**Chisquare**	**Pvalue**
Loss of sensation	39	39.0	10.64	0.014
Putting to sleep	19	19.0		
Loss of responses	22	22.0		
I do not know	20	20.0		
Total	**100**	**100**		

Table (3) shows that 13.0% of the study participants said just one drug should be used to induce anesthesia, while 79.0% of the participants answered that more than one drug should be used to induce anesthesia, and 08.0% did not know how many drugs should be used to induce anesthesia. The Chi-square test revealed 94.220 ($p<0.001$) which means a high significant difference between the participants in terms of drugs that should be used to induce anesthesia. It can be seen that the highest percentage of drugs that should be used to induce anesthesia is more than one drug.

Table 3: Knowledge about drugs used to induce anesthesia

	n	**%**	**Chisquare**	**P value**
Just one drug should be used to induce anesthesia	13	13.0	94.220	< 0.001
More than one drug should be used to induce anesthesia	79	79.0		
Did not know how many drugs should be used to induce anesthesia	8	8.0		
Total	**100**	**100**		

Table (4) shows that 07.0% of the study participants say that route of administration of general anesthesia is inhaled gas, 03.0% of the study participants say that route of administration of general anesthesia is IV, while 84.0% of the study participants say that route of administration of general anesthesia is inhaled gas and IV, 02.0% of the participants say that route of administration of general anesthesia is oral pills and inhaled gas, and 04.0% of the participants do not know what is route of administration of general anesthesia is used?. The Chi-square test revealed 256.700 ($p<0.001$) which means a highly significant difference between sample studies in terms of the route of administration of general anesthesia. It can be seen that the highest percentage of using the route of administration of general anesthesia is inhaled gas and IV.

Table 4: Knowledge about the route of administration of general anesthesia

	n	**%**	**Chisquare**	**Pvalue**
Route of administration of general anesthesia is inhaled gas	7	7.0	256.700	<0.001
Route of administration of general anesthesia is IV	3	3.0		
Route of administration of general anesthesia is inhaled gas and IV	84	84.0		
Route of administration of general anesthesia is oral pills and inhaled gas	2	2.0		
Do not know what is route of administration of general anesthesia is used?	4	4.0		
Total	**100**	**100**		

Table (5) shows that 75.0% of the participants think that co-existing diseases affect the anesthesia, while 04.0% of the participants think that co-existing diseases do not affect the anesthesia and 21.0% of the participants do not know. The Chi-square test revealed 82.460 ($p<0.001$) which means there is a highly significant difference

between the participants in terms of do co-existing diseases affect the anesthesia. It can be seen that the highest percentage is that co-existing diseases affect the anesthesia is inhaled gas and IV.

Table 5: Participants' answers if co-existing diseases affect the anesthesia

	n	**%**	**Chisquare**	**Pvalue**
Co-existing diseases affect the anesthesia	75	75.0	82.460	<0.001
Co-existing diseases do not affect the anesthesia	4	4.0		
Do not know	21	21.0		
Total	**100**	**100**		

Table (6) shows that 35.2% of the respondents think that cardiac diseases may affect the anesthesia, 11.4% of the respondents think that diabetes mellitus might affect the anesthesia, 19.3% of the respondents think that high blood pressure may affect the anesthesia, and 34.1% of the responses do not know that.

Table 6: Diseases assumed by participants that might be affected by general anesthesia

Diseases	**Frequency**	**%**
Cardiac disease	31	35.2
Diabetes mellitus	10	11.4
High blood pressure	17	19.3
Asthma	30	34.1
Total	**88**	**100**

Table(7) shows that 38.0% of the participants think that if the patient has hypertension, he/she should take their medicine before surgery, 07.0% of the participants think that if the patient has hypertension, he/she should take their medicine after surgery, while 50.0% of the participants think that if the patient has hypertension, he/she should take their medicine depends on the type of drug, and 05.0% of the participants do not know. The Chi-square test revealed 60.720 ($p<0.001$) which means the high significant difference between the participants in terms of patient have hypertension, he/she should take their medicine. It can be seen that the highest percentage of patient has hypertension; they should take their medicine depending on the type of drug.

