Research and Reviews: Journal of Medical and Health Sciences

Anesthetic Pathology

Sravanthi Reddy1*, Lavanya B2

¹Sri Padmavathi Mahila Viswavidyalayam, Tirupati, AP, India ²Department of Medicinal Chemistry, Sri Lakshmi Venkateswara Institute of Pharmaceutical Sciences, Kadapa, AP, India

Review Article

Received: 11/07/2016 Accepted: 25/07/2016 Published: 02/08/2016

*For Correspondence

Sri Padmavathi Mahila Viswavidyalayam, Tirupati, AP, India

E-mail: sravanthigkcp@gmail.com

Keywords: Local and General anesthesia, Anesthetics Pathophysiology, Mechanism action. Anesthesia is an integral and important part of any major surgical procedure. With time and gained knowledge this term has become a sub discipline of medical science. Established medical tips are offered for native and general anesthesia. Numerous factors are vital throughout application of physiological condition protocol wherever patient's age, actual malady condition etc. ought to be thought of with care.

ABSTRACT

ANESTHESIA

Anesthetics are drugs that are generally used to generate anesthesia ^[1-3]. We've got totally different categories of anesthetics in apply corresponding to anesthetic, local, regional anesthetic. Some anesthetics like desflurane, cocaine, lidocaine, propaine, inert gas square measure few can be used for generate anesthesia to avoid pain and discomfort. These anesthetics result in reversible loss of sensation ^[4,5].

Despite the fact that the clinical world cannot cure each disorder, the management of pain to make sure patient comfort ought to be a goal. Cacaine is an oldest anesthetic in 1860 and it was extracted from the leaves of the Erythroxylon coca bush ^[6-8]. Sigmund Freud and Karl Koller have been the primary used anesthetic agents in 1884 for the prolongation of ophthalmologic processes ^[9,10].

Procaine, an artificial alternative to cocaine, wasn't developed till 1904. This Procaine is an ester anesthetic, generally metabolized in plasma and through hydrolysis releases PABA as metabolic product which is an allergen product ^[11,12]. Using of procaine and other ester-type anesthetic marketers was limited because of their extreme allergies. So in 1930s Tetracaine and some other ester-type anesthetics were developed ^[13,14]. Tetracaine is stronger than procaine, and it causes comparable hypersensitive reactions.

When Lofgren was developed local anesthetic (lidocaine) in 1943, then alternative classes of anesthetics were discovered ^[14-17]. This developed lidocaine is an amide spinoff of diethylaminoacetic acid, now not PABA; thus, it has the benefit of low allergic capabilities. In view that then, more than one amide-variety anesthetics were offered into scientific use. Moderate chemical changes to the compounds have imparted important traits, together with extended duration and efficiency ^[18-20], to each. These compounds present the healthcare professional extra picks, and anesthetics will also be thoroughly matched to special techniques.

General Anesthesia

To induce deep sleep the method which is used is General anesthesia. Loss of reversible consciousness can be induced by using these general anesthetics ^[21-23]. With the help of this method patient will go into deep sleep during the surgery and will not be aware of it.

When the patient receives medications for amnesia, analgesia, muscle paralysis, and sedation then condition produced is called general anesthesia ^[24-27]. The patient who is anesthetized feels himself that everything is in his

control. Surgical procedures that would inflict "unbearable pain which potentiate extreme physiologic exacerbations, and result in unpleasant memories" this condition can be tolerable by giving anesthesia ^[28-30].

Patient feels following conditions when given with combination of anesthetic agents during general anesthesia.

- 1. Even the patient is secondary to surgery or any other treatment he feels Unarousable pain.
- 2. He can't even remember what happened during his treatment (amnesia).
- 3. Because of muscle paralysis the patient was not able to maintain adequate airway protection and/or spontaneous ventilation.

Local Anesthesia

To avoid pain and discomfort during the surgical and medical procedures the method used is local anesthesia which is used to induce the anesthesia that involves numbing on a specific part of the body. Local anesthetics are safer to perform minor surgeries and in pain management to provide anesthesia ^[31-34].

