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THE EFFECT OF AMINO ACIDS IN REDUCING TREMOR DURING LAPAROSCOPIC SURGERY OF CHOLECYSTECTOMY FOR WOMEN AGED 20-50 Y/O AT IRAN

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ABSTRACT

Introduction: Post-anesthetic shivering is reduced by preventing the occurrence of hypothermia during anesthesia. It is so difficult to maintain normothermia during general anesthesia. Amino acids produce heat by stimulating energy consumption during general anesthesia. The aim of this study is to investigate the effect of amino acids to prevent Shivering after anesthesia. **Methods and materials**: In this clinical trial, 80 female patients undergoing elective laparoscopic cholecystectomy were randomly divided into two groups each comprising 40 patients. After premedication, similar method of general anesthesia was performed to all patients. Patients in group A received amino acid 10% (2 ml/kg/h) immediately after anesthesia induction, and continued until the end of surgery (max 1gr/kg). Patients in control group received saline normal with similar manner. After awake extubation, all patients transferred to recovery room immediately. Oral temperature, heart rate, blood pressure and arterial oxygen saturation (SaO2) were recorded during surgery. Post-anesthesia shivering was recorded by a nurse not aware from the research method. We used ANOVA, Chi-square and Tukey test to analyze the data. **Results:** Shivering rate in amino acid group, in minutes 10, 20 and 30 after anesthesia was less than control group (P value<0.05). Also, increasing systolic blood pressure and heart rate in amino acid group was less than control group in minutes 10, 20 and 30 after anesthesia (P value<0.05). Mean body temperature in minutes 20 and 30 after anesthesia was higher in amino acid group. Post-anesthetic shivering in amino acid group was less than control group (Pvalue<0.05). **Conclusion:** Amino acid infusion 10% (2ml/kg/h), immediately after anesthesia induction until end of surgery (maximum 1gr/kg), is effective to reduce the frequency and severity of post-anesthetic shivering in women undergoing laparoscopic cholecystectomy. Also, it reduces increasing systolic blood pressure, heart rate, body temperature and shivering.

KEYWORDS: Post-anesthesia, tremor, Amino acid.

INTRODUCTION

Post-anesthesia shivering is not only related to patients, it can relate to physiological changes such as increased tissue oxygen consumption, resulting in raised cardiac output.[1] The incidence of postoperative shivering may occur at 65% (range 5% to 65%) after general anesthesia In addition to significant patient discomfort, postoperative shivering increases oxygen consumption, carbon dioxide production, and sympathetic tone.[2] These effects prevent shivering, especially in the patients with a low cardiopulmonary reservation.[3] Although various drugs such as Meperidine and Ondansetron have been used to treat or prevent the problem, the ideal drug has not yet been found.[4] The incidence of this complication is reduced by preventing hypothermia during general anesthesia, but maintaining normothermia during general anesthesia is very difficult.[5]

During anesthesia and surgery core body temperature gradually declines because of slow and impaired heat production. The stress of surgery and anesthesia leads to a series of changes at the metabolic level, catabolism exceeds anabolism, and increasing the physiological load of patients undergoing surgery (6). Proteins and amino acids stimulate heat production. Previous studies have demonstrated that amino acid infusions enhance thermogenic effects during general anesthesia and causes re-warming.[7]

J. Widman et al. showed that amino acid infusion before surgery increases level of energy consumption about 50-60% more than baseline. Also, they showed that amino acid infusion prevents hypothermia by increasing heat accumulation and stimulating heat production.[8]

The aim of amino acid infusion in stressed patients is to reduce the loss of endogenous proteins, which provides an alternative amino acid source for gluconeogenesis and protein synthesis. Amino acids solution 5% and 10% are available, that, contain protein substrates and are used to maintain protein or prevent nitrogen excretion, and are used to treat its negative equilibrium. Their dosage is 1-1.7 g / kg / day in stressed patients and 0.8-1.2 g / kg / day in stress less patients. To infuse through peripheral veins, they should be diluted with 5% dextrose solution. The infusion rate is about 2ml per minutes. Unfortunately, no information is available on the distribution, metabolism and disposal of this drug.[9]

The method of surgery may affect thermal effects of amino acids. Amino acid infusion during anesthesia prevents hypothermia through heat accumulation and delayed heat stimulation.[10]

A. Sahin et al. in 2002 showed that, in combination with amino acid solutions, anesthesia with Propofol has more thermogenetic effects than Isofulrane anesthetics.[11]

Considering previous studies and regard to maintain normothermia, preventing hypothermia during surgery causes less post-anesthetic shivering; so, we studied the effect of amino acids to access normothermia maintenance during anesthesia and prevent shivering after anesthesia.

METHOD

In this double blind clinical trial, 80 women aged from 20 to 50 years with ASA class I and II candidates for elective laparoscopic cholecystectomy referred to the Qazvin (velayat) hospital in the four months entered the study after confirming the Ethics Committee of the Qazvin University of Medical Sciences, this year (or until the completion of the sample size). Patients were randomly divided into two groups with color card, each comprising 40 patients; A group (amino acid group) and C group (control group).

