Original Article

ISSN (0): 2347-3398; ISSN (P): 2277-7253

A Comparison of Perioperative Hemodynamic Stability with Amlodipine and Telmisartan during Laparoscopic Cholecystectomy in known Hypertensive Patients

Mandeep Manohar Harison Madia[1], Atul Kumar Singh[2], Subhdeep Manohar Wrangler Richi[3], Ram Badan Singh[4]

[1]Junior Resident, Department of Anaesthesiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, [2]Assistant Professor, Department of Anaesthesiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi, [3]Senior Resident, Department of Anaesthesiology, Rajkiye Medical College, Orai, [4]Professor, Department of Anaesthesiology, Institute of Medical Sciences, Banaras Hindu University, Varanasi.

Abstract

Background: There are many antihypertensive agents available for optimal control of elevated blood pressure. The agent with better safety profile and minimal side effects are the agents of choice. The aim of this study is to compare the perioperative hemodynamics stability with Amlodipine and Telmisartan during laparoscopic cholecystectomy in known hypertensive patients. **Subjects and Methods:** A comparative, prospective, randomized interventional study was conducted in 60 known hypertensive patients of either sex of ASA PS II and III class, aged 40-70 years undergoing laparoscopic cholecystectomy. Patients were randomly allocated to Group A: taking Amlodipine 5 mg once daily, and Group B: taking Telmisartan 40 mg once daily. Hemodynamic monitoring was done including heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure and brain natriuretic peptide (BNP) as cardiac marker. **Results:** Among the hemodynamic variables there was significant difference (p-value<0.05) in heart rate, mean arterial pressure, brain natriuretic peptide. Heart rate, mean arterial pressure was better controlled in patients receiving Telmisartan. Rise in BNP level was significantly less during intraoperative period in patients receiving Telmisartan. HR, SBP, DBP and demographic profile were comparable between two groups. **Conclusion:** One of the major responsibility of anaesthesiologist is to maintain hemodynamic stability during intra-operative and post-operative period. Hemodynamic stability if not managed successfully particularly in hypertensive patients can lead to poor outcomes during intra-operative and post-operative period. Antihypertensive medications are administered for at least 1-2 weeks for returning of normal autoregulation and optimum blood pressure control. Telmisartan has better control over blood pressure in comparison to amlodipine.

Keywords: Heart Rate, Systolic Blood Pressure, Diastolic Blood Pressure, Brain Natriuretic Peptide, Amlodipine, Telmisartan.

Corresponding Author: Dr. Atul Kumar Singh, Assistant Professor, Department of Anaesthesiology, Banaras Hindu University, Varanasi.

Received: July 2019
Accepted: July2019

Introduction

The use of laparoscopic technique in general surgery has gained increasing popularity in the last few decades. The small limited incisions are well accepted by the patients and there is the benefit of faster recovery. The physiological changes observed during laparoscopic surgery are a result of patient position, introduction of exogenous insufflation gas, CO2, and increased intra-abdominal pressure due to pneumoperitoneum. The extent of hemodynamic changes associated with the creation of pneumoperitoneum depends on the intra-abdominal pressure attained, volume of CO2 absorbed, patient's intravascular volume, ventilatory technique, and surgical conditions.[1,2]

Amlodipine, initially approved by the FDA in 1987, is a popular antihypertensive drug belonging to the group of drugs called dihydropyridine calcium channel blockers. Due to their selectivity for the peripheral blood vessels, dihydropyridine calcium channel blockers are associated with a lower incidence of myocardial depression and cardiac conduction abnormalities than other calcium channel blockers. Amlodipine is commonly used in the treatment of high blood pressure and angina. Amlodipine has antioxidant properties and an ability to enhance the production of nitric oxide (NO), an important vasodilator that decreases blood pressure.

Telmisartan is an angiotensin II receptor antagonist that is highly selective for type 1 angiotensin II receptors. Telmisartan, a long-acting angiotensin receptor blocker (ARB), has therapeutic effects that go beyond BP control.

1. The very high lipophilicity and high volume of distribution give it the clinically important advantage of good tissue penetration.
2. It has multiple positive effects not only on BP, but also on target organ protection.

Blockade of the renin-angiotensin system with ACE inhibitors, which inhibit the biosynthesis of angiotensin II from angiotensin I, is widely used in the treatment of hypertension.

Subjects and Methods

After Institutional Ethical Approval and written informed consent, 60 known hypertensive patients receiving antihypertensive drugs between age of 40-70 years, of either sex, of American Society of Anaesthesiologist (ASA PS) grade II or III scheduled for laparoscopic cholecystectomy under general anaesthesia between March 2018 to February 2019were included in this prospective, randomized, controlled, binterventional double-blinded trial. Patients with history of upper respiratory tract infections, restrictive or obstructive lung disease, anticipated difficult airway, allergy to the drugs used in the study, diabetic patients, patients with uncontrolled hypertension were excluded.