Table 7: Knowledge about the time at which hypertensive patient should take their medicine

State	**n**	**%**	**Chi square**	***P***
Before surgery	38	38.0	60.72	0.00
After surgery	7	7.0		
Depends on of drug type	50	50.0		
Idon't know	5	5.0		
Total	**100**	**100**		

Table (8) shows that 61.0% of the participants think that one of the most common side effects that might happen for hypertension patients during surgery is an increase in blood pressure, 03.0% of the participants think that one of the most common side effects that might happen for hypertension patients during surgery is malignant hyperthermia, while 18.0% of the participants think that one of the most common side effects that might happen for hypertension patients during surgery is lung collapse, and 18.0% of the participants do not know. The Chi-square test revealed 75.120 ($p<0.001$) which means a high statistically significant difference between sample studies in terms of one of the most common side effects that might happen for patients with hypertension during surgery. It can be seen that the highest percentage of one of the most common side effects that might happen for patients with hypertension during surgery is an increase in blood pressure.

Table 8: Knowledge about side effects that might happen for hypertensive patients during surgery

State	**n**	**%**	**Chi square**	***P***
Increase in blood pressure	61	61.0	75.120	<0.001
Malignant hyperthermia	3.0	3.0		

State	n	%	Chi square	*P*
Lung collapse	18	18.0		
I do not know	18	18.0		
Total	**100**	**100**		

Table (9) shows that 36.0% of the participants think that if the patient has hypertension, the drug should be used to control blood pressure during surgery is sodium nitroprusside, 08.0% of the participants think that the drug should be used to control blood pressure during surgery is clevidipine, while 39.0% of participants think that if the patient has hypertension, the drug should be used to control blood pressure during surgery is furosemide, and 17.0% of the sample study do not know. The Chi-square test revealed 26.80 ($p<0.001$) which means a significant difference between participants in terms of patient has hypertension, and what drug should be used to control blood pressure during surgery. It can be seen that the highest percentage of patient has hypertension, what drugs should be used to control blood pressure during surgery are furosemide and sodium nitroprusside.
Further, data shows that 80.0% of the responses say that for hypertension patients, the drug used in their hospital to anesthetize is propofol, while 20.0% of the responses say that for hypertension patients, the drug used in their hospital to anesthetize is sodium thiopental.

Table 9: Knowledge about what drug should be used to control blood pressure during surgery

State	n	%	Chi square	*P*
Sodium nitroprusside	36	36.0		
Clevidipine	8.0	8.0		
furosemide	39	39.0	26.80	<0.001
I do not know	17	17.0		
Total	**100**	**100**		

DISCUSSION
In this study, we interviewed 100 clinical pharmacists about their knowledge of anesthesia and how anesthetic medications affect hypertensive patients. These pharmacists, who are 80.0% female and 20.0% male, are between the ages of 20 and 50 on average, and work at public hospitals 67.0% of the time and private hospitals 33.0%. They typically hold a bachelor's degree in pharmacy and at least a diploma. They have a few months to several years of experience. A regulated condition of unconsciousness followed by a partial or whole absence of defensive reflexes is known as general anesthesia[17]. According to the current study, 39.0% of pharmacists define general anesthesia as a loss of sensation, 22% as a loss of responses, and 19.0% as putting the patient to sleep. To induce and sustain general anesthesia, a variety of IV and inhalational medicines are available. These drugs are frequently taken in combination [18].
According to the current study, 84.0% of the CPs suggested administering these drugs via inhalation and intravenous routes. When asked if co-existing diseases affect anesthesia, 75.0% of the pharmacists said that they do, while 04.0% said that the disease has no effect on anesthesia. Only 13.0% of the pharmacists thought that only one anesthetic agent was required, while 79.0% said that multiple agents are. Patients also need a preoperative assessment to rule out any conditions that can interfere with the anesthetic management process. Reducing the morbidity and mortality of perioperative surgical and anesthetic operations and restoring the patient to desired functionality as soon as feasible should be taken into account[19].
Respondents' responses varied when asked which conditions the anesthetic drugs might impact: 35.0% mentioned heart disease, 34.0% mentioned asthma, 19.0% mentioned hypertension, and 11.0% mentioned diabetic mellitus. We specifically assessed pharmacists' knowledge of hypertension in the current survey to find out if they knew about the illness, how it affected anesthesia, and if a specific drug was used to put patients to sleep. A clinical anesthetic physician and a clinical pharmacist should be familiar with the most commonly used hypertensive medications, even if there are multiple approaches to managing hypertension. The morning before the operation, patients should continue taking CCBs, and Blocking medications, agonists, and other medications for sedation or general anesthesia. With a missed dosage of and/or blocking drugs and the agonists, rebound hypertension is a particular worry. Due to the possibility of experiencing refractory hypotension during induction, angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and direct renin inhibitors may be stopped before undergoing general anesthesia.
The cornerstone of anesthetic management has always been to keep blood pressure within physiologic ranges for a specific patient based on preoperative readings. To avoid serious hypotension, it's crucial to avoid anesthetic problems [20]. During the surgery, 39.0% of them answered that furosemide which is a diuretic is used to control the increase in blood pressure, while nitroprusside is the most used agent because it has an immediate onset of action and duration of effect of two minutes. 36.0% answered with nitroprusside which reflects a weakness in the

