

Low Dose Hyperbaric Bupivacaine 5 mg Combined with 50 mcg Fentanyl for Caesarean Section Delivery in Patient with Maternal Heart Disease

Husodo DP¹, Isngadi I¹, Hartono R¹ and Prasedya ES^{2,3*}

¹Department of Anesthesiology and Intensive Care, Faculty of Medicine, Brawijaya University, Jawa Timur 65145, Indonesia

²Bioscience and Biotechnology Research Centre, Faculty of Mathematics and Natural Sciences, University of Mataram, Nusa Tenggara Bar 83115, Indonesia

³Department of Cellular and Integrative Physiology, Fukushima Medical University, Fukushima, Japan

*Corresponding author: Dr. Eka Prasedya, Department of Cellular and Integrative Physiology, Fukushima Medical University, Fukushima, Japan, E-mail: ekaprasedya@gmail.com

Received date: May 09, 2019; Accepted date: June 10, 2019; Published date: June 17, 2019

Copyright: © 2019 Husodo DP, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

Abstract

Most of women with cardiovascular diseases show worsen clinical condition during pregnancy. That is caused by cardiovascular physiological change during pregnancy and increased demand of oxygen-metabolic system. Spinal anesthesia is the most used technique in section caesaria patient, but there's worried about using spinal anesthesia in patient with cardiac disease due to sudden hemodynamic decrease. Recent studies have proved hemodynamic changes in spinal anesthesia is dose dependent. Dose decreased of spinal anesthesia have potency of inadequate block and change of maternal-fatal hemodynamic due to pain or uncomforted feeling. It can be prevented by using opioid adjuvant that has good effect in anesthesia block. This is retrospective study in 33 patients with maternal heart disease undergoing CS under low dose spinal anesthesia in Saiful Anwar Hospital Malang Indonesia from September 2017 until September 2018. The spinal regimen was 5 mg bupivacaine heavy 0,5% combined with 50 mcg fentanyl. We evaluated the hemodynamic preoperative, post injection of spinal anesthetics, post-delivery, at the end of surgery. We also evaluated bromage score, Apgar score of the baby, and relaxation satisfaction from obstetrician. Combination low dose spinal and opioid for the CS delivery show no significant hypotension effects. It stabilized the hemodynamic prior to injection, post injection, after delivery, post-operative as well as in the recovery room. Furthermore, target blocked was reached well in all cases, no significant changes in Apgar score of the baby, and obstetrician satisfied with motoric relaxation. Low dose spinal anesthesia using 5 mg of bupivacaine heavy 0,5% and adjuvant opioid fentanyl 50 mcg can be successfully used for the performance of CS delivery as regards to onset, adequacy, level, duration of the block and hemodynamic stability and good fetal outcome, with impressive cardiovascular stability.

Keywords: Spinal anesthesia; Cardiac abnormalities; Caesarean section

Introduction

Cardiac abnormalities in pregnancy are still the main non-obstetric factors causing morbidity and mortality in pregnant women [1]. In the United States, complications of heart disease are found in about 4% of all pregnancies. Maternal heart diseases have a mortality risk of (10%-25%) [2]. Pregnant women with heart disorders due to congenital heart disease, acquired heart disease, and cardiomyopathy, require special attention and treatment, because of physiological changes during pregnancy will increase due to higher workload of the heart, whereas the heart itself has abnormalities with the ability to compensate and adapt to imperfect pregnancy [3]. Every cardiac disease have their own's special consideration, but the main goal in patient with heart disease patient who's undergoing section caesarean is same to maintain hemodynamic stability for the mother and baby.

