ISSN No:-2456-2165

Comparison of Random Blood Sugar Levels on Inductions Using a Combination of Ketamine and Propofol (Ketofol) and Single Ketamine in Patients Undergoing Total Intravenous General Anesthesia at Haji Adam Malik General Hospital

Ongta Gibson Quatro Sirait, Soejat Harto, Cut Meliza Zainumi
Department of Anesthesiology and Intensive Care, Medical Faculty, North Sumatera University, Haji Adam Malik General Central Hospital, Medan, Indonesia

Abstract:-

- ***Introduction:***

Increased blood sugar levels in patients undergoing surgery and anesthesia is one of the important problems in perioperative management, so that the selection of appropriate induction drugs is needed in patients with hyperglycemia.

- ***Objective:***

This study aims to determine the comparison of blood sugar levels when induced using a combination of ketamine and propofol (ketofol) and single ketamine in patients undergoing total intravenous general anesthesia at H. Adam Malik General Hospital of Medan.

- ***Method:***

This research is an experimental study with double blind. The study was conducted at the H. Adam Malik General Hospital of Medan from June to July 2019. The total sample obtained was 62, of which 31 samples were given ketofol treatment, while the other 31 samples were given ketamine treatment. The blood sugar level was then measured at 5, 10, 15, and 20 minutes after induction. Data collection was done using questionaires and blood sugar level sticks.

- ***Results:***

The mean value of blood sugar levels in the group given ketamine increased compared to the group given ketofol after observation for 5 minutes (T1) and 10 minutes (T2) but not significant, whereas in T3 (15 minutes) and T4 (20 minutes) a significant difference was found.

- ***Conclusion:***

The combination of intravenous ketamine and propofol (ketofol) and single ketamine only has an influence on the blood sugar levels in patients undergoing total intravenous general anesthesia, where ketamine further increases blood sugar levels when compared to ketofol.

Keywords:- *Hyperglycemia, Ketofol, Ketamine, Blood Sugar Levels*

I. INTRODUCTION

Blood sugar level is one of the important things that must be considered in the body's metabolism. Metabolism always occurs in the body and most of the fuel for metabolism is blood sugar. Blood sugar metabolism also occurs when operative action is performed and is a challenge in its control during the perioperative period. Special conditions that must be considered are in patients with hyperglycemia or diabetes mellitus. This is a complication in handling the perioperative period in patients with diabetes mellitus.[1]

In Indonesia, the regulation of blood sugar levels cannot be separated from the phenomenon diabetes mellitus, which is also one of the problems of metabolic diseases in teh country. According to the *International Diabetes Federation*, as many as 382 million people lived with diabetes in the world in 2013. By 2035 it will increase to 592 million people and this number will grow continuously; this includes those who have not been diagnosed or treated properly so that they are at the stage of quite severe complications. The proportion of diabetes mellitus in Indonesia in 2013 was around 6.9%, which was obtained from routine blood sugar checks in people over the age of 15 years[1,2].

The regulation of blood sugar in patients with diabetes mellitus (DM) is of particular concern in the field of anesthesiology. Good control of blood sugar levels during surgery will reduce the morbidity and mortality rates of DM patients. Surgery induces many stress responses mediated by the neuroendocrine system which then releases catecholamines, glucagon and cortisol. Non-diabetic patients are able to maintain glucose homeostasis by secreting enough insulin to balance the increase in glucose due to the stress response. Regulation blood sugar levels in the use of general anesthesia needs to be considered carefully. Some induction agents for general anesthesia have the side effects of increasing blood sugar level.[2,3].

ISSN No:-2456-2165

The system of ERAS, or Enhanced Recovery After Surgery, is one of the methods or provisions in the preparation and final follow-up of operative measures. Based on several hypotheses regarding carbohydrate levels, regulation of blood sugar levels is one of the key elements of ERAS in the preoperative period in individuals with diabetes (such as aspiration pneumonia due to delayed gastric emptying, hyperglycemia and some of the remaining symptoms). Patients with diabetes will have problems when emptying the stomach. Chronically, elevated glucose level can cause autonomic neuropathy and sympathetic nervous system dysfunction in cellular targets, such as neurons, that will produce nitric oxide, interstitial cells in the intestine, and intestinal hormone level. Regulation of blood sugar level is needed in pre, intra and post-operative measures on DM.[4].