Reversible regional loss of sensation is generally produced by these local anesthetics. By reducing pain these local anesthetics facilitates many surgical procedures. Delivery techniques include topical anesthesia ^[35,36], infiltrative anesthesia ^[37], ring blocks ^[38], and peripheral nerve blocks have broaden the clinical applicability of local anesthetics.

Pathophysiology

Before any discussions it is very important to know about the nerve conduction physiology in local anesthetics. Due to the propagation of electrical impulses, nerves transmit sensation occurs ^[39,40]; this electrical impulses propagation is achieved across the nerve cell wall, or axolemma by alternating the ion gradient.

The negative membrane potential of -70 mV is indicates that, the nerve is in normal resting state. This resting potential is determined by 2 major ions, Na+ and K+ relative membrane permeability and concentration gradients of these major ions (also known as leak currents) and these concentration gradients are maintained by the sodium/potassium ATP pump process. This Na+/K ATP pump process accomplished by transporting potassium ions into the cell and sodium ions out of the cell. So the concentration gradient which was created by this active transport favors the extracellular diffusion of potassium ions. Because the process of nerve membrane is impermeable to sodium ions and permeable to potassium ions, condition happens is 95% of the ionic leak in excitable cells is caused by K+ ions in the form of an outward flux, and leads to the negative resting potential of the nerve. The reason for leaking of this K+ currents was believed to be recently identified 2-pore domain potassium (K2P) channels ^[41-45].

Impulse propagation progresses and depolarization of the nerve occurs when the nerve is stimulated. Initially, through the nerve cell membrane sodium ions are gradually enter the cell and this entry of sodium ions causes the trans-membrane electric potential to increase from the resting potential ^[46-48]. Reaching of approximate potential -55 mV indicates the condition called threshold level and once it happens, rapid influx of sodium ions increases and in the cell membrane sodium channels becomes activated, so permeability of sodium ions increases and the nerve membrane is depolarized to a level of +35 mV or more ^[49,50].

Once the above process (membrane depolarization) is complete, the permeability of potassium ions into the cell is increases and permeability of sodium ions across the membrane becomes impermeable again ^[51-53]. Because of this process negative resting membrane potential can be bring back by restoring the excess of extracellular sodium and intracellular potassium. The changes in potential of nerve cell membrane are known as action potential.

MECHANISM OF ACTION

By interfering with Na+ and K+ currents local anesthetics can inhibit depolarization of the nerve membrane. Here threshold level is never reached so the action potential will not be propagated ^[57-59]. The exact mechanism of retarding influx of sodium ions into the cell by using local anesthetics is unknown. So to make it clear 2 theories have been proposed:

Coming to 1st theory called membrane expansion theory. That postulates that cell membrane absorbs local anesthetics and gets expanded, that leads to sodium channel narrowing. This hypothesis has given way to the specific receptor theory ^[60-62]. Diffusion of local anesthetics across the cell membrane and binding to a specific receptor at the opening of the voltage-gated sodium channel was proposed by this theory. When the excitation rate of the neuron increases then the affinity of local anesthetics to the voltage-gated Na+ channel is also increases markedly. This binding to voltage-gated Na+ channel causes alterations in the function/structure of the Na+ channel and inhibits its movement.

Coming to 2nd theory, Blockade of leak K+ currents by local anesthetics is now also believed to contribute to conduction block by reducing the ability of the channels to set the membrane potential ^[63-65].

Nerve fibers are classified into three types on basis of their diameter. Type A fibers are largest fibers and they are responsible for pressure conducting and motor sensations ^[66,67]. Type B fibers are moderate in size and myelinated. Type C fibers are small, unmyelinated and they transmit pain and temperature sensations. When compared to type A fibers anesthetics can block type C fibers more easily. Because of this unblocked type A fibers patients still feel pressure and have mobility even he has blocked pain sensation ^[68-70].

