# Research & Reviews: Journal of Pharmaceutics and Nanotechnology

## A review on different anesthetic agents and possible risks during surgery

Midhat Fatima Rizvi<sup>1</sup>, Mohammed Asadullah Jahangir<sup>2</sup> and Yamini K<sup>\*3</sup>

<sup>1</sup>MBBS, Tripura Medical College, Tripura, India <sup>2</sup> Research Scholar, School of Pharmacy, Glocal University, Saharanpur, India \*<sup>3</sup>Research Scholar, Department of Pharmaceutical Sciences, JNTU, Hyderabad, India

#### **Review Article**

Received: 04/04/2016 Accepted: 15/06/2016 Published: 27/06/2016

\*For Correspondence

Yamini K, Research Scholar, Department of Pharmaceutical Sciences, JNTU, Hyderabad, India

E-Mail: yaminik.yk@gmail.com

**Keywords:** Anesthesia, Surgery, General anesthesia, Local anesthesia, Regional anesthesia Anesthesiologists play a very important role during surgery. Different anesthising agents have been developed over the last 100 years. However, the question of safety and efficacy of most of the available anesthising agent had been questioned over the years. Every patient hopes for a painless surgery. But still the period of emergence from anesthesia is very critical. Optimum pain management plays a key role in maintaining the individual anesthetic treatment. This review article conducts a literature review of the different researches and data regarding anesthesia and its possible risk available online.

ABSTRACT

#### INTRODUCTION

Whenever a patient is going for a major or minor operation, the family members of patients pray for painless procedure and speedy recovery of their loved ones. The question now arises what is the patient feeling when the operation is going on? In the operation theatre with the doctors there is also a team of anesthesiologists to ensure the patient is properly immobilized, with no sense of pain and do not come up with the waking memory of the procedure <sup>[1]</sup>. The other question is whether the patient is in restful peace? However the answer is not as relaxing as general anesthising agents have the potential of disrupting a patient's photo entrained circadian rhythm <sup>[1]</sup>.

Neuromuscular blocking agents (NMBAs) are commonly utilized to paralyze skeletal muscles <sup>[2]</sup> and used as an adjuvant to the anesthetic agents during surgery. These medications are extensively used in the emergency departments, intensive care units, interventional radiology areas as well as in medical and surgical units <sup>[2]</sup>.

There are basically three types of anesthising agents- local, regional and general. Depending on the type of operation, anesthesiologists choose the best possible anesthising agent as a solo medicine or with adjunctive NMBA.

#### Different surgeries require different approach and different anesthising agents:

General anesthesia along with endotracheal intubation is among the commonest technique for open renal surgeries <sup>[3]</sup>. However, with high incidence of side effects, regional anesthetic agents are gaining popularity. Regional anesthesia can be safely used for renal surgeries <sup>[3]</sup> and it comes with the advantage of stable hemodynamics, decrease blood loss with prolonged postoperative analgesia and fewer side effects<sup>[3]</sup>.

Eldaba A and Amin SM reported that combined spinal/paravertebral block can be safely and effectively used in patients undergoing open renal surgeries <sup>[3]</sup>.

Dental surgeries usually require the administration of local anesthesia <sup>[4]</sup>. Local anesthetic agent like xylocaine is very commonly used.

Atia AM and Abdel-Rahman KA studied the combined effect of thoracic epidural bupivacaine on the requirement doses of general anesthetic agent and muscle relaxants during major abdominal surgery. The researcher concluded that the induction and maintenance dose of propofol, fentanyl and atracurium was reduced in the combination group as compared to the group having general anesthesia alone <sup>[5]</sup>.