Trans-intravenous anesthesia is the main topic in this study. Study after study pretty much dominates this matter. Some well-known agents such as barbiturates, thiopental, propofol, ketamine, etc., are widely used as induction drugs in trans-intravenous anesthesia. Implementers of trans-intravenous anesthesia must know several principles such as TCI, or Target Controlled Infusion, which will also depend on the concentration. Thiophental is widely used in patients with ASA 1, while ketamine is the best and most widely used because of its few side effects. Meanwhile, propofol is very good for the effects of sedation and has a protective effect on the brain.[5]

The side effects of ketamine on increasing blood sugar levels are now receiving special attention. Ketamine works very significantly to increase blood flow to the brain, oxygen consumption, and intracranial pressure. Ketamine does not depress breathing. Muscle tone of the airways will be well controlled and airway reflexes are usually not disturbed. The use of ketamine has been linked to postoperative disorientation conditions, sensory illusions, perceptions and life-like dreams (which are called *emergent phenomena*). Several studies have proven that ketamine has a glucocorticoid effect, which is increasing blood sugar levels after administration in anesthesia. This is enough reason to give special attention to patients with diabetes mellitus and patients with prolonged use of steroid drugs[3,6].

In its administration, Propofol also has an effect blood sugar levels. In some conditions, propofol and ketamine are often used together. Some studies explain that propofol lowers blood sugar levels or tends to cause hypoglycemia.[2] In another comparison, it was found that isoflurane would increase blood sugar levels.[7,8].

Comparison of changes in blood sugar levels in the system has been widely studied in several studies. Acute hyperglycemia is one condition that often gets special attention after surgeries. Several studies found that ketamine increases blood sugar levels more than propofol. Other studies also compared adjuvants such as midazolam with propofol, in which there were no specific differences in the increase in blood sugar levels.[9,10].

According to study conducted by Andolfatto et al (2012), the combination of ketamine-propofol (ketofol) resulted in an increase in blood glucose levels and was statistically related to an increase in blood glucose with a p value <0.01. A study conducted by Sharma I et al on 100 patients who underwent surgery in India found that administration of ketamine 2 mg/kgBB caused an increase in blood glucose levels. This is because ketamine has a sympathomimetic effect and causes stimulation on adrenocortical function. Meanwhile, according to study by Kaviani et al (2014), administration of propofol caused a decrease in blood glucose levels. [11]

II. RESEARCH METHODS

A. Research Design

This is an experimental study that aims to determine the comparison of blood sugar levels when induced using a combination of ketamine and propofol (ketofol) and single ketamine in patients undergoing total intravenous general anesthesia at H. Adam Malik General Hospital of Medan.

B. Place and Time of Research

The study was conducted at the Central Surgical Installation and Integrated Diagnostic Installation of H. Adam Malik General Hospital of Medan and began after ethical clearance was published until the number of samples was met.

C. Research Population and Samples

The population of this study was all patients who underwent total intravenous general anesthesia at the Central Surgical Installation and Integrated Diagnostic Installation of H. Adam Malik General Hospital of Medan. The sample was patients who met the inclusion and exclusion criteria. After being calculated statistically, all samples were divided into 2 groups:

a. Group A, who were given intravenous ketofol, namely ketamine and propofol (ratio 1: 1), where 100 mg of ketamine (50 mg/ml) was diluted with NaCl 0.9% to achieve a volume of 10 ml + 100 mg propofol 1%. The total volume was 20 ml and each ml contained 5 mg of propofol + 5 mg of ketamine. The dose given was 1 ml for every 5 kg (31 samples)
b. Group B, who were given intravenous ketamine 1 mg/kg (31 samples)

D. Research Criteria

All patients underwent total intravenous general anesthesia at the Central Surgical Installation and Integrated Diagnostic Installation of H. Adam Malik General Hospital of Medan. The **Inclusion Criteria** included patients aged 18-65 years, patients with preoperative ASA I-II, patients with normoglycemia and patients with a BMI of 18.5-24.9 kg/m². The **Exclusion Criteria** included patients who had contra indications for propofol administration and patients who had contra indications for ketamine. And the **Drop-Out Criteria** included patients who experienced cardiac and pulmonary emergencies and patients who received rescue and or sedation within 20 minutes after induction.

