PERIODICUM BIOLOGORUM
VOL. 115, No 2, 283–288, 2013

UDC 57:61
CODEN PDBIAD
ISSN 0031-5362

Clinical experience

Sudden cardiorespiratory arrest following spinal anesthesia

SINIŠA ŠOŠTARIĆ
KREŠIMIR OREMUŠ

Akromion
– Special Hospital for Orthopedic Surgery
Krapinske Toplice, Croatia
E-mail: sinisa.sostaric@akromion.hr

Key words: Spinal anesthesia, Sudden cardiorespiratory arrest, Apnea, Asystole.

Received May 15, 2013.

INTRODUCTION

Sudden cardiac arrest after spinal anesthesia is a relatively rare but potentially catastrophic event. The true incidence of cardiac arrest during neuraxial anesthesia is not as low as it was traditionally believed to be; it varies between 1.3 and 18 in 10,000 *(1"12)*. A review by Sprung *et al. (1)* reported the frequency of arrest for patients during regional anesthesia to be 1.5 per 10,000, which was less than the reported frequency of arrest for patients receiving general anesthesia (5.5 per 10,000). These facts do not necessarily imply greater safety of regional anesthesia. Rather, this may reflect the fact that a wider variety of more complex surgical cases are performed under general anesthesia, and also that there may be a bias toward general anesthesia in the emergency setting. Two large prospective studies designed to evaluate the incidence of complications during spinal anesthesia reported 2 cardiac arrests in 1881 patients *(9)* and 26 arrests in 40,640 patients *(2)* for an overall incidence of 7 in 10,000 (0,07%). This incidence is high compared with the rate of one cardiac arrest for every 10,000 cases (0,01%) reported for epidural anesthesia *(2)*. Equally important are the long--term survival and outcome after such events. Auroy *et al. (2, 3)* reported 29 cardiac arrests among 40,640 spinal and 30,413 epidural anesthetics, only 6 of which were fatal. Importantly, no neurologic deficits were observed in the 23 (79%) patients who survived cardiac arrest. In another large 20-yr prospective study, Kopp *et al. (13)* showed that median time to arrest was 50 min (range 0-210 min) after last local anesthetic administration (intrathecal/epidural/caudal). Because the time of onset of cardiac arrest cannot be predicted, it is of utmost importance that all the patients who receive neuraxial anesthesia get constant monitoring and vigilance. Also, in order to achieve satisfactory neurologic outcome, resuscitative measures of an advanced cardiac life support protocol have to be promptly initiated.

CASE REPORT

A 64 years old woman (weight 69 kg, height 160 cm, BMI 26,95 kg/m^2) was scheduled for elective total hip replacement surgery. Preoperative assesment was unremarkable except for a hystory of arterial hypertension and hyperlipidemia. Medications consisted of lisinopril, hydrochlorotiazide and atorvastatin. Physical examination, laboratory evaluation and ECG were unremarkable. She was classified as ASA II patient according to the ASA classification. For premedication patient received oral midazolam 7,5 mg. Upon arrival in the operating room, ECG, automated blood pressure cuff and pulse oximeter monitors were aplied