Inguinal herniorrhaphy (IH) is one of the commonest types of surgeries in adults <sup>[6]</sup>. The major cause of IH is the loss of strength in the inguinal area. Mireskandari SM, et al. compared the effect of general anesthesia (GA) and epidural anesthesia (EA) in IH for incidence of urinary retention. In GA, premedication with midazolam (0.02  $\mu$ g/kg) and fentanyl (2  $\mu$ g/ kg) was done, induction of anesthesia was performed by NA-thiopental (5 mg/kg) and atracurium (0.6 mg/kg) and proper size of endotracheal tube was applied for all patients. He anesthesia was maintained by 1.2-1.5% isoflurane Fentanyl and atracurium were repeated in 30 minutes intervals as needed. At the end of the procedure the muscle relaxant reversed in the operative room and patients were extubated before transferring to post anesthetic care unit (PACU). In EA performed for all patients by the same anesthesiologist in sitting position and at the L3-L4 level. Bupivacaine 0.5% (15-20 ml) was administered in the beginning and are achieving the desired level of epidural anesthesia all patients received intravenous sedation by midazolam (2 mg). Epidural injection was repeated in one hour interval as needed. At the end of the surgery the patients were transferred to PACU by remaining the epidural catheter in place. The administered intravenous fluid in both groups was exactly recorded. The researcher concluded that with epidural anesthesia the incidence of UR was reduced as compared to GA <sup>[7]</sup>.

Patient suffering from benign thyroid disorders may either go for subtotal thyroidectomy or total thyroidectomy <sup>[8-9]</sup> lidocaine 2% gel is not an anesthetic agent of choice as it can disrupt the EMG reading <sup>[10]</sup>. Total thyroidectomy can also be performed under local/regional anesthesia via intravenous sedation accompanied by bilateral cervical blocks <sup>[11]</sup>. The use of a short acting opioid such as fentanyl or remifentanil has been reported to reduce coughing and bucking during recovery <sup>[10]</sup>.

According to different studies it is evident that the alignment of eyeballs during general anesthesia provides intraoperative support, as an alternative to possible adjustable sutures not adoptable in pediatric field <sup>[12]</sup>. Milgliorini R, et al. studied the effect of sevoflurane and desflurane on the ocular deviation in strabismus surgery. In which he concluded that sevoflurane is the inhalational anesthetic of choice in strabismus surgery <sup>[12]</sup>.

In most of the industrialized countries, the number of cesarean deliveries is increasing day by day. Anesthetic agents are used to reduce the pain during cesarean operation. General anesthesia is regarded as safe, however it is less commonly used than epidural or spinal anesthetic agents <sup>[13]</sup>. Spinal anesthesia comes with mild side effects such as vomiting, head ache, and hypotension <sup>[14-15]</sup>.

However, general anesthesia may affect hematological parameters by increasing the WBC count and decreasing hemoglobin concentration, RBC count and platelet count <sup>[13]</sup>.

Apart from all this complications, informed consent to the patient must be followed in cesarean deliveries [16].

Thoracotomy is a painful surgery and post thoracotomy pain syndrome occurs in 5% to 80% of patients <sup>[17]</sup>. Thoracic epidural analgesia remains the most effective anesthetic for thoracotomy but different options can be used to control post-thoracotomy pain, such as nerve block, paravertebral block or a paravertebral catheter <sup>[18]</sup>. Julien DW, et al. in his study concluded that epidural induction before starting surgery as well as the dose of levobupivacaine used during surgery play an important part to decrease acute post thoracotomy pain <sup>[19]</sup>.

In the recent past different researchers are exploiting the role of magnesium sulphate as an anesthetic and analgesic sparing drug in anesthesia practice. Its role has been linked to decrease mortality in in critical care patients with sepsis and diabetes <sup>[20]</sup>.

Dexmedetomidine (DEX) was approved as a sedative and analgesia for short duration in Intensive Care Unit by USFDA in 1999. It was later found that it preserves the respiratory function with smooth recovery when used as an adjunct to general anesthesia. In 2009, DEX was successfully used in laboring parturient, as an adjunct to epidural analgesia <sup>[21]</sup>. Zhou C and Zhao J in their study concluded that DEX has potential to be used as premedication in anesthesia <sup>[22]</sup>. In an another study by Noss C, et al., the researchers concluded that DEX is a promising adjuvant, which prolongs the duration of analgesia in brachial plexus nerve blockade <sup>[23]</sup>.

Prostate biopsy is usually related to a procedure with moderate to severe pain. Obi AO and Nnodi PI concluded in their study that low dose spinal saddle block anesthesia (0.3 ml of 0.5% hyperbaric bupivacaine in dextrose injection USP) can be used as an alternative anesthetic technique for prostate biopsy <sup>[24]</sup>.

Endotracheal intubation may cause Acquired subglottic stenosis. In a study by Choi JJ, et al., the researchers came to the conclusion that Monitored Anesthetic Care (MAC) based on propofol and remiferitanil provides the advantage of reducing the risk of airway fire. It also provides good visualization of the operative field with minimal respiratory depression <sup>[25]</sup>.