knowledge about an important drug that saved the lives of many patients this weakness might be raised from the isolating the pharmacist from the operation room [10].

When we asked the CP if the operation should be canceled if the patient had a marked increase in blood pressure, 53.0% answered that it depends on the type of surgery 23.0% agreed that it should be canceled but studies showed that it is normal to have elevated blood pressure before surgery especially if the patient was stressed this phenomenon is called preoperative blood pressure which we asked about it, 90.0% of the pharmacist agreed that stress may cause an elevation in blood pressure [21]. However, the most important thing is blood pressure should be mild to moderate and should be controlled if not, the surgery should be canceled if possible but if necessary special protocols are applied for safe surgery licensed [22, 23], and if the patient is already hypertensive and taking medication, 38.0% of the pharmacists think that the patient should take their medicine until the morning of the surgery and 50.0% answered that it depends on the type of medication.

The last questions about hypertension discussed the primary factor that raises blood pressure during surgery the responses were very close and it is fair because the main reason that causes an increase in blood pressure is the activation of the sympathetic nervous system and this activation is caused by several reasons such as the anesthetic drugs or hypoxia [24], and about what the medication that is used for a hypertensive patient in the hospital where they work, the answers were different and mostly incorrect. It should be mentioned that one of the main issues we faced was the number of pharmacists who had good experience as clinical pharmacists, which is considered limited or negligible in hospitals.

CONCLUSION

This study showed that certain pharmacists had flaws that led to a large number of incorrect responses to different queries. These shortcomings could be the consequence of the pharmacist's lack of training or insufficient educational preparation prior to working in hospitals. The absence of a pharmacist with clinical experience in the operating room coincided with these findings.