and routine monitoring (with ECG, non-invasive arterial pressure and oxygen saturation) was started. One wide-bore 14-gauge intravenous access was secured and 20-gauge arterial catheter was inserted in left radial artery, according to our local protocol. Arterial blood was drawn for preoperative analysis (blood gases, electrolytes, glucose, lactates). Lab results: pH 7,43, pO_2 10,1 kPa, pCO_2 5,1 kPa, sO_2 95%, HCO_3 25,2 mM, sodium 137 mM, potassium 3,5 mM, calcium 1,13 mM, glucose 5,0 mM, lactate 0,9 mM. The preoperative blood pressure was 150/85 mmHg, heart rate was 62 beats/min with sinus rythm and peripheral oxygen saturation was 99%. Sufentanyl 5 μg was given, and nasal oxygen supplementation at 4 L/min was begun. Fluid preload consisted of 500 mL of Ringer lactate solution. After positioning the patient to the sitting position, 0,5% levobupivacaine 15 mg mixed with morphine hydrochloride 125 μg was injected with a Whitacre 27-gauge spinal needle at L_2-L_3 interspace. Spinal puncture was uneventful. She was returned to supine position and urinary bladder was catheterised. Ten minutes after the spinal puncture sensory level to pinprick was noted to be at Th8 bilaterally. The patient was then turned to left lateral decubital position and a preparation for surgery had started. For 25 minutes after the intrathecal administration of local anesthetic, patient was fully responsive, oriented, hemodynamically and respiratory stable, with only a slight decrease of arterial blood pressure and heart rate (135/75 mmHg and 55 beats/min, respectively), and oxygen saturation was consistently 100%. Then suddenly the patient becomes unresponsive, apneic, with unmeasurable traces of oxygen saturation and pulseless on carotid artery. P-wave asystole was noted on ECG monitor. She was immediately turned supine, sterile drapes that were already in place were removed, external cardiac massage was started by a surgeon, while airway was easily secured with endotracheal tube. No muscular relaxant was needed for intubation because the patient was flaccid and completely areflectic. After the confirmation of the tube position by auscultation, ventilation with 100% oxygen was asynchronously started. Atropine 0,5 mg and ephedrine sulphate 20 mg were administered, while epinephrine 1 mg, diluted to 1:10,000 solution, was prepared. After approximately one minute of CPR patient status was checked: blood pressure was 125/65 mmHg and stable, heart rate was 78 beats/min with synus rythm, oxygen saturation was 100% and end-tidal CO_2 was 4,7 mmHg. Arterial blood was drawn for analysis: pH 7,36, pO_2 52,4 kPa, pCO_2 6,0 kPa, sO_2 100%, HCO_3 24,7 mM, sodium 137 mM, potassium 3,8 mM, calcium 1,21 mM, glucose 5,5 mM, lactate 1,0 mM. Inhalational anesthesia with sevoflurane 1,2 vol% was carefully started, and after ten minutes of observation during which patient remained fully hemodynamically and respiratory stable and without a need for inotropic support, a consensus was made to begin with surgery. Invasive arterial blood measurement was started. Surgery lasted for 92 minutes and went uneventful, intraoperative blood loss was 250 mL, diuresis was 500 mL. Patient received our standard intravenous fluid load consisting of Ringer lactate 1000 mL and 6% hydroxyethyl starch 130/0.42/6:1 balanced solution (Tetraspan® *6%*, BBraun) 500 mL. General anesthesia was mainained only with sevoflurane 0,8–1,2 vol%. At the end of the surgery patient was awaked and extubated. Postoperative laboratory analysis was normal. She was fully oriented but completely amnestic and unaware of the event. No neurologic deficit or cognitive dysfunction was observed, except for mild confusion and retrograde amnesia. Early recovery and physical rehabilitation on the ward was normal, and the patient was on 4th postoperative day discharged to rehabilitation clinic according to preoperative plan.

DISCUSSION

Cardiac arrest fatalities during spinal anesthesia are becoming increasingly recognised by many representative case reports throughout medical science literature of 21st century. As it is described in introduction, although such fatalities were usually described as unexpected or extremely rare, they were actually surprisingly common *(1, 2, 3, 13, 14, 46, 50)*. In a study including 20,000 spinal anesthetics, fatal cardiac arrest was reported in healthy young patients less than 30 years of age *(15)*. A closed claims analysis by Caplan *et al. (14)* reported 14 arrests with six mortalities in young healthy patients undergoing minor surgical procedures. Of the eight survivors, seven had serious neurological damage. Such a situation should attract attention that many of these fatalities may be avoidable and that the working mechanism should be cleared.

A responsible mechanism for cardiac arrest after spinal anesthesia is of a possible respiratory, cerebral and circulatory origin.

RESPIRATORY MECHANISM

It may be considered as a cause for cardiac arrest after spinal anesthesia, because most of those patients also receive a sedative drug that may be responsible for inadequate ventilation. But the evidence for a respiratory etiology is sparse. Spinal anesthesia sensory levels up to Th4 do not lead to hypoventilation; they are actually associated with mild hyperventilation *(16, 17)*. And after the widespread use of pulse oximetry in routine monitoring, it is now difficult to invoke hypoxemia as the primary cause, because cardiac arrests occur in the setting of oxygen saturation readings of 95–100% at the time *(18, 19, 20)*. However, for safety, one should consider that oversedation may increase the risk of bradycardia *(14)* and the patient may not be able to communicate symptoms of early warning of a vasovagal attack *(21)*. In our patient that wasn't the case; she received only premedication with subhypnotic dose of oral midazolam together with a low-dose sufentanyl intravenously, and was fully responsive, with oxygen saturation reading of 100%, until the moment of sudden cardiac arrest.