In a study by Okcelik S, et al., reported the application of spinal anesthesia in Fahr's syndrome patient. The study concluded that varicocelectomy under spinal anesthesia can be performed for Fahr's syndrome patient safely [26].

Apart from all the advantages an anesthetic agent provides there is many reports available which highlights the risk factors associated with the use of anesthetic agents.

Compared to the normal population postoperative complications are 9.5 time more frequent in patients with pre-existing pulmonary diseases <sup>[27]</sup>. In particular, patients with chronic obstructive pulmonary disease (COPD) have a very high mortality risk of 5-13 times <sup>[28-29]</sup>.

In a study conducted by Alvi N, it was reported that aspiration is one the most common cause of anesthesia related fatality <sup>[30]</sup>.

A rare autosomal disease namely, Brugada Syndrome (BrS) is caused by genetic mutation. It has been reported that some routinely used anesthetic agents' triggers spontaneous ventricular arrhythmias on BrS patients which leads to sudden cardiac arrest <sup>[31]</sup>.

Perioperative acute myocardial infarction (PAMI) is a serious complication which is the one of the leading cause of death within the first 30 days of non-cardiac surgery <sup>[32]</sup>. In a study conducted by Mansuroglu C, et al., it was concluded that spinal anesthesia increase hs-cTnT, which can be harmful to cardiac tissues <sup>[33]</sup>.

Nausea and vomiting are the two most common complaints following anesthesia and surgery. It was reported by Al Jabari A, et al., that patient suffering from diabetes, hypertension and hypothyroidisms as chronic illness have the higher incidence of nausea and vomiting. Although, non-smokers also have higher incidence of nausea and vomiting [34].

It has been reported that during spinal/epidural anesthesia, direct puncture damages the conus medullaris <sup>[35]</sup>. Spinal anesthesia is also associated with hypotension (33%) and bradycardia (13%) <sup>[36-38]</sup>. However, Sigdel S, et al., reported that prophylactic IV atropine or IV ephedrine after one minute of induction of spinal anesthesia reduces the severity of spinal anesthesia induced hypotension and bradycardia <sup>[38]</sup>. It is also reported that complete lower limb motor block after administering spinal anesthesia can cause negative memory in certain patients <sup>[39]</sup>.

Gokahmetoglu G, et al., reported a very rare incidence of Froin Syndrome with spinal anesthesia <sup>[40]</sup>. Froin Syndrome is a rare disease which is characterized with xanthochromic cerebrospinal fluid, high CSF protein content, and complete blockage of CSF circulation <sup>[41-42]</sup>.

Pituitary abscess is another rare disease, with merely 200 cases described in literature <sup>[43]</sup>. Baallal H, et al., reports a typical case where a patient was reported with intercreanial hypertension after surgery for prostate adenoma operated under spinal anesthesia. The histopathological report confirmed the presence of abscess cavity featuring multiple fragments of fibrous <sup>[43]</sup>.

Some researchers also suggest the use of alternative options to be used in case of spinal anesthesia with regard to its associated risks <sup>[44]</sup>.

Laryngospasm is another complication reported in the perioperative period during induction of anesthesia or during emergency <sup>[45]</sup>.

The period of emergence from anesthesia is very critical, owing to consciousness, neuromuscular conduction and airway protective reflexes <sup>[46]</sup>.

Some adjuvants to anesthesia add up to the risk provided by the anesthetic agent. Ong YY, et al., reported that use of propofol for the management of anesthesia, may cause the urine to get cloudy. This cloudiness of urine is due to the precipitation of uric acid crystals <sup>[47]</sup>. However, this can be exploited as beneficial effect for patient having history of hyperuricemia <sup>[47]</sup>.

It has been reported by Monsef JB and Boettner F that hypotensive anesthesia may result in creating false anemia and thus may create a situation for increase transfusion in Total Hip Arthroplasty <sup>[48]</sup>.

Dental traumas post dental surgeries have also been discussed by various researchers. Anesthesiologist must conduct a thorough preoperative evaluation of patient's mouth in order to avoid complications <sup>[49]</sup>.