Coming to structure of local anesthetics almost all local anesthetics have similarity in their chemical structure, which composed of 3 components: an amine group, intermediate chain, an aromatic portion (Figure 1). The aromatic portion consist of a benzene ring is lipophilic and the amine portion is responsible for its hydrophilic properties ^[71-75]. For any anesthetic degree of lipid solubility is an important property because its diffusion across the highly lipophilic nerve membrane is determined by this lipid solubility nature only. So this lipophilicity nature of the anesthetic's is directly related to its efficacy ^[76-80].

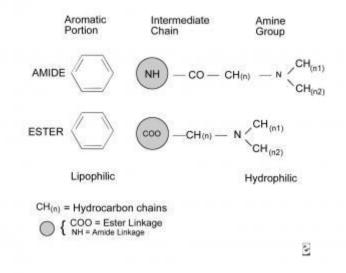


Figure 1: Molecular diagram.

The composition of local anesthetics are addition of HCl salt to the water so they are weak bases and easily injectable ^[81-83]. In aqueous solution between unionized and ionized form salt get equilibrates. Although the ionized form is injectable, the lipophilic properties of unionized base has responsible for its diffusion into the nerve cell membrane, so equilibration is very important process ^[84,85]. An anesthetic protein-binding activity determines it's duration of action and/or period during which it remains effective, because the anesthetic receptors along the nerve cell membrane are proteins ^[86-90].

From the figure chain that connects the amine and aromatic portions is intermediate chain and it is composed of amide/ester linkage (Figure 1). Classification of local anesthetics can be done by using this intermediate chain only ^[91-93].

Anesthesia providers can access all factors that influence medical condition of patient's and suitable anesthetic technique will be select accordingly ^[94,95].

ANESTHESIA SIDE EFFECTS

Many side effects of anesthesia were minimized because of its research development and quality practice by anesthiologists, but to reduce fewer side effects like "after subjected to anesthesia patients might feel sick, feeling like [0] vomiting, sometimes faint, sore throat which may last for few hours to few days based on the individual and anesthetics," furthermore development in its research is also require ^[96-98].

Compared to other procedures like medical and surgical, to provide unconsciousness the safe procedure is anesthesia. Even though some adverse actions like mental confusions, shivering, fainting will evolve by application of anesthesia and these conditions may last for few hours to few days ^[99,100]. Some rare cases death also takes place including stroke, heart attack, bladder problem etc.

SUMMARY

Compared to general and systemic anesthetics, Local anesthetics are safe. So they were use whenever require. In addition, these are available easily and mode of administration is also easy. From centuries research and development of local anesthetics have been undergoing, and still research is required to provide patients with maximum safety and great efficacy anesthtics. Also development of different variety of anesthtics with different pharmacological activity is needed to provide the surgeons with advanced anesthetics and to treat patient with safer anesthetics.

REFERENCES

1. Seidler N. General Anesthesia and Sleep. J Anesth Clin Res. 2016;7:e116.

2. Nisa N. Is it Time That We Start Using Sonovisible Catheters in Regional Anesthesia?. Gen Med (Los Angel). 2016;4:250.

3. Laycock H and Bantel C. Objective Assessment of Acute Pain. J Anesth Clin Res. 2016;7:630.

4. Hahn RG, et al. Fluid Retention is Alleviated by Crystalloid but Not by Colloid Fluid after Induction of General Anesthesia: An Open-Labeled Clinical Trial . J Anesth Clin Res. 2016;7:597.

5. Kishimoto N, et al. Optimal Concentration of Sevoflurane to Prevent Cardiovascular Depression after Induction of General Anesthesia with Remifertanil and Propofol. J Anesthe Clinic Res. 2011;2:149.

6. Swati Srabani N, et al. Anesthesia and Intensive Care. J Anesthe Clinic Res. 2012;4:310.

7. Mcguire TR, et al. IL6 Plasma Concentrations in Patients with Sepsis Receiving SLED and Antibiotics: A Predictor for Survival. In Vivo. 2014;28:1131-1134.