CEREBRAL MECHANISM

There is some evidence in the older literature that cerebral hypoxia might occur during spinal anaesthesia in some patients *(22, 23)*. More recently, Atallah *et al. (26)* proved that following spinal anaesthesia and during TURP, some patients developed impaired cerebral oxygenation. Although impaired cerebral oxygenation seems not to be a primary etiology for fatal cardiac arrest during spinal anaesthesia, it can be suggested that a disturbance in cerebral oxygen balance might be a precipitating factor for the occurrence of cardiac arrest in specific surgical situations during spinal anaesthesia. In our patient that wasn't the case either.

CIRCULATORY MECHANISM

A circulatory etiology for cardiac arrest during spinal anaesthesia is directly or indirectly related to the blockade of sympathetic efferents *(25, 26)*. Local anesthetics injected into subarachnoid space block not only motor and somatic sensory fibres; they also produce preganglionic sympathetic denervation, and the level of sympathetic block is always 2 to 6 segment higher than somatic levels, which are usually assessed by pinprick. Skin discrimination of temperature may be used as a clinical correlate of the level of sympathetic denervation during regional anaesthesia. The cardiac sympathetic outflow emerges from C5 to Th5 levels, with the main supply to the ventricles from Th1 to Th4. A significant part of the chronotropic and inotropic control of the heart and its oxygen demand is mediated through the upper four thoracic spinal segments. The major determinant of heart rate is the balance between sympathetic and parasympathetic systems with the latter predominating. A high thoracic sympathetic blockade covering the cardiac segments (Th1-Th4) produces significant reduction in heart rate. However, high sympathetic blockade may leave some cardiac sympathetic activity intact, since sympathetic responses to hypercarbia are not totally suppressed by high Th1 to Th5 blockade *(27, 28)*.

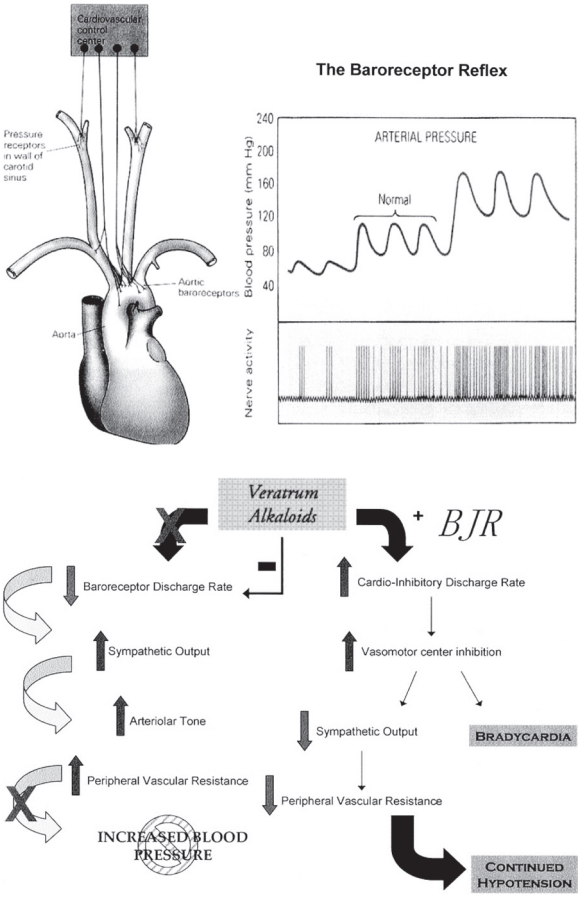
A more important effect of sympathetic inhibition during spinal or epidural anaesthesia is a significant decrease in venous return due to dilatation of resistance and capacitance vessels *(27)*. Reductions of the right atrial pressure of 36% and 53% have been reported after low and high spinal blocks respectively *(17)*. It is clear that a circulatory etiology underlies the occurrence of severe bradycardia and asystole, given the blockade of sympathetic efferents and the profound decrease in venous return associated with higher levels of spinal sympathetic blockade (29). Those decreases in preload after spinal anaesthesia initiate reflexes that cause severe bradycardia.

Mackey *et al. (19)* have suggested three working reflexes:

1. The pacemaker stretch reflex: the rate of firing of the pacemaker cells within the myocardium is proportional to the degree of stretch. Decreased venous return results in decreased stretch and a slower heart rate.