#### What is the possible way out of the risk provided by different anesthesia?

The answer to this question can be very diverse, the one possible way out is Optimum Pain Management, which is defined as balance between effective analgesic modalities, treatment of side effects and patient safety <sup>[50-51]</sup> and to ensure safe and effective delivery of postoperative analgesia. Like anesthetic decision-making regarding upper respiratory tract infection in children is presented in numerous literature. However, it is still very challenging to evaluate the same <sup>[52]</sup>.

Open-globe injury which is defined as a full thickness defect in the cornea and/or sclera is a common cause of blindness <sup>[53]</sup>. The global incidence is approximately 3.5/100.000 persons/year, which means 203.000 open-globe injuries each year <sup>[54]</sup>. General anesthesia is usually used however; regional eye blocks or topical anesthesia can be approached. But there must be a close communication and planning between ophthalmologist and anesthesiologists <sup>[55]</sup>.

For surgeries which require hemodynamic stability, better adjuvant must be used. In a research Shokhri H and Ali I reported that Nalbuphine may better provide hemodynamic stability and post-operative pain relief than morphine in patients of postcardiac surgery <sup>[56]</sup>.

For anesthesia induced with opioid agents, Patient-controlled analgesic system must be followed <sup>[57]</sup>. However, use of regional anesthesia or improved oral analgesics must be promoted.

## CONCLUSION

It is very difficult to conclude which is the best possible anesthising agent for a particular surgery. However, it is very important that a close relation and communication between the surgeons and anesthesiologist is required for optimizing the best possible anesthising agent for an individual patient. Optimum pain management is another possible outcome.

### COLLECTION OF DATA

The data was collected from different free online sources like-Google scholar, Jamia Hamdard University database etc.

#### ACKNOWLEDGEMENT

The authors would like to acknowledge the support of all the seniors who played a vital role in shaping the review article.

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## REFERENCES

- 1. Seidler N. General Anesthesia and Sleep. J Anesth Clin Res. 2016 7: e116.
- 2. Manish Pal Singh, et at. Neuromuscular Blocking Agents (NMBAs): An Overview. J. Chem. Pharm. Res. 2010, 2: 264-273.
- Eldaba A and Amin SM (2016) A Comparative Evaluation of General Anesthesia versus Spinal Anesthesia Combined with Paravertebral Block for Renal Surgeries: A Randomized Prospective Study. J Anesth Clin Res. 2016;7:632.
- 4. Shimoji S, et al. (2016) Influence of Local Anesthesia on Autonomic Nervous Activity in Healthy Young Adults: Evaluation of Heart Rate Variability. Dentistry. 2016;6:378.
- Atia AM and Abdel-Rahman KA. Combined Thoracic Epidural with General Anesthesia vs. General Anesthesia Alone for Major Abdominal Surgery: Anesthetic Requirements and Stress Response. J Anesth Clin Res. 2016;7:616.
- 6. Su Y, et al. Efficacy of ropivacaine by the concentration of 0.25%, 0.5%, and 0.75% on surgical performance, postoperative analgesia, and patient's satisfaction in inguinal hernioplasty: a randomized controlled trial. Patient Prefer Adherence. 2015;9:1375-1379.
- 7. Mireskandari SM, et al. Comparison between General Anesthesia and Epidural Anesthesia in Inguinal Herniorrhaphy Regarding the Incidence of Urinary Retention. J Anesth Clin Res. 2016;7:614.
- Gough IR and Wilkinson D. Total thyroidectomy for management of thyroid disease. World J Surg. 2000;24:9622-9965.
- 9. Serpell JW and Phan D. Safety of total thyroidectomy. ANZ J Surg. 2007;15-19.
- 10. Chan TN. Anesthesia Management of Total Thyroidectomy Using a NIM EMG Endotracheal Tube: A Case Report. J Gen Practice. 2016;4:248.
- 11. Milan SA, et al. Thyroidectomy under local anesthesia. Curr Surg Rep. 2014;2:37.
- 12. Migliorini R, et al. Anesthesia in the Surgery of Strabismus: Role of Anesthetic Agents in the Ocular Deviation and Surgical Outcome. J Anesth Clin Res. 2015;6:572.
- Alnour TM, et al. Shaktur AT, Ayyad RA, Alhewat MM, Shaban EH, et al. Comparison between the Side Effects of Spinal and General Anesthesia during Caesarean Section in Tripoli-Libya. J Anesth Clin Res. 2015;6:560.
- 14. Mekonen S, et al. Maternal and Neonatal outcomes in mothers who undergo caesarean section under General and spinal Anesthesia in Gandhi Memorial Hospital, Addis Ababa. Adv Tech Biol Med. 2015;3:119.
- 15. Abd El-Hakeem EE, et al. How Long Can Patients Sit Up for Before Lying Down after Combined Spinal-Epidural Anesthesia For Cesarean Delivery? A Randomized Trial. J Anesth Clin Res. 2014;5:482.
- 16. Ajmal M. A Study of the Quality of Informed Consent of Anesthesia for Cesarean Deliveries: What and Whatnot was Discussed with Parturients. J Anesth Clin Res. 2014;5:438.