ISSN No:-2456-2165

E. Procedure

The procedure of this research is as follows:

1. After obtaining approval from the ethics commission to conduct research, the research was started by collecting research subjects according to inclusion and exclusion criteria.
2. After patients were given an explanation on the objectives, benefits and procedures of the research and signed an agreement to participate, interviews were conducted with a questionnaire to find out the data needed by the researcher.
3. After the patients arrived in the surgical waiting room, they were re-examined for their identity, diagnosis, anesthesia plan, access to infusion before signing in.
4. The patients were then taken to the operating room and fitted with a standard monitor (ECG, blood pressure, heart rate, breathing frequency, oxygen saturation).
5. Blood sugar levels were measured before induction.
6. Both groups of patients were then given an SA injection of 0.01 mg/KgBB and midazolam injection of 0.05 mg/kgBB.
7. Two anesthetic agents were given for induction in each group; group A was given a combination of ketamine and propofol (ketofol) and group B a single ketamine
8. Blood sugar levels were measured at 5, 10, 15, and 20 minutes after induction.
9. Data were then recorded in each experimental group
10. Data analysis was performed with SPSS

F. Statistic Analysis

Data will be analyzed descriptively to see the frequency distribution of the studied variable. If the data is normally distributed, a difference test will be performed using an unpaired t-test with a significance of $p < 0.05$.

III. RESEARCH RESULTS

➢ *Sample Characteristics*

This research was conducted for 1 month, in June-July 2019, at the H. Adam Malik General Hospital of Medan. This study aims to determine the comparison of blood sugar levels when induced using a combination of ketamine and propofol (ketofol) and single ketamine in patients undergoing total intravenous general anesthesia at H. Adam Malik General Hospital of Medan.

Samples obtained in this study amounted to 62 samples that fit the inclusion and exclusion criteria, with a group of 31 samples given ketofol and group 31 samples given ketamine. Characteristics of the sample are shown in Table 1.

Characteristics	**Treatment**				**Total**		**p *value***
	Ketofol		**Ketamine**				
	n	**%**	**n**	**%**	**n**	**%**	
Gender, n (%)							
Male	15	41,7	21	58,3	36	67,7	0.001
Female	16	61,5	10	38,5	26	32,3	
Age (mean±SD)	41,42±1.36		45,58±0,44				0.001
Types of procedure, n (%)							
Gastroscopy	13	43,3	17	56,6	30	48,4	
ERCP	3	50,0	3	50,0	6	9,7	0.001
Bronchoscopy	8	57,1	6	42,9	14	22,6	
Colonoscopy	7	58,3	5	41,7	12	19,4	
ASA, n (%)							
1	7	53,8	6	46,2	13	21,0	0.001
2	24	49,0	25	51,0	49	79,0	
RBS Level Before Treatment (T0) (mean±SD)	119,4 ± 5,1		100,7 ± 2,3				0,166*
Total	31	100.0%	31	100.0%	62	100.0%	

Table 1:- Sample Characteristics

** Kolmogorov-Smirnov Normality Test*

Table 1 shows the distribution of sample characteristics by treatment groups. The male patients in both ketofol and ketamine groups were 41.7% and 67.7% respectively, while the female patients in the ketofol and ketamine groups were 61.5% and 38.5%, respectively. From the test results for the characteristics of age, sex, type of procedure, and ASA, the p value obtained in the normality test was less than 0.05, which meant that the data were not normally distributed. However, on the characteristics of RBS Level before treatment (T0), the p value was greater than 0.05, which meant that the data were normally distributed.

The samples in this study were mostly from the type of gastroscopy procedure, which were 30 samples (48.4%), followed by bronchoscopy with 14 samples (22.6%). Meanwhile, the least number of samples came from ERCP patients, which was 6 samples (9.7%). Most of the patients in this study received ASA 2, amounting to 49 cases (79%). The ketofol group included 24 samples (49%); while in the ketamine group, the majority had ASA 2, which was 51%.

- *Comparison of random blood sugar levels on induction using a combination of ketamine and propofol (ketofol) and single ketamine in patients undergoing total intravenous general anesthesia at T1 (Minute 5)*

Comparison of random blood sugar levels in the group of ketamine and propofol (ketofol) combination and the group of single ketamine at T1 (Minute 5)

Group	RBS Level (Mean±SD) mg/dl	p Value
Ketofol	126.8±22.5	0.58
Ketamine	121.5±18.9	
α Value <0.05		

Table 2:- Comparison of random blood sugar levels in the group of ketamine and propofol (ketofol) combination and the group of single ketamine at T1 (Minute 5)

Based on Table 2, it was found that the mean value of random blood sugar (RBS) level in the group given Ketofol at T1 observation was 126.8±2 22.5 mg/dl and in the group given single ketamine was 121.5±18.9 mg/dl. There was no statistically significant difference between the RBS values in the ketofol and single ketamine groups on T1 observation with p = 0.58.