2. Low pressure baroreceptors in the right atrium and vena cava when stimulated may cause bradycardia. With progressive hypovolemia, there may be a paradoxical recurrence of baroreceptor discharge, the so-called "collapse firing" *(21)*.

3. The Bezold-Jarisch reflex: mechanoreceptors in the left ventricle when stimulated may cause bradycardia. The Bezold-Jarisch reflex includes reactions triggered by cardiac mechano-receptor activation and it has been used to describe perioperative bradycardia with hypotension *(19, 30, 51)*. Some unmylenated afferent pathways from the inferoposterior wall of the left ventricle pass via the glossopharyngeal and vagus nerves to the brain stem and may respond to decreased venous return due to relative hypovolemia by bradycardia. This bradycardia is a protective reflex that prevents the heart from contracting when relatively empty *(31, 37)*. The Bezold-Jarisch reflex overlaps with the vasovagal syncope *(52)* as it became a term which includes reactions triggered by cardiac mechanoreceptors and describes perioperative bradycardia with hypotension *(19, 31, 32, 37, 46)*. The Bezold-Jarisch reflex was originally described in 1867 by von Bezold and Hirt *(40)*. They observed that an intravenous injection of veratrum alkaloids cause a profound decrease in blood pressure and heart rate in conjunction with apnea. In the late 1930s Jarisch and Richter confirmed that the depressor effect initially observed by von Bezold was, in fact, a



reflex in origin. In 1947 Dawes *et al. (41)* finally showed that the reflex apnea was caused by a separate mechanism from that mediating the hemodynamic changes. Today, the term Bezold-Jarisch connotes the reflex as describes by Dawes: bradycardia, vasodilation, and hypotension resulting from stimulation of cardiac receptors.

We have assumed that in our patient the Bezold-Jarisch reflex, possibly together with the other two cardiac reflexes proposed by Mackey, is responsible for sudden onset of cardiac arrest. Because we have managed to achieve hemodynamic stability in the patient in less than one minute, our presumption is that the circulatory reflex originated from the heart was the main cause of the event, rather than an unexpectedly high sympathetic blockade.

Risk factors for cardiac arrest following spinal anesthesia

John B. Pollard *(5)* has summarized six risk factors for bradycardia < 50 beats/min during spinal anaesthesia: baseline heart rate < 60 beats/min, ASA physical status I, age < 50 years, sensory level block above T6, prolonged P-R interval and the use of â-blocking drugs. He holds the opinion that the presence of a single risk factor out of these six, does not make it certain that a patient will experience severe bradycardia or cardiac arrest. However, when two or more of these six factors are present, the patient may be considered at high-risk for bradycardia and cardiac arrest during spinal anaesthesia. Patient in our case report didn't have any of these warning signs, but had still developed a sudden cardiac arrest. Considering this, a continuous vigilance and monitoring is mandatory, while providing anesthetic care for every patient after spinal anesthetic.

Possible prevention of cardiac arrest

1. Proper selection of patient and operation

It is strongly adviced that it should be appropriate to reconsider the use of spinal anaesthesia for a patient with vagotonia *(5)*. Similarly, it may be prudent not to use spinal anaesthesia when significant blood loss or the use of vasodilators is anticipated *(48, 49),* because the vasodilatation caused by spinal anaesthesia can make resuscitation ineffective.

2. Fluid support

Although one might assume that maintaining preload during spinal or epidural anaesthesia is a uniform practice of anaesthetists, the literature demonstrates otherwise as many cases with cardiac arrest reported in literature occurred in settings without volume preloading *(33, 46)*.

With decrease of venous return due to hypovolemia or a redistribution of blood volume, blood pressure is initially maintained by vasoconstriction. During progressive and continuing decrease in venous return, there may be a sudden fall in blood pressure, heart rate and peripheral resistance. Restoration of venous return is always urgent as spontaneous recovery from asystole may occur if this is achieved *(34, 51)*. A simple manouvre as leg elevation if possible should not be ignored *(14, 51)*. In an original study, Mirt and Vesna *(38)* compared the use of 12ml/kg Ringer Lactate solution within 20 min before spinal anaesthesia versus within 20 min starting immediately after spinal anaesthesia. In the first group of patients, the cardiac output (CO) increased by 20% after the infusion and returned to baseline value 30 min after spinal block. In the second group, CO increased after spinal block and was still 11.3% above the baseline 30 min after the spinal block. They (38) concluded that the decrease in CO after spinal anaesthesia can be prevented by the infusion of Ringer lactate solution, with CO reaching the highest value while the infusion is running.