8. Srilatha B and Hima Bindu A. A Retrospective Review on Complications related to Anesthesia. J Anesthe Clinic Res. 2012;3:180.

9. Vanita P and Jhansi K. Metabolic Syndrome in Endocrine System. J Diabetes Metab. 2011;2:163.

10. Ekweghariri C, et al. V-Scope Extendable Intubation Stylet. In 38th Annual Northeast Bioengineering Conference. 2012.

 Jimnez-Almonte JH, et al. Is local infiltration analgesia superior to peripheral nerve blockade for pain management after THA: A network meta-analysis. Clinical Orthopaedics and Related Research?. 2015:1-22.
Srilata M, et al. Airtraq and Pediatric Cervical Spine Surgery. Journal of neurosurgical anesthesiology. 2015;27:79-80.

13. Lim FM, et al. Development of an Automatic Blood Aspiration Device for Periodic Measurement of Blood Glucose Level. J Med Device. 2015;9:20932.

14. Theodoraki K, et al. The impact of two different transfusion strategies on patient immune response during major abdominal surgery: a preliminary report. J Immunol Res. 2014.

15. Hurtado EM, et al. Orgaz ovdispositivos? PTICOS. 2014.

16. Arai YCP, et al. Intravenous lidocaine and magnesium for management of intractable trigeminal neuralgia: a case series of nine patients. J Anesth. 2013;27:960-962.

17. Carmelina G, et al. Acute cardiac failure after muscle block reversal with sugammadex for unexpected difficult intubation. World J Med Surg Case Rep. 2014:3.

18. Doleman B et al. A systematic review and meta-regression analysis of prophylactic gabapentin for postoperative pain. Anaesthesia. 2015;70:1186-1204.

19. Krishnan P and Kartikueyan R. Spontaneous spinal epidural hematoma: A rare cause of paraplegia in pregnancy. Neurology India. 2014;62:205.

20. Harjai MM, et al. Absent upper blind Pouch in a case of tracheo-esophageal fistula. J Indian Assoc Pediatr Surg. 2015;20:37.

21. Velasco-P, rez G. Escalera analg, sica en pediatria. Acta Pedi trica de Maxico. 2014;35:249-255.

22. Parasa M. Utility of Stroke Volume Variation as a Predictor of Fluid Responsiveness Using Third Generation Vigileo Device in Patients Undergoing Brain Surgery. 2011.

23. Veroniki F, et al. Intraoperative oxygenation impairment: A comparison between three alveolar recruitment strategies. 2015.

24. Mynbaev OA, et al. Is there only CO: insufflation pressure impact on surgical field visualization during robotic surgery. Arch Gynecol Obstet. 2015.

25. Gautami J. Research and Reviews: Journal of Pharmaceutics and Nanotechnology. 2015.

26. Pham JC, et al. The prevalence of long QT interval in post-operative intensive care unit patients.ÿJournal of clinical monitoring and computing. 2015:1-7.

27. Hanish B, et al. Evaluation of changes in serum phenytoin level after craniotomy and its relation to intra operative blood loss. The Indian Journal of Neurotrauma. 2014;11:109-112.

28. Eldaba A and Lofty M. Different local anesthetic technique for postoperative analgesia in open cholecystectomy. Ain-Shams J Anaesthesiol. 2015;8:252.

29. Michalek P, et al. Complications Associated with the Use of Supraglottic Airway Devices in Perioperative Medicine. BioMed Research International. 2015.

30. Anikwe EE, et al. Influence of Nerve Flossing Technique on acute sciatica and hip range of motion. International Journal of Medicine and Biomedical Research. 2015;4:91-99.

31. Danninger T, et al. The Effect of Incremental Airway Resistance on Cardiac Performance and Pulmonary Pressure in Spontaneously Breathing Volunteers. J Anesthe Clinic Res. 2013.

32. Kahsay S, et al. Determinants of Caesarean Deliveries and its Major Indications in Adigrat Hospital.ÿNorthern Ethiopia: A Case Control Study. Epidemiology-sunnyvale. 2015;5:2161-1165.