- 17. d'Amours RH, et al. Pathogenesis and management of persistent post thoracotomy pain. Chest Surg Clin N Am. 1998;8:703-722.
- 18. Koop O, et al. The role of intercostal nerve preservation in pain control after thoracotomy. Eur J Cardiothorac Surg. 2013; 43:808-812.
- 19. Julien DW, et al. Effect of Induced Epidural Anesthesia before Surgical Incision on Acute Pain and Postoperative Pulmonary Events: Results from a Population with Lung Resection by Thoracotomy. J Anesth Clin Res. 2015;6:548.
- 20. Bansal T. Magnesium: Emerging Potentials in Anesthesia Practice. J Anesth Clin Res. 2015;6:547.
- 21. Mahrous RSSE. Study of the Effect of Dexmedetomidine in Reducing Hemodynamic Responses to General Anesthesia for Elective Cesarean Section in Patients with Preeclampsia. J Anesth Clin Res. 2015;6:544.
- 22. Zhou C, and Zhao J. Dexmedetomidine versus Midazolam as Premedication in Anesthesia: A Meta-Analysis from Randomized Controlled Clinical Trials. J Anesth Clin Res. 2014;5:457.
- 23. Noss C, et al. Dexamethasone a Promising Adjuvant in Brachial Plexus Anesthesia? A Systematic Review. J Anesth Clin Res. 2014;5:421.
- 24. Obi AO and Nnodi PI. Low Dose Spinal Saddle Block Anesthesia (With 1.5 Mg Bupivacaine) For Transrectal Prostate Biopsy-Experience with 120 Cases. J Anesth Clin Res. 2014;5:469.
- 25. Choi JJ, et al. Monitored Anesthesia Care Using Target-Controlled Infusion with Propofol and Remiferitanil in a Patient with Subglottic Stenosis. J Anesth Clin Res. 2014;5:443.
- 26. Okçelik S, et al. Subinguinal Varicocelectomy Under Spinal Anesthesia in a Fahr's Syndrome Patient with Non-Obstructive Azoospermia. Andrology. 2016;5:163.
- 27. Savas JF, et al. Regional anesthesia as an alternative to general anesthesia for abdominal surgery in patients with severe pulmonary impairment. Am J Surg. 2014;188:603-605.
- 28. Mallon JS, and Edelist G. Risk factors of importance-the patient. Probl Anesth. 1992;6:193-204.
- 29. Chavan GN and Chavan AG. Spinal Anesthesia as an Alternative to General Anesthesia for Emergency Laprotomies in ASA Grade III and IV Patients. An Observational Study at RIMS, Adilabad, Telangana. J Anesth Clin Res. 2016;7:618.
- 30. Alvi NI. Anesthesia Fatality due to Bile Aspiration: Lessons to be Learnt. J Anesth Clin Res. 2016;7:631.
- 31. Venus J. A Case Report on Brugada Syndrome and Anesthesia Considerations. J Gen Practice. 2016;4:241.
- 32. Landesberg G, et al. Perioperative myocardial infarction. Circulation. 2009;119:2936-2944.
- 33. Mansuroglu C, et al. Comparison of Spinal or General Anesthesia for Cardiac Complications with Using High Sensitive Cardiac Troponins in Non-cardiac Surgeries. Angiol. 2016;4:172.
- 34. AlJabari A, et al. Post-Operative Nausea, Vomiting and Pain Score in Post Anesthesia Care Unit (PACU) at Jordan University Hospital . J Anesth Clin Res. 2016;7:595.
- 35. Melloni C, et al. Conus Medullaris/Cauda Equina Syndrome Following a Repeated Bupivacaine 1% Spinal Anesthesia- Analysis of a Case with Review of the Literature. J Anesth Clin Res. 2015;6:575.
- 36. Carpenter RL, et al. Incidence and risk factors for side effects of spinal anesthesia. Anesthesiology. 1992;76:906-916.
- 37. Arndt JO, et al. Incidence and time course of cardiovascular side effects during spinal anesthesia after prophylactic administration of intravenous fluids or vasoconstrictors. Anesth Analg. 1998;87:347-354.
- Sigdel S, et al. (2015) Prevention of Spinal Anesthesia Induced Hypotension in Elderly: Comparison of Prophylactic Atropine with Ephedrine. J Anesth Clin Res. 2015;6:557.
- 39. Santiago J. Low-Dose Low-Concentration Spinal Anesthesia for Inguinal Herniorraphy in a Patient with Claustrophobia. J Anesth Clin Res. 2014;5:473.
- 40. Gokahmetoglu G, et al. Incidental Finding of Froin Syndrome during Spinal Anesthesia in a 72-Year-Old Patient. J Pain Relief. 2014;3:1000158.
- 41. Froin G. Inflammations méningées avec choramatique, fibrineuse et cytologique du liqude céphaloravhidien. Gazette des hopitaux. 1903;76: 1005-1006