Spinal anesthesia is the most used technique in section caesarean patient, but there's worried about using spinal anesthesia in patient with cardiac disease due to sudden hemodynamic decrease. Some literature also said, it's contraindication to use spinal anesthesia in some specific heart disease such like mitral stenosis due to risk of fallen vital sign. Recent studies have proved hemodynamic changes in spinal

anesthesia is dose dependent. Dose decreased of spinal anesthesia. Have potency of inadequate block and change of maternal-fatal hemodynamic due to pain or uncomforted feeling. The addition of opioids could reduce the dose requirements of local anesthetics and prevent hemodynamic fluctuations and increase the effects of intraoperative and postoperative analgesia. In this retrospective study, we evaluate the outcome of the low dose spinal anesthesia technique in pregnant patients with cardiac abnormalities undergoing caesarean section. This study would be a consideration in determining anesthetic techniques in pregnant patients with heart diseases.

Methods

This study was an observational descriptive retrospective study that evaluated maternal and fetal outcomes parameters in the low dose spinal anesthesia technique during the lower section caesarean section in pregnant patients with cardiac abnormalities. The study was conducted at Saiful Anwar Malang Hospital in November 2018 by observation of the patient's one year medical record from September 2017 to September 2018. The patients that observed in this study were pregnant patients with cardiac abnormalities who underwent CS both elective and emergency with a low dose spinal anesthesia technique under regimen hyperbaric bupivacaine 5 mg and fentanyl 50 mcg. The exclusion criteria in this study were patients undergoing anesthetic changes into general anesthesia or received additional other anesthesia

techniques during surgical, patients who have additional vasopressors preoperatively and surgery duration, and patients with incomplete medical record. Medical records about the outcome of the mother and fetus were observed, such as:

Hemodynamic conditions (blood pressure and pulse) at the 0, 3, 6, and 9 minutes after the anesthetic technique was performed.

Apgar score of the baby.

The bromage score and block height are reached in how many minutes and lost in how many minutes.

The level of obstetrician's satisfaction with the anesthetic technique used.

The data obtained was analyzed using the SPSS 15.0 program. Data on hemodynamic changes (blood pressure and pulse) were analyzed for homogeneity and sample distribution. The homogeneous and normal distribution data were analyzed using one way ANOVA test. Other data whose abnormal were analyzed with Kruskal Wallis. The average bromage score and block target were reached descriptively analyzed with the mean median. The infant Apgar score and Obstetrician's satisfaction levels were analyzed descriptively with the mean median.

Results

1. Patient characteristics

A total of 33 pregnant patients with heart disease undergoing CS with low dose spinal anesthesia hyperbaric bupivacaine 5 mg combine with fentanyl 50 mcg during the period of September 2017 -

September 2018 were observed. The patients demography was consist of 13 patients that were primigravida and 20 other patients that were multipara. Furthermore, the age range was <20 years old (n=3), 21-30 years old (n=18), 31-40 years old (n=12), and no patients were aged over 40 years old.

Types of heart abnormalities in these patients include mitral stenosis (n=6), mitral regurgitation (n=6), atrial septal defect (ASD) (n=6), ventricular septal defect (VSD) (n=3), patent ductus arteriosus (PDA) (n=3), pulmonary hypertension (PH) (n=3), tetralogy of fallot (TOF) (n=2), aorta regurgity (n=1), cardiomyopathy (n=2), others heart diseases (n=4). From exclusion criteria, there's no cardiac patient whose undergoing section caesarean with low dose spinal combine opioid who use any vasopressor (phenylephrine, nor ephinephrine, dopamin, ephedrine, etc.) pre-duranre-post operative. There're two medical records that exclude because incomplete records.

2. Hypothesis testing and descriptive analysis

Based on the normality testing of the observation results with the Kolmogorov Smirnov test, the patient's diastole and pulse data showed p value greater than 0.05 which suggests the data is statistically significant. Hence, the patient's diastole and pulse data were considered normal (Table 1). In the other hand, systole and MAP data show were not statistically significant (p<0.05). Hence, it could be concluded that the systole and MAP data were not normally distributed. So the analyses could not be subjected to ANOVA but was analyzed with the Kruskal wallis test. By using a levene test, the patient's diastole and pulse data was statistically significant (p>0.05), so it can be concluded that the diastole and pulse data of these patients had homogeneous variances (Table 1).