3. Pharmacological support

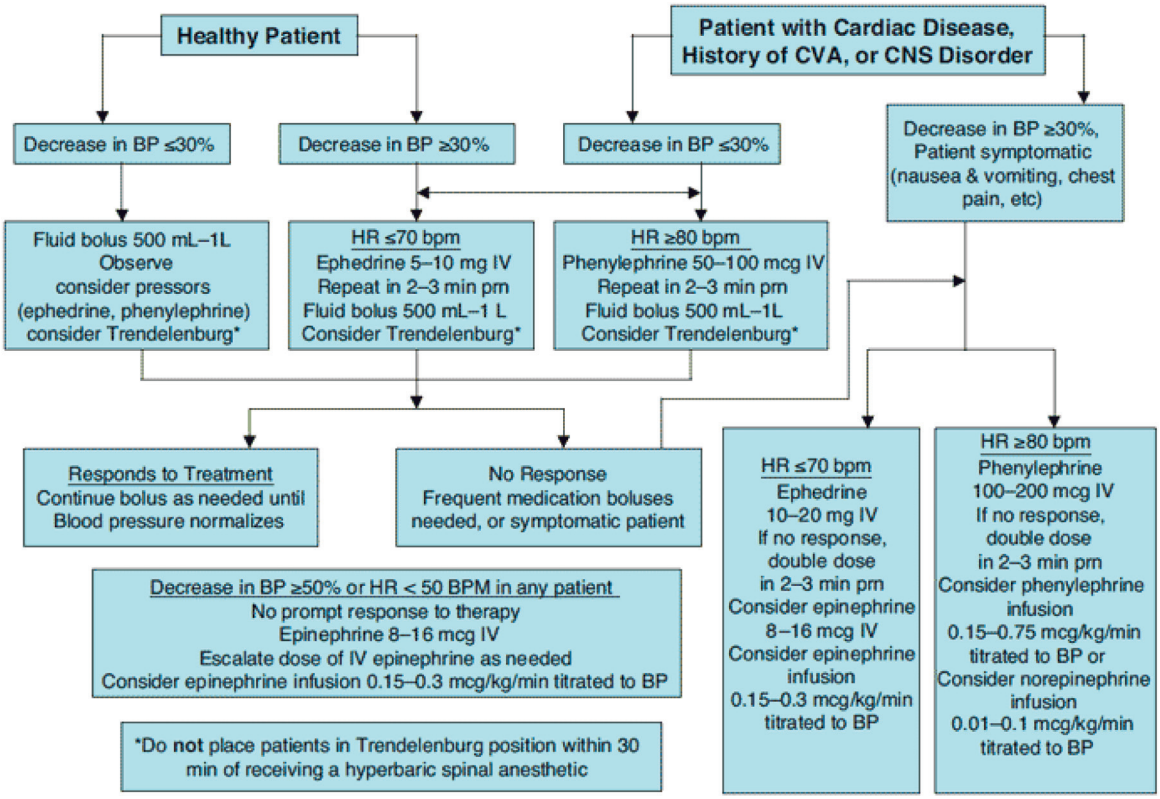
Inspite of emphasizing the importance of volume loading and prompt replacement of fluid loss during spinal anaesthesia, decreases in preload can occur so quickly with altering the patient position, releasing a tourniquet or similar perioperative events that there may not be enough time to give sufficient fluid volumes over several minutes. Here, the administration of pharmacological drug support may be appropriate. In such situations, or when bradycardia is the presenting sign, atropine may decrease the incidence of cardiac arrest during spinal anaesthesia *(7, 9)*. Brown *et al. (39)* advised vigilance of the anaesthetist and the willingness to utilize iv. atropine (0.4–0.6 mg), ephedrine (25–50 mg) and epinephrine (0.2–0.3 mg) in stepwise escalation of therapy, when bradycardia develops following spinal analgesia. Successful resuscitation was carried out in all settings where atropine was typically used as the first line of therapy *(8, 42, 43, 46)*. Atropine may not be the best single agent if bradycardia is accompanied by vasodilatation as hypotension may persist after the relief of bradycardia by atropine *(7)*.