33. Overstreet S, et al.Cardiopulmonary exercise testing after laryngectomy: A connection conundrum.Respiratory Medicine Case Reports. 2015;16:11-14.

34. Ganguly S, et al. Measurement of distance and angle between the arytenoids in eastern Indian population and their applied importance. 2015.

35. Kencana WS. Perbandingan Efek Koinduksi Ketamin 0 3 MG/KGBB IV Dengan Midazolam 0, 03 MG/KGBB IV Terhadap Pengurangan Dosis Induksi Propofol. 2015.

36. Neelima K. Research and Reviews: Journal of Nursing and Health Sciences. 2013.

37. Fergo C, at al. Tredimensional laparoskopi har potentiale til at erstatte todimensional laparoskopi ved abdominalkirurgi. Ugeskr L'ger. 2015;177:V11140635.

38. Baronica R, et al. Indications for blood transfusions in critical illness. SIGNA VITAE 2015;10:35-40.

39. Strong KL, et al. NMDA receptor modulators: an updated patent review. Expert opinion on therapeutic patents. 2014;24:1349-1366.

40. Bodea A and Popa AR. Orectic And Anorectic Peptides And Their Implication In Obesity And The Metabolic Syndrome. Romanian J Diabetes Nutr Metab Dis. 2015;22:187-191.

41. Choleva P and Sale S. Caring for children undergoing eye surgery: from admission to discharge. Int J Ophth Pract. 2014;5:124-128.

42. Wu X, et al. Rocuronium blockade reversal with sugammadex vs. neostigmine: randomized study in Chinese and Caucasian subjects. BMC anesthesiology. 2014;14:53.

43. Jadon A, et al. Interscalene brachial plexus block for shoulder arthroscopic surgery: Prospective randomised controlled study of effects of 0.5% ropivacaine and 0.5% ropivacaine with dexamethasone. Indian J Anaesth. 2015;59:171.

44. Machado HS, et al. Oxygen Increases Lung Inflammatory Response in Spontaneous One-Lung Ventilation in Rabbits: A Prospective Randomized Experimental Study. J Anesth Clin Res. 2014;5:489.

45. Ukpaka CP and Douglas IE. Model Development for pH, Salinity and Conductivity Monitoring and Predicting the Diffusion Concentration in Stagnant Water. Chem Sci. J 2016;7:120.

46. Denu AZ et al. Perioperative Hypothermia and Predictors of Intra-Operative Hypothermia among Patients Operated at Gondar university Hospital from March to April 2015. J Anesth Clin Res. 2015;6:656.

47. Lam DM, et al. Efficacy of Pregabalin in Acute Postoperative Pain Under Different Surgical Categories: A Meta-Analysis. Medicine. 2015;94:e1944.

48. Hassan AA. Knowledge and Attitude of Oncology Practitioners towards Complementary and Alternative Medicine for Cancer Care in Qatar. J Anesth Clin Res. 2015;5:477.

49. Hofmann FB. Einfluss des Anasthesieverfahrens auf den Apnoe-Hypopnoe-Index und weitere Parameter bei Patienten mit obstruktivem Schlafapnoe syndrome. 2015.

50. Phillips A and Mehl AA. Diabetes mellitus and the increased risk of foot injuries. J Wound Care. 2015;24:4-7.

51. Peng YG, et al. Essential training steps to achieving competency in the basic intraoperative transesophageal echocardiography examination for Chinese anesthesiologists. Front Med. 2015;9:123-128.

52. Srilatha B. A Retrospective Review on Complications related to Anesthesia. J Anesthe Clinic Res. 2012;3:180.53. Soleimani M, et al. Evaluation of patient mortality in intensive care units using the APACHE Ilscoring system.Koomesh. 2014;15:289-294.

54. Tessler MJ, et al. Association between anesthesiologist age and litigation. Survey of Anesthesiology. 2012;116:574-579.