Maternal hemodynamic	Minute				p value
	0	3	6	9	
Diastole A	76.06 ± 18.3	68.70 ± 15.1	67.45 ± 13.8	69.45 ± 14.4	0.112
Sistole K	134.97 ± 11.2	123.09 ± 14.3	122.21 ± 13.5	121.58 ± 13.6	0.071
Pulse A	95.21 ± 9.93	90.67 ± 11.74	89.88 ± 11.51	89.64 ± 13.13	0.178
MAP K	95.70 ± 20.7	86.83 ± 17.1	85.71 ± 16.1	86.83 ± 16.2	0.157

A: ANOVA Analysis; K: Kruskal Wallis

Table 1: Comparison of maternal hemodynamics.

Based on the maternal hemodynamic comparison table, it was evidenced that every minute showed differences for maternal hemodynamic parameters, where blood pressure (systole and astole), pulse and MAP tended to decrease from 0, 3 and 6 minutes, but at the 9th minute there is a slight increase. Whereas, in the 0th minute, the 33 diastole average of the patients was 76.06 mmHg, then decreased in the 3rd minute to 68.70 mmHg, and the 6th minute to 67.45 mmHg, but in the 9th minute it increased to 69.45 mmHg (Table 2).

Based on the 4th average value of the observation time, then the p value of the ANOVA test results is 0.112 (p>0.05), so it can be concluded that there were no significant differences in diastolic means at the minute 0, 3, 6, or 9th minute. In other words, the difference in the average diastole between the four lengths of observation is relatively small, so it is not statistically significant. The average for MAP in the 0th minute was 95.7 mmHg. However, it decreased at the

3rd minute to 86.83 mmHg, and the 6th minute to 85.71 mmHg, finally at 9th it increased to 86.83 mmHg. Based on the 4th average value of the observation time, the p value of the Kruskal wallis test result is 0.157 which is greater than alpha 0.05 (p>0.05). Hence it could be concluded that there were no significant differences in the average MAP at the minute to 0, 3, 6, and 9th minute. In other words, the differences in the average of MAP values between the 4 intervals of observation times were relatively small, so that it is statistically meaningless. In the 0th minute, the average pulse of the 33 patients was 95.21 times/minute, then decreased in the 3rd minute to 90.67 times/minute, the 6th minute to 89.88 times/minute, and in the minute to -9 becomes 89.64 times/ minute. Based on the average pulse at the 4th observation time, the p value of the ANOVA test results is 0.178 which is greater than alpha 0.05 (p>0.05), so it can be concluded that there is no significant difference in mean pulse in the minute to -0, 3, 6, and 9th minute. The next step was to process the existing data using

the post hoc test method as multiple comparisons with the Tukey's test as one of the multiple benchmarking tests that has high enough sensitivity to test for differences between treatments in multiple comparisons. With this method multiple comparisons will be made of the average data between the 4 lengths of observation time, with the results there were no significant differences in the 0, 3, 6, and 9th minute minutes.

Parameter	Mean	Std. Deviation	Minimum	Maximum
Anesthesia block (min)				
Bromage 2	1.45	0.90	0.5	3
Bromage 3	2.85	1.04	1.2	5
Bromage 0	119.85	18.48	80	180
T10	2.33	1.22	1	5
T6	3.87	2.01	1.2	8
Hemodynamic of infant				
Apgar Score 1	6.52	1.15	3	8
Apgar Score 2	8.36	0.99	5	10
Obstetrician				
Relaxation satisfactions	7.59	0.82	6	9.5

Table 2: Descriptive statistics of several parameters of anesthesia block, infant Hemodynamics and satisfaction of obstetrician field relaxation.