It may be useful to note that epinephrine and external cardiac massage were also needed in some cases. None of these patients suffered morbidity after the event, reinforcing Caplan *et al. (14)* suggestion that immediate treatment of bradycardia or asystole under these circumstances is crucial. If initiating the measures of basic and advanced life support is delayed, the mortality becomes extremely high, approaching 90.9% among the patients that arrested in the Thailand prospective registry of 40,271 cases of spinal anesthesia reported by Charuluxananan *et al. (50)*. It should be clear that bradycardia with heart rate of 50 beats/min is consistent with cardiac sympathetic nerve inhibition associated with mid-thoracic block level *(44)*. However, the development of sudden bradycardia over a few heart beats and the potential for the reversal of bradycardia by postural changes that increase venous return, can only be explained by a vasovagal reaction *(21, 44, 52)*.

When bradycardia is profound or a full cardiac arrest occurs after spinal anaesthesia, the early administration of epinephrine is crucial. The vasodilatation caused by spinal anaesthesia can make cardiopulmonary resusci-

TABLE 1

Treatment for Hypotension after Spinal Anesthesia (www.nysora.com).



tation ineffective. Successful resuscitation requires a coronary perfusion pressure gradient of 15 to 20 mmHg and during spinal anaesthesia this may require epinephrine 0.01 to 0.1 mg/kg *(35)*. Currently, epinephrine is administered during only 25–40% of these arrests after spinal anaesthesia and up to 25% of these arrests are fatal *(2, 8, 9)*. Earlier and more consistent use of epinephrine has been recommended *(8, 14, 35, 49)* and could improve outcomes after cardiac arrest during spinal anaesthesia. Sympathomimetic drugs can counteract the vasodilation in both the arterial and venous circulations *(14, 47, 49)*. Unfortunately, not all of the arrests that occur during spinal anaesthesia are successfully treated, and fatal cardiac arrest still occurs in young healthy patients. It is important to consider that if hypotension persists after adequate doses of ephedrine or epinephrine, an alpha-agonist like phenylephrine should be given. It is only in this situation that selective alpha-agonists have therapeutic place, because these agonists if given to a patient with bradycardia, heart rate may be reduced further if baroreceptor function remains active *(36, 37)*. A standard sequence using atropine, ephedrine and then epinephrine to treat bradycardia during spinal anaesthesia has been advocated *(35)*. But, although flexibility is necessary, Kinsella and Tuckey *(21)* have recently suggested that ephedrine, due to its cardiac and vascular actions, is the most logical choice for a single agent to treat profound bradycardia during regional anaesthesia, given the lack of vasoconstrictor effect of atropine and the potential for heart rate reduction with alpha-agonists. As mentioned before, with the occurrence of asystole or persistent severe bradycardia, epinephrine should be used early.

CARDIOPULMONARY RESUSCITATION

Severe bradycardia (<40 beats/min), if persistent despite pharmacological therapy, should be managed like asystole by cardiopulmonary resuscitation, comprising its usual principles of basic and advanced life support. Once persisting cardiac arrest occurs, external cardiac massage must be started to ensure circulation of drugs and perfusion of vital organs. Prompt treatment with epinephrine has been emphasized as crucial for successful recovery *(5, 13, 33, 35, 46)*. In our case, we have managed to achieve sustained hemodynamic stability in our patient with external chest compressions, atropine and ephedrine. Epinephrine, although already prepared, was not needed.

REFERENCES

1. SPRUNG J, WARNER M E, CONTRERAS M G *et al.* 2003 Predictors of survival following cardiac arrest in patients undergoing noncardiac surgery: a study of 518,294 patients at a tertiary referral center. *Anesthesiology 99:* 259–69
2. AUROY Y, NARCHI P, MESSIAH A *et al.* 1997 Serious complications related to regional anesthesia. *Anesthesiology 87:* 479–86