55. Velazquez Cuenca I and Contreras Leon E. Comparacion De La Analgesia Postoperatoria En Pacientes Sometidos A Colecistectomia Laparoscopica Bajo Anestesia General Balanceada Cuando Se Administra Dosis. 2013.

56. Kumar A. Assessment Effectiveness of Surgeries in Human Safety. J Clinic Exp Ophthalmol. 2011;2:201.

57. El Hamd MA, et al. Simultaneous determination of propofol and remifentanil in rat plasma by liquid chromatography-tandem mass spectrometry: application to preclinical pharmacokinetic drug-drug interaction analysis. Biomed Chromatogr. 2015;29:325-327.

58. Onizuka S, et al. Local Anesthetics with High Lipophilicity are Toxic, While Local Anesthetics with Low pka Induce More Apoptosis in Human Leukemia Cells. J Anesthe Clinic Res. 2011;2:116.

59. Srinivas P. Effect of n-Alkanols on G-Protein α Subunits. J Anesthe Clinic Res. 2011;2:153.

60. Fozzard HA, et al. The Sodium Channel as a Target for Local Anesthetic Drugs. Front Pharmacol. 2011; 2:68.

61. Taiwanica AA. Anesthetic management of a patient with thoracic aortic aneurysm scheduled for cesarean section. Acta Anaesthesiologica Taiwanica. 2014;52:91-92.

62. Scheuer T. Local anaesthetic block of sodium channels: raising the barrier. J Physiol. 2007;581:423.

63. Girard AC, et al. Local Anesthetics: Use and Effects in Autologous fat Grafting. Surgery Curr Res. 2013;3:142.

64. Maghawry KM and Rayan AA. Tracheal intubation with the aid of fiberoptic bronchoscopy with or without the C-MAC device in patients with a suspected difficult airway undergoing elective uvulopalatopharyngoplasty. Ain-Shams J Anesthesiol. 2015;8:308.

65. Green-Hopkins I, et al. Video Laryngoscopy in the Pediatric Emergency Department: Advantages and Approaches. Clin Pediatr Emerg Med. 2015;16:195-202.

66. Maghawry KM and Rayan AA. Tracheal intubation with the aid of fiberoptic bronchoscopy with or without the C-MAC device in patients with a suspected difficult airway undergoing elective uvulopalatopharyngoplasty. Ain-Shams J Anesthesiol. 2015;8:308.

67. Jacobs-Martin GG, et al. Labour epidural analgesia audit in a tertiary state hospital in South Africa. South Afr J Anaesth Analg. 2014;20:174-178.

68. Vanheukelom V, et al. Behavior, production results and meat quality of intact boars and gilts housed in unmixed groups: A comparative study. Appl Anim Behav Sci. 2012;142:154-159.

69. Swati Srabani N, et al. Anesthesia and Intensive Care. J Anesthe Clinic Res 2012;4:310.

70. Pham JC, et al. The prevalence of long QT interval in post-operative intensive care unit patients. J Clin Monit Comput. 2016;30:437-443.

71. Kizilay D et al. Comparison of neostigmine and sugammadex for hemodynamic parameters in cardiac patients undergoing noncardiac surgery. J Clin Anesth. 2016;28:30-35.

72. Seife C. Research Misconduct Identified by the US Food and Drug Administration: Out of Sight, Out of Mind, Out of the Peer-Reviewed Literature. JAMA Intern Med. 2015;175:567-577.

73. Cheek D. Worldwide Experience With Sugammadex Sodium: Implications for the United States. AANA journal. 2015;83:107.

74. Renyu L. Anesthesia, Surgery and Dementia. J Anesthe Clinic Res. 2012;3:e103.

75. Jildenstl PK, et al. Perioperative management in order to minimise postoperative delirium and postoperative cognitive dysfunction: Results from a Swedish web-based survey. Ann Med Surg. 2014;3:100-107.