Based on the 4th average value of the observation time, then the p value of the ANOVA test results is 0.112 ($p > 0.05$), so it can be concluded that there were no significant differences in diastolic means at the minute 0, 3, 6, or 9th minute. In other words, the difference in the average diastole between the four lengths of observation is relatively small, so it is not statistically significant. The average for MAP in the 0th minute was 95.7 mmHg. However, it decreased at the 3rd minute to 86.83 mmHg, and the 6th minute to 85.71 mmHg, finally at 9th it increased to 86.83 mmHg. Based on the 4th average value of the observation time, the p value of the Kruskal wallis test result is 0.157 which is greater than alpha 0.05 ($p > 0.05$). Hence it could be concluded that there were no significant differences in the average MAP at the minute to 0, 3, 6, and 9th minute. In other words, the differences in the average of MAP values between the 4 intervals of observation times were relatively small, so that it is statistically meaningless. In the 0th minute, the average pulse of the 33 patients was 95.21 times/minute, then decreased in the 3rd minute to 90.67 times/minute, the 6th minute to 89.88 times/minute, and in the minute to -9 becomes 89.64 times/ minute. Based on the average pulse at the 4th observation time, the p value of the ANOVA test results is 0.178 which is greater than alpha 0.05 ($p > 0.05$), so it can be concluded that there is no significant difference in mean pulse in the minute to -0, 3, 6, and 9th minute. The next step was to process the existing data using the post hoc test method as multiple comparisons with the Tukey's test as one of the multiple benchmarking tests that has high enough sensitivity to test for differences between treatments in multiple comparisons. With this method multiple comparisons will be made of the average data between the 4 lengths of observation time, with the results there were no significant differences in the 0, 3, 6, and 9th minute minutes.

Results in Table 2 shows that Bromage score 2 of 33 patients was 0.5 minutes at the latest, 3 minutes at the most, and an average of 1.45 ± 0.9 minutes, for Bromage score 3 was reached fastest at 1.2 minutes, for maximum of 5 minutes, and on average 2.85 ± 1.04 minutes, while for the return time Bromage score 0 from 33 patients was reached at 80 minutes and at most 180 minutes, and an average of 119.85 ± 18.48 minutes. Furthermore, the fastest time to reach T6 block of 33 patients was 1.2 minutes for at the least 8 minutes and an average of 3.87 ± 2.01 minutes. Finally, the time to reach T-10 was 1.0 minutes for a maximum of 5 minutes, and an average of 2.33 ± 1.22 minutes.

Apgar scoring was applied for observations of infant hemodynamics. Apgar score (AS) 1 from 33 patients was at least 3 and at most 8 with an average of 6.52 ± 1.15 . AS 2 was at least 5 and at most 10 with an average of 8.36 ± 0.99). As for the score for relaxation satisfaction evaluated by obstetricians from 33 patients was at least 6 and at most 9.5 with an average of 7.59 ± 0.82 .

Discussion

Determination of the time and type of labor during delivery in patients with heart disease depends on the condition of the mother and fetus in the womb. Factors that must be considered to determine the anesthetic technique administered include parturient hemodynamic status, type of heart disease, previous drug use, and elective surgery [4]. General anesthesia is more widely used in patients that are classified in higher classes based on New York Heart Association (NYHA) classification and previous history of heart surgery [5]. General anesthesia is still an option in cases where regional anesthesia could not be performed. Such as patients that are predicted to experience a lot of bleeding and haemodynamically unstable patients. However, general anesthesia has several risks of hemodynamic disorders due to the administration of induction drugs, laryngoscopic actions, difficult intubation and risk of aspiration [6]. General anesthesia has been known to depress cardiac contractility increase pulmonary vascular resistance through positive pressure ventilation and positive end-expiratory pressure (PEEP). This cause general anesthesia to have a four times greater risk of maternal mortality.

Regional anesthesia according to some literatures is contraindicated in patients with severe valve stenosis and uses anticoagulants [7]. Patients with NYHA class III-IV should not use spinal anesthesia but epidural techniques because the block height can be adjusted easily. In some cases of CHD, regional anesthesia is a preferred option because hemodynamic stability can be well maintained [8]. However, if regional anesthesia is the chosen technique, the anesthetist must determine how to conduct the procedure with a single shot spinal, epidural, or combination of low-dose spinal followed by titration of epidurals.