- *Comparison of random blood sugar levels on induction using a combination of ketamine and propofol (ketofol) and single ketamine in patients undergoing total intravenous general anesthesia at T2 (Minute 10)*

Comparison of random blood sugar levels in the group of ketamine and propofol (ketofol) combination and the group of single ketamine at T2 (Minute 10)

Group	RBS Level (Mean±SD)	p Value
Ketofol	152.8±26.6	0.067
Ketamine	169.3±43.1	
α Value <0.05		

Table 3:- Comparison of random blood sugar levels in the group of ketamine and propofol (ketofol) combination and the group of single ketamine at T2 (Minute 10)

Based on Table 3, it was found that the mean value of random blood sugar (RBS) level in the group given ketofol at T2 observation was 152.8±26.6 mg/dl and in the group given single ketamine was 169.3±43.1 mg/dl. There was no statistically significant difference between the RBS values in the ketofol and single ketamine groups on T2 observation with p = 0.067.

- *Comparison of random blood sugar levels on induction using a combination of ketamine and propofol (ketofol) and single ketamine in patients undergoing total intravenous general anesthesia at T3 (Minute 15)*

Comparison of random blood sugar levels in the group of ketamine and propofol (ketofol) combination and the group of single ketamine at T3 (Minute 15)

Group	RBS Level (Mean±SD)	p Value
Ketofol	166.1±28.1	0.001
Ketamine	202.7±49.8	
α Value <0.05		

Table 4:- Comparison of random blood sugar levels in the group of ketamine and propofol (ketofol) combination and the group of single ketamine at T3 (Minute 15)

Based on Table 4, it was found that the mean value of random blood sugar (RBS) level in the group given ketofol at T3 observation was 166.1±28.1 mg/dl and in the group given single ketamine was 202.7±49.8 mg/dl. There was no statistically significant difference between the RBS values in the ketofol and single ketamine groups on T3 observation with p = 0.001.

- *Comparison of random blood sugar levels on induction using a combination of ketamine and propofol (ketofol) and single ketamine in patients undergoing total intravenous general anesthesia at T4 (Minute 20)*

Comparison of random blood sugar levels in the group of ketamine and propofol (ketofol) combination and the group of single ketamine at T4 (Minute 20)

Group	RBS Level (Mean±SD)	p Value
Ketofol	177.8±28.1	0.001
Ketamine	226.5±49.8	
α Value <0.05		

Table 5:- Comparison of random blood sugar levels in the group of ketamine and propofol (ketofol) combination and the group of single ketamine at T4 (Minute 20)

Based on Table 5, it was found that the mean value of random blood sugar (RBS) level in the group given ketofol at T4 observation was 177.8±28.1 mg/dl and in the group given single ketamine was 226.5±49.8 mg/dl. There was no statistically significant difference between the RBS values in the ketofol and single ketamine groups on T4 observation with p = 0.001.

- *Comparison of random blood sugar levels in the group induced with a combination of ketamine and propofol (ketofol) and the group induced with single ketamine on observations T1 to T4*

Comparison of random blood sugar levels in the group induced with a combination of ketamine and propofol (ketofol) and the group induced with single ketamine on observations T1 to T4 it was found that the mean value of random blood sugar (RBS) levels in the group given ketofol on observations T1 to T4 tended to increase, with the highest value of random blood sugar level of 177.8 mg/dl; likewise, the mean value of random blood sugar (RBS) levels in the group given ketamine on observations T1 to T4 also tended to increase, with the highest value of random blood sugar level of 226.5 mg/dl.

IV. DISCUSSION

This study was conducted in July 2019 using data obtained directly from all patients undergoing total general intravenous anesthesia at the Central Surgical Installation and Integrated Diagnostic Installation at H. Adam Malik General Hospital of Medan. This study aims to determine the comparison of random blood sugar levels on inductions using a combination of ketamine and propofol (ketofol) and single ketamine in patients undergoing TOTAL INTRAVENOUS GENERAL ANESTHESIA. This research is an experimental study with 62 research samples.

Based on Table 1, it was found that the majority of the samples in this study received gastroscopy procedure, which was 30 samples (48.4%). This is consistent with the data at the Integrated Diagnostic Installation of H. Adam Malik General Hospital of Medan for the last 3 years (2016-2018), where gastoscopy was the most frequently performed procedure: 806 times in 2018, 852 times in 2017, and 821 times in 2016.