It included pre-anaesthetic check-up and clinical examination, investigations which included tests i.e. CBC (complete blood counts), FBS (fasting blood sugar), LFT (liver function test), RFT (renal function test), electrocardiogram (for patients over 40 years of age), chest X-ray. Pre-anaesthetic evaluation was done on the previous day of surgery.

All patients was pre-medicated with Tab. Alprazolam 0.25mg orally, Tab. Ranitidine 150mg orally and Tab. Metoclopramide 10mg orally on the night before surgery and 2hrs prior to surgery. A peripheral intravenous line with 18 gauze cannula was secured in one of the upper limb. Morning dose of antihypertensive medication was given. Before arriving at the operation room an18-gauge peripheral venous cannula will be inserted and all patients will be preloaded with 500ml of Lactated Ringer solution. Patients will receive Inj. midazolam 30mcg/kg.

In the Operating room base line readings of Heart Rate (HR), Systolic Blood Pressure(SBP), Diastolic Blood Pressure(DBP), Mean Arterial Pressure(MAP), Oxygen Saturation(Sa02), and End Tidal CO2(ETCO) will be measured. Thereafter measurements of HR, SBP, DBP, MAP, ETCO2 will be taken at intervals of 1, 5 and 10 minutes will be recorded. Patients will be induced with 1% of Inj. Propofol 2mg/kg and depth of anaesthesia will be monitored by loss of following verbal commands. Inj. Vecuronium 0.1mg/kg will be administered. After mask ventilation for three minutes, the appropriate sized airway device will be inserted. Effective ventilation with device was defined as a square wave capnograph trace and bilateral chest movements on manual ventilation. Patients will be maintained with 33% of oxygen in air, isoflurane and intermittent dose of vecuronium. Perioperative analgesia will be provided with Inj Fentanyl 2 mcg/kg. The tidal volume and respiratory frequency will be adjusted and intermittent positive pressure ventilation (IPPV) will be continued by mechanical ventilator to maintain end tidal carbon dioxide level between 35-45 mm Hg. Pneumoperitonium will be created by insufflation of carbon dioxide and operation table will be tilted 15 degree reverse Trendelenburg position. Intraabdominal pressure will not be not allowed to exceed 14 mm Hg throughout the surgery. Any regurgitation of fluid through the gastric channel or airway tube will be noted. Heart rate(HR), non-invasive Systolic blood pressure(SBP), Diastolic Blood pressure(DBP), Mean arterial blood pressure (MAP), oxygen saturation (SpO2), end tidal carbon dioxide(EtCO2) will be recorded at 1,5 and 10 minutes after insertion of device. After pneumoperitoneum at 5,10,15,30,45,60,90 and 120 minutes and just after removal of device. At the end of surgery residual neuromuscular block will be reversed with appropriate dose of Inj. neostigmine and Inj. glycopyrrolate intravenously. After reversal patients will be monitored in the post anaesthesia care area.

Complications such as incidence of any airway complications caused by supraglottic devices will be managed accordingly.

Statistics

The analysis was done using SPSS IBM Version 20. Proportions were compared with Chi square or Fisher's exact test. The two groups were compared using Statistical analysis of various parameters using SPSS for ordinally scaled Data by Mann-Whitney U, Sign Test, and Wilcoxon test.

Results

Table 1: Comparison of Heart Rate among two groups

	Group A Mean±SD N=30	Group B Mean±SD N=30	t-value	p-value
HR baseline	85.00±14.856	80.57±13.738	1.200	0.235
HR post induction	89.93±14.475	86.47±13.135	0.971	0.335
After insertion				
HR 1min	92.47±14.345	89.43±16.504	0.760	0.450
HR 3 min	94.13±15.704	89.33±15.925	1.176	0.245
HR 5 min	87.70±16.605	83.93±17.935	0.844	0.402
HR 10 min	89.43±14.913	87.10±13.555	0.634	0.528
After Pneumoperitoneum				
HR 5 min	84.27±15.074	81.27±13.861	0.802	0.426
HR 10 min	87.80±8.965	77.67±9.241	4.311	<0.001
HR 15 min	81.60±8.881	74.10±7.092	3.614	<0.001
HR 30 min	81.77±11.367	73.03±10.005	3.159	0.003
HR 45 min	78.70±12.885	77.13±12.364	0.481	0.633
HR 60 min	77.47±14.911	76.07±15.369	0.358	0.722
HR 90 min	75.10±11.339	73.20±10.260	0.681	0.499
HR 120 min	72.10±12.135	68.43±10.129	1.271	0.209
HR After removal	74.27±11.444	69.37±9.611	1.796	0.078

Despite the potential advantages, laparoscopic procedures are associated with physiological changes, which present the anaesthesiologist with many challenges and especially in hypertensive patients. Besides, these procedures are associated with potentially life-threatening complications that are usually not encountered with the traditional open procedure. Thus there is a need to optimize the blood pressure in hypertensive subjects to allow this surgical procedure to be performed safely.