A sudden decrease in preload and afterload due to spinal single shot is a condition that aggravates the patient's condition, so in some literature this technique is contraindicated to use in patient with heart disease [9]. Administration of fluids and drugs as prophylaxis to prevent hypotension or bradycardia due to regional anesthesia can be a new problem for patients with low cardiovascular reserves.

There are several ways to reduce the incidence of post-spinal anesthesia hypotension, namely by using preloading/coloadng fluid, uterine displacement, use of vasoconstrictors, and the use of a low dose bupivacaine technique. Spinal low dose technique is one technique to reduce the possibility of hypotensive events from regional anesthesia

[10]. Several studies have revealed that hemodynamic changes in spinal anesthesia (especially hypotension) are caused by sympathetic blocks, the amount of which depends on the dose and concentration of local anesthetics used. Therefore, low-dose and low-concentration spines are expected to have minimal effects on hemodynamics of the mother and baby. The low dose technique using hyperbaric bupivacaine can be with lower volumes below 8 mg or lower concentrations below 0,25%. The addition of opioids could reduce the dose requirements of local anesthetics and prevent hemodynamic fluctuations and increase the effects of intraoperative and postoperative analgesia.

The uterine blood flow was not auto regulated, so the uteroplacental perfusion was directly related to maternal blood pressure [11]. Hence, maternal blood pressure can be tolerated only by the mother but not by the fetus. One strategy to maintain both stable hemodynamics and adequate anesthesia block during spinal anesthesia in Cesarean section (CS) surgery is to use low-dose bupivacaine combined with opioid adjuvant [12]. In our study, the outcomes of the low dose spinal anesthesia technique in pregnant patients with cardiac abnormalities undergoing caesarean section were evaluated. The low doses of hyperbaric bupivacaine (5 mg) combined with fentanyl 50 mcg produced adequate blocks with minimal systemic side effects, among others, to minimize the decrease in vascular systemic resistance and prevent the onset of hypotension in spinal anesthesia.

In this retrospective study we also did not find any episodes of hypotension and desaturation. There's no use of any vasopressor (phenylephrine, nor ephinephrine, dopamin, ephedrine, etc.) pre-durante-post operative.

Intrathecal local anesthesia works by inhibiting voltage-gated sodium channels on the spinal cord which will affect the motor and sensory impulses of afferent and efferent fibers [13]. This level of sensory and motor blocks depends on the technique, agent and dosage given. Opioids given to intrathecal space selectively produce an analgesic effect through interaction with opioid receptors in the dorsal horn of the spinal cord and thus can minimize the dosage and supraspinal effects of local anesthetics such as hypotension, respiratory depression, sedation and nausea and vomiting [14]. The main location of the opioid receptor is in the substantia grisea of the substantia gelatinosa. This is the basis of the anatomy of selective analgesia after intrathecal opioids are given.

Fentanyl works synergistically with bupivacaine in reducing the pain threshold without increasing sympathetic and motor blockade [15]. There have been many studies that prove the effectiveness of opioid use in spinal anesthesia especially in CS surgery. Previous studies have shown that lipophilic opioids, for example fentanyl, can accelerate the onset and extend the duration of bupivacaine blocks, and prolong the duration of postoperative analgesia [16]. The combination of both has a 5-minute intrathecal onset speed and 10 minutes through the epidural and relatively has a shorter duration of action due to the presence of redistribution (2-4 intrathecal and epidural hours). No active metabolites were found and were 800 times more lipid soluble than morphine. And because of its very high solubility in fat it will quickly bind to opioid receptors in the dorsal horn of the spinal cord, and this rapid onset is very beneficial both as analgesia in normal labor and in cases of emergency CS. The optimal dose fentanyl for adjuvant spinal anesthesia are 12,5 mcg- 50 mcg, there's no more beneficial effect in dose more than 50 mcg. The combination of hyperbaric bupivacaine 5 mg and fentanyl 50 mcg

result's bupivacaine 0,25% hyperbaric with faster onset and prolong post-operative analgesia [17].