3. AUROY Y, BENHAMOU D, BARGUES L *et al.* 2002 Major complications of regional anesthesia in France. *Anesthesiology 97:* 1274–80
4. LIU S S, MCDONALD S B 2001 Current issues in spinal anesthesia. *Anesthesiology 94:* 888 –906
5. POLLARD J B 2001 Cardiac arrest during spinal anesthesia: common mechanisms and strategies for prevention. *Anesth Analg 92:* 252– 6
6. PHILLIPS O C, EBNER H, NELSON A T, BLACK M H 1969 Neurologic complications following spinal anesthesia with lidocaine: a prospective review of 10,440 cases. *Anesthesiology 30:* 284 –9
7. LIGUORI G A, SHARROCK N E 1997 Asystole and severe bradycardia during epidural anesthesia in orthopedic patients. *Anesthesiology 86:* 250 –7
8. GEFFIN B, SHARPIRO L 1998 Sinus bradycardia and asystole during spinal and epidural anesthesia: a report of 13 cases. *J Clin Anesth10:* 278–85
9. TARKKILA P J, KAUKINEN S 1991 Complications during spinal anesthesia: a prospective study. *Reg Anesth16:* 101– 6
10. MOORE D C, BRIDENBAUGH L D 1966 Spinal (subarachnoid) block: a review of 11,574 cases. *JAMA 195:* 907–12
11. CARPENTER R L, CAPLAN R A, BROWN D L *et al.* 1992 Incidence and risk factors for side effects of spinal anesthesia. *Anesthesiology 76:* 906–16
12. OLSSON G L, HALLEN B 1988 Cardiac arrest during anaesthesia: a computer aided study in 250,543 anaesthetics. *Acta Anaesthesiol Scand 32:* 653– 64
13. KOPP S L, HORLOCKER T T, WARNER M E *et al.* 2005 Cardiac Arrest During Neuraxial Anesthesia: Frequency and Predisposing Factors Associated with Survival. *Anesth Analg100:* 855–65
14. CAPLAN R A, WARD R J, POSNER K *et al.* 1998 Unexpected cardiac arrest during spinal anesthesia: a closed claims analysis of predisposing factors. Anesthesiology 68: 5–11.
15. SADOVE M S, LEVIN M J, RANT-SEJDINAJ I 1961 Neurological complications of spinal anaesthesia. *Can Anaesth Soc J 8:* 405-16
16. KENNEDY W F, BONICA J J, AKAMATSU T J *et al.* 1968 Cardiovascular and respiratory effects of subarachnoid block in the presence of acute blood loss. *Anesthesiology 29:* 29 –35
17. SANCETTA S M, LYNN R B, SIMEONE F A, SCOTT R W 1952 Studies of hemodynamic changes in Humans following induction of low and high spinal anesthesia. *Circ 6:* 559 –71
18. KREUTZ J M, MAZUZAN J E 1990 Sudden asystole in a marathon runner: The athletic heart syndrome and its anesthetic implications. *Anesthesiology 3:* 1266–8
19. MACKEY D C, CARPENTER R L, THOMPSON G E *et al.* 1989 Bradycardia and asystole during spinal anesthesia: a report of three cases without morbidity. *Anesthesiology 70:* 866–8
20. JOSHI G P, SHEARER V E, RACZ T *et al.* 1997 Ruptured aortic aneurysmand cardiac arrest associated with spinal anesthesia. *Anesthesiology 86:* 244 –7
21. KINSELLA S M, TUCKEY J P 2001 Perioperative bradycardia and asystole: relationship to vasovagal syncope and the Bezold-Jarisch reflex. *Br J Anaesth 86:* 859–68
22. SIVARAJAN M, AMORY D W, LINDBLOOM L E 1976 Systemic and regional blood flow during epidural anesthesia without epinephrine in the rhesus monkey. *Anesthesiology 45:* 300–10
23. MURKIN J M 1994 Monitoring cerebral oxygenation. *Can J Anaesth 41:* 1027–32
24. ATTALAH M M, ANDREAS H, EL-GHOROURI M A, GOLINAR E H 1998 Does spinal anesthesia affect cerebral oxygenation during transurethral prostatectomy? *Reg Anesth &Pain Medicine 23(2):* 119–25
25. COOK P R, MALMQVIST L, BENGSTSSON M 1990 Vagal and sympathetic activity during spinal analgesia. *Acta Anaesthesiol Scand 34:* 271–5
26. BARON J, DECAUX-JACOLOT A 1986 Influence of venous return on baroreflex control of heart rate during lumber spinal and epidural anesthesia in humans. *Anesthesiology 64:* 188–93