- 42. Adams RD, and Victor M. Special techniques for neurologic diagnosis. In: Adams RD, Victor M editors. Principals of neurology. 4th edition New York: Mc Graw- Hill. 1989; 10-52
- 43. Baallal H, et al. Pituitary Abscess in Post Spinal Anesthesia. J Neuroinfect Dis. 2014;5:153.
- 44. Gopinadh G. Spinal anesthesia: a system review and update. Research & Rev.2015.
- 45. Haile M, et al. Magnitude and Associated Risk Factors of Perioperative Pediatrics Laryngospasm under General Anesthesia. InternMed. 2015;5:203.
- 46. Ali MA, et al. Critical Incidents in Post Anesthesia Care Unit (PACU) at a Tertiary Care Hospital: A Prospective Internal Audit. J Anesth Clin Res. 2014;5:486.
- 47. Ong YY, et al. Cloudy Urine after Propofol Anesthesia; A Rare Occurrence after a Routine Anesthetic. J Anesth Clin Res. 2014;5:432. doi:10.4172/2155-6148.1000432
- 48. Monsef JB and Boettner F. Hypotensive Anesthesia may Result in False Anemia and Increase Transfusion Requirements in Total Hip Arthroplasty. J Anesth Clin Res. 2014;5:425.
- 49. Idrees SR, et al. Dental Trauma related to General Anesthesia: Should the Anesthesiologist Perform a Preanesthetic Dental Evaluation? OHDM. 2014;13:271-274.
- 50. Goldstein DH, et al. Recommendations for improved acute pain services: Canadian collaborative acute pain initiative. Pain Res Manag. 2004;9:123-130.
- 51. Cogan J, et al. Transforming the Concept of "State of the Art" Into "Real Pain Relief" for Patients after Cardiac Surgery – A Combined Nursing-Anesthesia Initiative. J Pain Relief. 2014;3:152.
- 52. Guimaraes J, et al. Anesthesia in a Young Infant with Unrecognized Pertussis Infection Mild Cold orSevere Infection? Reinforcing the Debate. J Anesth Clin Res. 2015;6:574.
- 53. Harlan JB and Pieramici DJ. Evaluation of patients with ocular trauma. Ophthalmol Clin North Am. 2002;15:153-161.
- 54. Harlan JB and Pieramici DJ. Evaluation of patients with ocular trauma. Ophthalmol Clin North Am. 2002;15:153-161.
- 55. Sekeroglu MA, et al. Alternative Methods of Anesthesia for the Repair of Open-Globe Injuries: Ophthalmologists' Perspective. J Anesth Clin Res. 2014;5:442.
- 56. Shokri H and Ali I. Nalbuphine versus Morphine as Part of Intravenous Anesthesia Post Cardiac Surgery. J Anesth Clin Res. 2014;5:463.
- 57. Hassani M and Atkinson T. Changing Trends in Use of IV-Patient-Controlled Anesthesia (IV-PCA) in a District General Hospital over the Last 15 Years and Proposed Factors behind this. J Anesth Clin Res. 2015;6:567.