Patients with NYHA class III and IV should not use conventional doses of spinal anesthesia given the possible reduction hemodynamics [18,19]. In patients with stable hemodynamics, pure epidural anesthesia and low-dose epidural spinal combinations according to some literature are more recommended than general anesthesia [20]. General anesthesia is known to depress cardiac contractility, increase pulmonary vascular resistance through positive pressure ventilation [21]. Laryngoscopic and intubation actions and possible aspiration can also cause hemodynamic changes in patients undergoing general anesthesia [22]. Low-dose spinal bupivacaine combined with fentanyl adjuvant in some research have been proved minimally decreased hemodynamic with adequate anesthesia blockage. As we know, patient with cardiac heart disease have susceptibility to any changes in cardiovascular function [23]. That's why we must avoid anything that can increase overwork cardiac and metabolic demand such like pain, hypovolemia, hypotension, shivering, etc. Every cardiac disease has different special consideration and therapy but the main goal is same to avoid drastically change in hemodynamic. Therefore using this technique in patients with cardiac diseases has advantage in producing stability of parturient vital sign.

Conclusion

From this research, there were no significant differences in the mean systole, diastole, and MAP at the 0th, 3rd, 6th and 9th minute post spinal low dose measures. There was no significant difference in mean pulse at the 0th, 3rd, 6th and 9th minute post spinal low dose measures. There's no use of any vasopressor (phenylephrine, nor ephinephrine, dopamin, ephedrine, etc.) pre-durante-post operative. We can conclude that there were no significant hemodynamic changes after spinal anesthesia using low dose bupivacaine 5 mg with combination fentanyl 50 mcg. The onset, duration, and blockage quality of anesthesia have been reached well in all case. Bromage score 2 after a spinal low dose of 33 patients was reached on average after 1.45 minutes. For Bromage score 3 the average is reached after 2.85 minutes, while for Bromage score 0 the average returns at 119.85 minutes. Block t-6 height after spinal low dose action of 33 patients reached an average of 3.87 minutes, and for block t-10 height reached an average of 2.33 minutes. Newborn hemodynamic in all 33 cases are good. Apgar score (as) 1 averages 6.52 and for apgar score (as) 2 8.36. Obstetrician relatively satisfied with the quality of sensoric and motoric blockage that produced by low dose spinal anesthesia. Score of field relaxation satisfaction by operator from 33 patients averaging 7.59 (satisfied).

Low dose hyperbaric bupivacaine 5 mg combined with fentanyl 50 mcg can be considerate as an anesthesia technique in CS delivery patients with heart diseases due to its onset, adequacy, level and duration of the block, hemodynamic stability and good fetal outcome. In conclusion, the choice of the anesthetic technique used must consider the hemodynamic status of the parturient at the time of arrival, type of heart disease, previous drug use, and the type of elective surgery or emergency surgery. Pre, durante, and postoperative management must involve multidisciplinary (involving cardiologist, obstetrician, and pulmonologist) to deal with possible complications.