27. VEERING B T, COUSINS M J 2000 Cardiovascular and pulmonary effects of epidural anaesthesia. *Anaesth Intensive Care 28:* 620–35
28. D'ALESSIO J G, WELLER R S, ROSENBLUM M 1995 Activation of the Bezold-Jarisch reflex in the sitting position for shoulder arthroscopy using interscalene block. *Anesth Analg 80:* 1158–62
29. KLEINERMAN J, SANCETTA S M, HACKEL D B 1958 Effect of high spinal anesthesia on cerebral ciruclation and metabolism in man. *J Clin Invest 37:* 285–293
30. HAMPL K F, SCHNEIDER M C 1994 Vasovagal asystole before induction of general anaesthesia. *Eur J Anaesth 11:* 131–3
31. HART P S, YANNY W 1998 Needle phobia and malignant vasovagal syndrome. *Anaesthesia 53:* 1002–4
32. UNDERWOOD S M, GLYNN C J 1988 Sick sinus syndrome manifest after spinal anesthesia. *Anesthesia 43:* 307–9
33. LOVSTAD R Z, GRANHUS G, HETLAND S 2000 Bradycardia and asystolic arrest during spinal anaesthesia: a report of five cases. *Acta Anaesthesiol Scand 44:* 48–52
34. SAPIRE D, CASTA A 1985 Vagotonia in infants, children, adolescents and young adults. *Int J Cardiol 9:* 211–22
35. ROSENBERG J, WAHR J, SUNG C 1996 Coronary perfusion pressure during cardiopulmonary resuscitation after spinal anaesthesia in dogs. *Anesth Analg 82:* 84–7
36. MARK A L 1983 The Bezold Jarisch reflex revisited: clinical implications of inhibitory reflexes originating in the heart. *J Am Coll Cardiol 1:* 90–102
37. CAMPAGNA J A, CARTER C 2003 Clinical Relevance of the Bezold-Jarisch Reflex. *Anesthesiology 98:* 1250–60
38. MIRT K, VESNA K 2001 The effect of lactated ringer solution infusion on cardiac output changes after spinal anaesthesia. *Anesth Analg 92:* 710–14
39. BROWN D L, CARPENTER R L, MOORE D C 1988 Cardiac arrest during spinal anesthesia [letter]. *Anesthesiology 68:* 971–2
40. VON BEZOLD A V, HIRT L 1867 Uber die physiologischen wirkungen des essigsauren veratrins. *Untersuchungen aus dem Physiologischen Laboratorium Wurzburg 1:* 75–156
41. DAWES G S, COMROE J H 1954 Chemoreflexes from the heart and lungs. Physiological Rev 34: 167–201.
42. JORDI E, MARSCH S C, STREBEL S 1998 Third degree heart block and asystole associated with spinal anesthesia. *Anesthesiology 89:* 257–60.
43. LIU S, PAUL G, CARPENTER R 1995 Prolonged PR interval is a risk factor for bradycardia during spinal anesthesia. *Reg Anesth 20:* 41–4
44. HOLMES F 1960 The supine hypotensive syndrome. Its importance to the anaesthetist. *Anaesthesia 15:* 298–306
45. KAMATH S H S, AMBARRESHA M 2006 Cardiac arrest following spinal anesthesia. A case report. *Indian J Anaesth 50(6):* 479–480
46. LIMONGI J A, LINS R S 2011 Cardiopulmonary arrest in spinal anesthesia. *Rev Bras Anestesiol 61(1):* 110–20
47. BARI S, ISLAM A, KHAN R H 2006 Case report on cardiac arrest under spinal anesthesia in a case of caesarean section. *Journal of BSA 19:* No 1–2
48. KOPP S L, HORLOCKER T T 2006 Bradycardia and asystole during neuraxial anesthesia. *Anesth&Analg 102:* 327–328
49. LEE L A, POSNER K L *et al.* 2004 Injuries associated with regional anesthesia in the 1980's and 1990's: a closed claims analysis. *Anesthesiology 101:* 143–52
50. CHARULUXANANAN S, THIENTING S *et al.* 2008 Cardiac arrest after spinal anesthesia in Thailand: a prospective multicenter registry of 40,271 anesthetics. *Anesth Analg 107:* 1735–41
51. AGRAWAL S, SRIVASTAVA V 2010 Bezold Jarisch reflex as a cause of haemodynamic alterations during surgery in prone position. *Anaesth Pain & Intensive Care 14(2):* 115–117
52. JANG Y E, DO S H, SONG I A 2013 Vasovagal cardiac arrest during spinal anesthesia for cesarean section. A case report. *Korean J Anesthesiol 64(1):* 77–81