Based on Table 2 and Table 3, it was found that the mean value of random blood sugar (RBS) level in the group given ketamine was higher than the initial mean value of random blood sugar (RBS) level (T0) compared to the group given ketofol after 5 minutes of observation (T1). Similarly on T2 observation, as described in Table 4.3, the mean value of random blood sugar (RBS) level in the group given ketamine was higher than the ketofol group, although there was no statistically significant difference between the mean values of random blood sugar (RBS) level in the ketofol combination group and the single ketamine group on T1 and T2 observations.

Based on observations T3 and T4 in Table 3 and Table 4, it was found that the mean values of random blood sugar (RBS) levels in the group given ketofol and in the group given ketamine experienced significant differences, with the ketamine group tending to have higher random blood sugar levels compared to the ketofol group. This is in accordance with the peak plasma time of ketamine which ranges from 5-10 minutes, so that in the next minute (15th minute and 20th minute), the random blood sugar level in patients given single ketamine increase significantly compared with patients given a combination of ketofol.

The results of this study are consistent with research conducted by Sharma et al on 100 patients who underwent surgery in India, where the administration of ketamine 2 mg/kgBB turned out to cause an increase in blood glucose levels. This is because ketamine has a sympathomimetic effect and causes the stimulation of adrenocortical function. While the study of Kaviani et al (2014) reported that Propofol administration resulted in a decrease in blood glucose levels. [11]

Ketamine has a sympathomimetic effect caused by the release of centrally mediated catecholamines and has an effect for catecholamine inhibition. Anesthetic drugs will basically have a sympathomimetic effect and affect the endocrine system in the human body, especially the regulation of blood glucose levels. The mechanism for increasing blood glucose levels is very complex. One opinion held is that anesthetic drugs directly suppress pancreatic beta cells through the release of catecholamines and result in decreased insulin production, while propofol will not increase blood sugar levels because it suppresses or decreases the stress response so that the levels of catecholamines and cortisol decline.[20]

The effect of propofol on blood glucose levels has also been examined by Johan et al in their study, which compared the effect of induction of propofol with etomidate on blood sugar levels. Johan et al's results found that propofol reduced blood sugar levels at a dose of 2.5 ml/kgBW. In some conditions,the combination of propofol and ketamine is often used together. Some studies explain that propofol lowers blood sugar levels or tends to cause hypoglycemia, whereas ketamine results in increased blood pressure.[2] The combination of propofol and ketamine is expected to maintain a more stable blood glucose level during a stress response. This might also be caused by the faster onset of propofol (40 seconds) compared to ketamine (2-4 minutes), so that on induction using a combination of ketamine and propofol (ketofol), the propofol effect first suppresses the sympathetic effect rather than the surgical response so that blood sugar levels can be pressed. So when the effects of ketamine start working to stimulate the sympathetic system which causes an increase in blood sugar level, the blood sugar level does not increased too high.

V. CONCLUSION

1. Induction using a combination of ketamine and propofol (ketofol) reduces random blood sugar levels more compared to single ketamine, especially at T3 (15th minute) and T4 (20th minute).
2. The combination of intravenous ketamine and propofol (ketofol) has an influence on random blood sugar levels in patients undergoing total intravenous general anesthesia.
3. Single intravenous ketamine has an influence on random blood sugar levels in patients undergoing total intravenous general anesthesia.

REFERENCES

[1]. Arphad T. General Anasthesia. Fac Pharm Univ Debreem. 2014;14–7.
[2]. Brown EN, Lydic R, Schiff ND. General Anesthesia, Sleep, and Coma. Schwartz RS, editor. N Engl J Med. 2010 Dec;363(27):2638–50.
[3]. Stevenson C. Ketamine: A Review. Updat Anaesth. 2007;1–5.
[4]. Pędziwiatr M, Mavrikis J, Witowski J, Adamos A, Major P, Nowakowski M, et al. Current status of enhanced recovery after surgery (ERAS) protocol in gastrointestinal surgery. Med Oncol. 2018 May;35(6):95.
[5]. Peltoniemi MA, Hagelberg NM, Olkkola KT, Saari TI. Ketamine: A Review of Clinical Pharmacokinetics and