Table 2: Comparison of Mean Arterial Pressure among study groups

	Group A Mean±SD N=30	Group B Mean±SD N=30	t-value	p-value
MAP baseline	106.56±4.348	106.21±3.481	0.339	0.736
MAP postinduction	108.88±3.613	108.77±3.316	0.124	0.902
MAP 1 min	110.10±4.325	110.17±3.958	-0.062	0.951
MAP 3 min	108.29±4.026	108.66±4.004	-0.354	0.725
MAP 5 min	102.54±5.081	103.44±5.377	-0.666	0.508
MAP 10 min	102.46±4.718	103.26±3.818	-0.722	0.473
After Pneumoperitoneum				
MAP 5 min	101.46±4.265	102.19±3.976	-0.689	0.494
MAP 10 min	101.07±4.142	98.14±2.543	3.293	0.002
MAP 15 min	101.07±4.142	98.14±2.543	3.513	0.001
MAP 30 min	98.72±4.575	95.88±2.830	2.896	0.005
MAP 45 min	100.43±4.766	100.30±4.331	0.113	0.910
MAP 60 min	98.66±3.700	98.56±3.705	0.105	0.917
MAP 90 min	100.84±3.706	100.56±3.761	0.300	0.766
MAP 120 min	100.63±4.411	100.31±3.461	0.315	0.754
MAP after removal	97.69±3.778	97.47±3.478	0.237	0.813

Table 3: Comparison of Values of different Cardiac Markers among study groups

	Group A Mean±SD N=30	Group B Mean±SD N=30	t-value	p-value
CKMB preop	0.7597±0.43101	0.8763±0.52756	-.938	0.352
CKMB intraop	1.0670±0.40192	1.0727±0.38850	-.056	0.956
CMKB postop	0.7390±0.21887	0.7423±0.22978	-.058	0.954
TNI preop	0.0052±0.00249	0.0056±0.00309	-.552	0.583
TNI intraop	0.0069±0.00173	0.0073±0.00152	-1.032	0.306
TNI postop	0.0057±0.00326	0.0058±0.00330	-.126	0.900
BNP preop	41.07±27.779	57.00±23.632	-2.393	0.020
BNP intraop	173.90±44.653	147.53±52.289	2.100	0.040
BNP postop	9.40±3.635	10.53±3.821	-1.177	0.244

Our result demonstrates that Telmisartan 40 mg once daily is as effective as Amlodipine 5mg once daily and has better hemodynamic stability. In our study, we compared Telmisartan and Amlodipine planned for laparoscopic cholecystectomy in 60 patients who were randomly selected in both groups. Each group had 30 patients and are demographically comparable. Baseline heart rate, EtCO2, oxygen saturation were all comparable and statistically nonsignificant.

After inserting airway devices hemodynamic changes were significant in both groups i.e. mean arterial pressure and heart rate was significant at 10,15 and 30 minutes after pneumoperitoneum. Mean arterial pressure and heart rate were less when Telmisartan was used compared to Amlodipine, which was observed by Tripathiet al4. Tripathiet al4 concluded that Telmisartan is a better alternative than Amlodipine for optimization of blood pressure in hypertensive patients since it produces lesser hemodynamic changes. Telmisartan produces fewer changes in MAP, Heart rate and BNP than amlodipine.

Other parameters like end-tidal CO2, SPO2, Troponin I and CPK-MB were comparable in both groups and was found to be statistically non-significant.

Discussion

Laparoscopic surgery has been shown to adversely affect intra-operative hemodynamic mechanics, thus providing the most severe test of the efficacy of antihypertensive medication in the optimization of raised blood pressure i.e. hypertensive subjects. Cardiac output is decreased with the elevation of systemic and pulmonary vascular resistance. The decrease in cardiac output is proportional to the increase in IAP. The mechanism of the decrease in cardiac output is multifactorial. A decrease in venous return is observed after a transient increase in venous return at low IAPs (<10 mm Hg). Increased IAP results in vena cava compression, pooling of blood in the legs and an increase in venous resistance. Consistent with these results, we observe that following pneumoperitoneum, Heart rate, MAP and BNP increased in both groups.

Tripathiet al,[4] concluded that hemodynamic control was better with Telmisartan. Both drugs provided optimal blood pressure control and BNP level and the adverse effects were also comparable.