REFERENCES

1. Bickham P, Golembiewski J, Meyer T, et al. ASHP guidelines on perioperative pharmacy services. Am J Health Syst Pharm, 76 2019:903–20.
2. Tefera GM, Zeleke AZ, Jima YM, et al. Drug therapy problems and the role of clinical pharmacist in surgery ward: prospective observational and interventional study. Drug Healthc Patient Saf 2020;12:71–83.
3. Nanji KC, Patel A, Shaikh S, et al. Evaluation of perioperative medication errors and adverse drug events. Anesthesiology 2016;124:25–34.
4. Neville HL, Chevalier B, Daley C, et al. Clinical benefits and economic impact of post-surgical care provided by pharmacists in a Canadian hospital. Int J Pharm Pract 2013;22:216–22.
5. Lovely JK, Hyland SJ, Smith AN, et al. Clinical pharmacist perspectives for optimizing pharmacotherapy within Enhanced Recovery After Surgery (ERAS®) programs. Int J Surg 2019;63:58–62.
6. Patel GP, Hyland SJ, Birrer KL, et al. Perioperative clinical pharmacy practice: responsibilities and scope within the surgical care continuum. J Am Coll Clin Pharm 2020;3:501–19.
7. Hadi MA, Neoh CF, Zin RM, Elrggal ME, Cheema E (2017) Pharmacovigilance: pharmacists' perspective on spontaneous adverse drug reaction reporting. Integrated Pharmacy Research and Practice. 6: 91-98. doi: 10.2147/ IPRP.S105881
8. Tefera GM, Zeleke AZ, Jima YM, Kebede TM (2020) Drug therapy problems and the role of clinical pharmacist in surgery ward: Prospective observational and interventional study. Drug Health and Patient Safety. 12: 71-83. doi: 10.2147/DHPS.S251200
9. Diao S, Ni J, Shi X, Liu P, Xia W (2014) Mechanisms of action of general anesthetics. Frontiers in Bioscience. 19 (5): 747-757. doi: 10.2741/4241
10. Estafanous FG (1989) Hypertension in the surgical patient: management of blood pressure and anesthesia. Cleveland Clinic Journal of Medicine. 56 (4): 385-393. doi: 10.3949/ccjm.56.4.385
11. Sonntag H, Hellberg K, Schenk HD, Donath U, Regensburger D, Kettler D, Larsen R (1975) Effects of thiopental (Trapanal) on coronary blood flow and myocardial metabolism in man. Acta Anaesthesiologica Scandinavica. 19 (1): 69-78. doi: 10.1111/j.1399-6576.1975.tb05224.x
12. Dundee JW (1974) Intravenous anaesthesia. Churchill Livingstone, distributed by Longman, Australia. ISBN: 0443009775.
13. Stanley TH, Bennett GM, Loeser EA, Kawamura R, Sentker CR (1976) Cardiovascular effects of diazepam and droperidol during morphine anesthesia. Anesthesiology. 44 (3): 255-260. doi: 10.1097/00000542-197603000-0
14. Garcia P, Kolesky S, Jenkins A (2010) General anesthetic actions on GABA(A) receptors. Current Neuro-pharmacology. 8 (1): 2-9. doi: 10.2174/157015910790909502
15. Dagnino J, Prys-roberts C (1984) Studies of anaesthesia in relation to hypertension. VI: Cardiovascular responses to extradural blockade of treated and untreated hypertensive patients. British Journal of

Anaesthesia. 56 (10): 1065-1073. doi: 10.1093/bja/56.10.1065
16. Goldman L, Caldera DL (1979) Risks of general anesthesia and elective operation in the hypertensive patient. Anesthesiology. 50 (4): 285-292. doi: 10.1097/00000542-197904000-00002
17. Reuven Pasternak L (1990) Anesthetic considerations in otolaryngological and ophthalmological outpatient surgery. International Anesthesiology Clinics. 28 (2): 89-100. doi: 10.1097/00004311 199002820-00005
18. Lauven PM, Helmut Schwilden H, Stoeckel H, Greenblatt DJ (1985) The effects of a benzodiazepine antagonist Ro 15-1788 in the presence of stable concentrations of midazolam. Anesthesiology. 63 (1): 61-64. doi: 10.1097/ 00000542-198507000-00009
19. Zambouri A (2007) Preoperative evaluation and preparation for anesthesia and surgery. Hippokratia. 11 (1): 13-21. PMID: 19582171; PMCID: PMC2464262.
20. Yancey R (2018) Anesthetic management of the hypertensive patient: Part II. Anesthesia Progress. 12 65 (3): 206-213. doi: 10.2344/anpr-65-03-17
21. Kulkarni S, O'Farrell I, Erasi M, Kochar MS (1988) Stress and hypertension. Wisconsin Medical Journal. 97(11): 34-38. PMID: 9894438.
22. Carey RM, Cutler J, Friedewald W, Gant N, Hulley S, Iacono J (1984) The 1984 report of the joint national committee on detection, evaluation, and treatment of high blood pressure. Archives of Internal Medicine. 144(5): 1045-1057. PMID: 6143542.
23. Lee TH, Marcantonio ER, Mangione CM, Thomas EJ, Polanczyk CA, Cook EF, Sugarbaker DJ, Donaldson MC, Poss R, Ho KK, Ludwig LE, Pedan A, Goldman L (1999) Derivation and prospective validation of a simple index for prediction of cardiac risk of major noncardiac surgery. Circulation. 100 (10): 1043-1049. doi: 10.1161/01.cir.100.10.1043
24. Dingle HR (1966) Antihypertensive drugs and anesthesia. Anaesthesia. 21 (2): 151-172. doi 10.1111/j.1365- 2044.1966.tb02595.x