References

1. Martins LC, Freire CMV, Capuruçu CAB, Nunes M do CP, Rezende CA de L (2016) Risk prediction of cardiovascular complications in pregnant women with heart disease. *Arq Bras Cardiol* 106:289-296.
2. Ashrafi R, Curtis SL (2017) Heart disease and pregnancy. *Cardiol Ther* 6: 157-173.
3. Michael E Hall, Eric M George, Joey P Grangerb (2011) The heart during pregnancy. *Rev Esp Cardiol* 64: 1045-1050.
4. Luthra A, Bajaj R, Jafra A, Jangra K, Arya V (2017) Anesthesia in pregnancy with heart disease. *Saudi J Anaesth* 11: 454-471.
5. Fisher JD (1972) New York Heart Association Classification. *Arch Intern Med* 129: 836.
6. Smith G, Goldman J (2018) *General Anesthesia for Surgeons*. StatPearls. Treasure Island (FL): StatPearls Publishing.
7. Johansson S, Lind MN (2017) Central regional anaesthesia in patients with aortic stenosis: A systematic review. *Dan Med J* 64: A5407.
8. Junghare SW, Desurkar V (2017) Congenital heart diseases and anaesthesia. *Indian J Anesth* 61: 744-752.
9. Han Y, Zhang Z, Sun Q, Ding K, Han L, et al. (2017) Combined spinal-epidural anesthesia for cesarean delivery in a patient with cor triloculare biventriculare. *BMC Anesthesiol* 17: 115.
10. Lairez O, Ferré F, Portet N, Marty P, Delmas C, et al. (2015) Cardiovascular effects of low-dose spinal anaesthesia as a function of age: An observational study using echocardiography. *Anaesth Crit Care Pain Med* 34: 271-276.
11. Venuto RC, Cox JW, Stein JH, Ferris TF (1976) The effect of changes in perfusion pressure on uteroplacental blood flow in the pregnant rabbit. *J Clin Invest* 57: 938-944.
12. Jain G, Singh DK, Bansal P, Ahmed B, Dhama SS (2012) Comparison of low doses of intrathecal bupivacaine in combined spinal epidural anaesthesia with epidural volume extension for caesarean delivery. *Anesth Essays Res* 6: 47-52.
13. Fozzard HA, Sheets MF, Hanck DA (2011) The sodium channel as a target for local anesthetic drugs. *Front Pharmacol* 2: 68.
14. Del Vecchio G, Spahn V, Stein C (2017) Novel opioid analgesics and side effects. *ACS Chem Neurosci* 8: 1638-1640.
15. Roussel JR, Heindel L (1999) Effects of intrathecal fentanyl on duration of bupivacaine spinal blockade for outpatient knee arthroscopy. *AANA J* 67: 337-343.
16. Chen Q, Shang Y, Xu Y, Li P, Li P, et al. (2016) Analgesic effect and pharmacological mechanism of fentanyl and butorphanol in a rat model of incisional pain. *J Clin Anesth* 28: 67-73.
17. Chu CC, Shu SS, Lin SM, Chu NW, Leu YK, et al. (1995) The effect of intrathecal bupivacaine with combined fentanyl in cesarean section. *Acta Anaesthesiol Sin* 33: 149-154.
18. Upadya M, Saneesh P (2016) Anaesthesia for non-obstetric surgery during pregnancy. *Indian J Anaesth* 60: 234-241.
19. Mung'ayi V, Mbaya K, Sharif T, Kanya D (2015) A randomized controlled trial comparing haemodynamic stability in elderly patients undergoing spinal anaesthesia at L5, S1 versus spinal anaesthesia at L3, 4 at a tertiary African hospital. *Afr Health Sci* 15: 466-479.
20. Zhu J, Zhang XR, Yang H (2017) Effects of combined epidural and general anesthesia on intraoperative hemodynamic responses, postoperative cellular immunity, and prognosis in patients with gallbladder cancer. *Medicine (Baltimore)* 96: e6137.
21. Alwardt CM, Redford D, Larson DF (2005) General anesthesia in cardiac surgery: a review of drugs and practices. *J Extra Corpor Technol* 37: 227-235.
22. Ko D-D, Kang H, Yang SY, Shin HY, Baek CW, et al. (2012) A comparison of hemodynamic changes after endotracheal intubation by the Optiscope™ and the conventional laryngoscope. *Korean J Anesthesiol* 63: 130-135.
23. Altaieb FF, Alshammari OM, Alanazi HM, Alijaber DA, Alanazi AB, et al. (2017) Pattern and factors associated with cardiovascular diseases among patients attending the cardiac center in Arar City, Northern Saudi Arabia. *Electron Physician* 9: 5459-5464.