Pharmacodynamics in Anesthesia and Pain Therapy. Clin Pharmacokinet. 2016 Sep;55(9):1059–77.
[6]. Kurdi MS, Theerth KA, Deva RS. Ketamine: Current applications in anesthesia, pain, and critical care. Anesth essays Res. 2014;8(3):283–90.
[7]. Anonymous. Propofol Injectable Emulsion. In USA: Hospira, Inc.; 2018. p. 1–30.
[8]. Metrot J, Vigreux J-M. Blood glucose and propofol in outpatient anaesthesia. Ambul Surg. 1993 Jun;1(2):101–2.
[9]. Anonymous. Propofol. Drug Enforc Adm. 2013;1.
[10]. Sahinovic MM, Struys MMRF, Absalom AR. Clinical Pharmacokinetics and Pharmacodynamics of Propofol. Clin Pharmacokinet. 2018 Dec;57(12):1539–58.
[11]. Kaviani N, Koosha F, Shahtusi M. Comparison of the changes in blood glucose level during sedation with midazolam and propofol in implant surgery: a prospective randomized clinical trial. J Dent (Shiraz, Iran). 2014 Sep;15(3):135–9.
[12]. Brown EN, Purdon PL, Van Dort CJ. General Anesthesia and Altered States of Arousal: A Systems Neuroscience Analysis. Annu Rev Neurosci. 2011 Jul;34(1):601–28.
[13]. De Kock M, Loix S, Lavand'homme P. Ketamine and Peripheral Inflammation. CNS Neurosci Ther. 2013 Jun;19(6):403–10.
[14]. Sanri E, Karacabey S, Akoglu H, Kaya B, Guneysel O. Comparison of ketamine/propofol (ketofol) and etomidate/fentanyl (etofen) combinations for procedural sedation and analgesia in the emergency department: An observational study. Turkish J Emerg Med. 2017 Sep;17(3):89–94.
[15]. Sehdev RS, Symmons DA, Kindl K. Ketamine for rapid sequence induction in patients with head injury in the emergency department. Emerg Med Australas. 2006 Feb;18(1):37–44.
[16]. Zeighami D, Akhlagh S, Khosravi M, Maghsoodi B, Azemati S, Alipour A, et al. The Effect of Low-Dose of Ketamine Infusion on Stress Responses in Coronary Artery Bypass Graft Surgery. Int Cardiovasc Res J. 2010 Mar;4(1).
[17]. Greenwood R. ICU Guideline: Adjusting Goal Feed Rates In The Patient Receiving A Propofol Infusion. In Critical Care Connections, Inc.; 2009.
[18]. Slavik VC, Zed PJ. Combination Ketamine and Propofol for Procedural Sedation and Analgesia. Pharmacotherapy. 2007 Nov;27(11):1588–98.
[19]. Lacoumenta S, Walsh ES, Waterman AE, Ward I, Paterson JL, Hall GM. Effects of ketamine anaesthesia on the metabolic response to pelvic surgery. Br J Anaesth. 1984 May;56(5):493–7.
[20]. Kumar M, Tripathi M, Malviya D, Malviya PS, Kumar V, Tyagi A. Influence of two anesthetic techniques on blood sugar level in head injury patients: A comparative study. Anesth essays Res. 2016;10(2):207–11.
[21]. Triplitt CL. Examining the mechanisms of glucose regulation. Am J Manag Care [Internet]. 2012 Jan [cited 2019 Mar 16];18(1 Suppl):S4-10. Available from: http://www.ncbi.nlm.nih.gov/pubmed/22559855
[22]. Güemes M, Rahman SA, Hussain K. What is a normal blood glucose? Arch Dis Child [Internet]. 2016 Jun [cited 2019 Mar 16];101(6):569–74. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26369574
[23]. Reddy M, Jugnee N, El Laboudi A, Spanudakis E, Anantharaja S, Oliver N. A randomized controlled pilot study of continuous glucose monitoring and flash glucose monitoring in people with Type 1 diabetes and impaired awareness of hypoglycaemia. Diabet Med [Internet]. 2018 Apr [cited 2019 Mar 16];35(4):483–90. Available from: http://www.ncbi.nlm.nih.gov/pubmed/29230878
[24]. Sudhakaran S, Surani SR. Guidelines for Perioperative Management of the Diabetic Patient. Surg Res Pract [Internet]. 2015 [cited 2019 Mar 16];2015:284063. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26078998
[25]. Pogatschnik C, Steiger E. Review of Preoperative Carbohydrate Loading. Nutr Clin Pract [Internet]. 2015 Oct 21 [cited 2018 Oct 29];30(5):660–4. Available from: http://www.ncbi.nlm.nih.gov/pubmed/26197803