76. Swati Srabani N, et al. Anesthesia and Intensive Care. J Anesthe Clinic Res 2012;4:310.

77. Mathew S, et al. Radiographic mislead: apparent arterial placement of subclavian central venous catheter due to mediastinal shift. Indian J Anaesth. 2014;58:69-71.

78. Onal O, et al. The effectiveness of trendelenburg positioning on the cross-sectional area of the right internal jugular vein in obese patients. Pak J Med Sci. 2015;31:770-774.

79. Krasuska-Stawinska E, et al. Treatment of massive labial and gingival hypertrophy in a patient with infantile systemic hyalinosis? A case report. Journal of Oral and Maxillofacial Surgery. 2015;73:1962-e1.

80. Shakeel F, et al. Solubility and Dissolution Improvement of Aceclofenac using Different Nanocarriers. J Bioequiv Availab. 2009;1:039-043.

81. Appelboom G, et al. The promise of wearable activity sensors to define patient recovery. J Clin Neurosci. 2014;21:1089-1093.

82. Callejo FJG, et al. Factores relacionados al dolor postamigdalectom_ja en adultos. Acta Otorrinolaringologica Espagola. 2016;67:23-32.

83. Jovanovic D. Analiza faktora udru?enih sa postoperativnim oporavkom kod bolesnika posle elektivne abdomenalne histerektomije. 2014.

84. Datta T. Thermodynamics, Equilibration, Conservation Principles, Scientific and Societal Change: Is this the 'Rich get Richer' all Over Again? J Thermodyn Catal 2014;5:e128.

85. Earla P. Transplantation: Unbelievable Evolution and an Amazing Gift to Human Population. J Transplant Technol Res. 2014;4:R1-001.

86. Positive end-expiratory KH. Observation, with particular attention to the patient?s respiratory status, is suggested in patients with PWS. The systemic problems associated with PWS are of great concern to the anesthesia. The International Student Journal of Nurse Anesthesia. 2012;63:22.

87. Krger W and Ludman AJ. Mechanical Ventilation. In Core Knowledge in Critical Care Medicine. Springer Berlin Heidelberg. 2014.

88. Liu R, et al. Binding Site and Affinity Prediction of General Anesthetics to Protein Targets Using Docking. Anesth Analg. 2012;114:947-955.

89. Krishnamoorthy K, et al. Evaluation of Efficacy of Epidural Clonidine with 0.5% Bupivacaine for Postoperative Analgesia for Orthopaedic Lower Limb Surgeries. Journal of clinical and diagnostic research: JCDR. 2015;9:UC14-UC18.

90. Imani F, et al. Comparison between the effect of 0.2% and 0.3% Bupivacaine in fascia iliac block on

postoperative pain in patients with femoral or hip fracture. Anesthesiology and Pain. 2015;5:59-68.

91. Laksono BH and Saleh SC. Tehnik Proteksi Otak pada Pembedahan Non Neurosurgery.Radical Neck Dissection) dengan Premorbid Space Occupying Lesion: dan Infark Serebri. 2013;3:157-163.

92. Laksono BH, et al. Tatalaksana Anestesi pada Direct Clipping Aneurisma Otak. 2015;4:193-202.

93. Swati Srabani N, et al. Anesthesia and Intensive Care. J Anesthe Clinic Res. 2012;4:2.

94. Siddiqui A. Is Clinical Research an Aid to Society. J Anesthe Clinic Res. 2012;3:179.

95. Liu R, et al. Binding Site and Affinity Prediction of General Anesthetics to Protein Targets Using Docking. Anesth Analg. 2012;114:947-955.

96. Wang C. Potential Neurotoxic Effects of Anesthetics during Development and Potential Protective Agents. J Bioequiv Availab. 2011.

97. Alnour TM, 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.

98. Haliloglu M, et al. Post Operative Effects: Anesthesia. J Anesth Clin Res. 2012;S7:007.

99. Cavus E and Dorges V. The development of direct laryngoscopy. Curr Anaesth Crit Care. 2014;4:3-9.

100. Wittkugel E. Quality improvement methods toreduce adverse events in anesthesia. 2014;S1:018.