Lacourcièreet al,[3] (1998) compared the antihypertensive effects and duration of action of the angiotensin II receptor antagonist, telmisartan, amlodipine, and placebo in patients with mild-to-moderate hypertension. Telmisartan and amlodipine treatments significantly decreased trough supine systolic blood pressure and DBP ($P < 0.001$, measured conventionally) to a similar extent (by 13.1/7.1 and 14.0/7.1 mmHg, respectively, at the end of 12 weeks' treatment) compared with placebo. Both drugs also significantly reduced 24 h mean systolic blood pressures and DBP compared with placebo ($P < 0.0001$), measured using ABP(ambulatory blood pressure monitoring), maintaining control of blood pressure throughout the dosing period. Reductions in DBP with telmisartan were greater ($P < 0.05$) than those with amlodipine during the night-time interval and the last 4 h of the dosing period. Twenty-four-hour mean ABPM DBP < 85 mmHg was observed in 71% of telmisartan patients and 55% of patients administered amlodipine. Also, heart rates in patients treated with telmisartan were lower than heart rates in those treated with amlodipine during the final 4 h of the dosing period ($P = 0.0003$) and the morning interval ($P = 0.005$). Generally,

both telmisartan and amlodipine were well tolerated, however, drug-related edema occurred significantly more commonly ($P < 0.05$) among the patients administered amlodipine than it did among patients administered either telmisartan or placebo. This study resembles our study in which 50% of the patients in the Amlodipine group had higher MAP, Heart rate and raised BNP and the result of the study was statistically significant (p value<0.05).

Different antihypertensive drugs and their mechanism of actions each have their advantages and disadvantages many anaesthesiologists after discussing with cardiologists consider the combination of two groups to be better than monotherapy. However using this combination may have other adverse effects like hypotension, lightheadedness, electrolyte disturbances and the most important is very fast blood pressure reduction leads to disturbances in brain and systemic autoregulation. These all problems considered the advantages of monotherapy (Amlodipine and Telmisartan) to begin the treatment.

Telmisartan provides better hemodynamic stability in hypertensive patients planned for laparoscopic cholecystectomy. Telmisartan doesn't let BNP rise that much as it is seen with Amlodipine.

Antihypertensive medications are required for the blood pressure control and returning of normal autoregulation at least for 1-2 weeks. In current practice, a patient with hypertension may already have developed complications, which must be detected before surgery. Different antihypertensive medications have a different mechanism of action. The first objective of preoperative evaluation is to know whether hypertension is controlled with medications or not. According to JNC 8 guidelines5 drug treatment to be initiated with angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, calcium channel blocker, or thiazide diuretic.

Conclusion

In Conclusion, One of the major responsibility of anaesthesiologist is to maintain hemodynamic stability during intra-operative and post-operative period. Hemodynamic stability if not managed successfully particularly in hypertensive patients can lead to poor outcomes during intra-operative and post-operative period. Antihypertensive medications are administered for at least 1-2 weeks for returning of normal autoregulation and optimum blood pressure control. Telmisartan has better control over blood pressor in comparison to amlodipine.

Acknowledgement

At the very outset I would like to pay the homage to founder of Banaras Hindu University, MahamanaPanditMadan Mohan Malviyaji, who made this glorious temple of training.

References

1. Hirvonen E A, Nuutinen L S, Kauko M: Hemodynamic changes due to Trendelenberg positioning and pneumoperitoneum during laparoscopic hysterectomy. ActaAnaesthesiolScand 1995;39:949.
2. Hirvonen E A, Nuutinen L S, Vuolteenaho O: Hormonal responses and cardiac filling pressors in head-up or head-down position and pneumoperitoneum I patients undergoing operative laparoscopy. Br J Anaesth 1997;78:128.
3. Lacourciere Y, Lenis J, Orchard R, et al. A comparison of the efficacies and duration of action of the angiotensin II receptors blockers telmisartan and amlodipine. Blood PresMonit 1998;3(5):295-302.
4. Tripathi N, Bohara S, Singh R Ret al. Comparative study of telmisartan and amlodipine to assess the effect on blood pressor, lipid profile and blood glucose level in Indian hypertensive patients.Int J Med Res Rev 2016;4(9):1693-1701.
5. James P A, Oparil S, Carter B L et al. 2014 Evidence based guideline for the Management of High Blood Pressure In adult, report from the Panel Members Appointed to the Eighth Joint National Committee (JNC 8). JAMA 2014;311(5):507-20.

How to cite this article: Madia MMH, Singh AK, Richi SMW, Singh RB. A Comparison of Perioperative Hemodynamic Stability with Amlodipine and Telmisartan during Laparoscopic Cholecystectomy in known Hypertensive Patients. Asian J. Med. Res. 2019;8(2):AN04-AN07.
DOI: dx.doi.org/10.21276/ajmr.2019.8.2.AN2

Source of Support: Nil, **Conflict of Interest:** None declared.