After an eight hour NPO period, patients were transferred to the operating room. All patients were under standard anesthesia monitoring and the intra venous catheter no 20.All pationts received 350-400 cc saline normal with room temperature in 15 minuts. 3 -5 minutes after receiving anesthesia premedication (Fentanyl 2 µg / kg and Meidazolam 0.02 mg / kg); induction of anesthesia performed with Propofol 2 mg / kg and Atracurium 0.5 mg / kg) and patients were intubated. Immediately after anesthesia induction and randomly, amino acid infusion 10% (2 ml / kg / h that diluted with D/W 5% equivolume) for women in group A performed and continued until the end of surgery (up to 1gr / kg) (we used Aminovent 10% Manufactured by:Fresenius Austria GmbH,Graz,Austria). Patients in control group received saline infusion with similar manner. Maintenance of anesthesia applied with Propofol (100µg / Kg / min), Alfentanil (1µg / kg / min), and Atrachiorium (0.15mg / kg) -if needed-. At the end of surgery, returning the effect of relaxant was done with atropine (0.02 mg / kg) and Neostygmine (0.04 mg / kg). By the end of surgery, all awake patients after extubation were transferred to the recovery room, under nasal oxygen therapy (2ml / min).

During the surgical period and during the recovery, the body temperature (thermometer probe was placed inside the patient's mouth), heart rate based on electrocardiography, blood pressure with automatic cuff and oxygen saturation (Sao2) was measured by a pulse oximeter and using SAADAT monitoring device. The mentioned items were recorded every 10 minutes by a nurse who did not know the research method. Also, Post-anesthesia shivering was evaluated and recorded on the basis of clinical observations.

Table 1: Post anesthetesia shivering gradation.[1]

Degree	Clinical symptoms
0	No shivering is detected by touching the muscles of the rodent, neck and chest
1 (mild)	Localized shivering in neck and thorax (alone)
2 (moderate)	moderate shivering in one group of muscles including upper limb, neck and thorax
3 (severe)	Visible muscular activity throughout the body including trunk, upper and lower limbs

All participants in this study were informed about the confidentiality of the information, as well as the purpose of the project, and were entered into the study with written consent.

Information obtained from patients in different groups was first introduced into the SSPS software. After collecting data, the findings were presented in the form of statistical tables and numerical indexes. ANOVA was used to analyze the findings. The ANOVA test was used to compare mean age, BMI and duration of operation. Chi-Square test was used for comparing other variables, and Tukey test was used to examine the difference between them. P value less than 0.05 was considered meaningful.

FINDINGS

In this study, there was no significant difference between

the two groups of amino acid and control groups in terms of age, weight, BMI and duration of surgery, based on ANOVA test (P value>0.05).

Table 2: Comparing demographic variables between two groups; amino acid and control groups.

Variable	Control group N = 40	Aminoacid group N = 40	P_{value}
	Mean ± Standard Deviation		
Age (year)	30.87 ± 4.99	31.92 ± 4.92	0.949
Weight (Kg)	70.10 ± 3.82	70.90 ± 4.12	0.772
height (cm)	165.07 ± 3.95	163.0 ± 3.74	0.547
BMI (kg/m²)	25.23 ± 1.1	24.67 ± 1.1	0.402
Duration of surgery (min)	94.34 ± 14.13	95.68 ± 19.43	0.602

There was no meaningful difference in systolic blood pressure in two groups before anesthesia induction. However, at minutes 10, 20 and 30 after anesthesia, the increase in systolic blood pressure in the amino acid group was lower than the control group (P value< 0.05).

There was no meaningful difference in diastolic blood pressure changes between two groups before and after anesthesia in the minutes after anesthesia (P value>0.05).

There was no significant difference in the number of heart rate in the two groups before anesthesia induction, but in minutes 10, 20 and 30 after anesthesia, increasing the heart rate in the amino acid group was lower than control group (P value<0.05).

Table 3: comparing clinical variables (vital signs) between two groups before anesthesia and at minutes 10, 20 and 30 after anesthesia: Amino acid and control groups.

Index	Control group N = 40	Aminoacid group N = 40	P_{value}
	Mean ± Standard Deviation		
SBP (before anesthesia)	120.12 ± 11.25	123.57 ± 4.40	0.057
SBP (at minute 10)	128.85 ± 10.59	121.35 ± 5.12	0.031
SBP (at minute 20)	129.95 ± 11.19	120.20 ± 4.23	0.014
SBP (at minute 30)	129.80 ± 10.96	120.65 ± 5.46	0.014
DBP (before anesthesia)	82.07 ± 4.57	81.75 ± 4.16	0.473
DBP (at minute 10)	85.92 ± 4.10	82.25 ± 4.27	0.645
DBP (at minute 20)	89.97 ± 4.09	83.00 ± 4.48	0.757
DBP (at minute 30)	85.80 ± 4.23	84.15 ± 4.51	0.867
HR (before anesthesia)	72.47 ± 9.61	73.20 ± 10.09	0.873
HR (at minute 10)	101.05 ± 7.93	73.72 ± 4.37	0.047
HR (at minute 20)	95.05 ± 3.20	76.65 ± 8.10	0.000
HR (at minute 30)	84.47 ± 3.54	74.97 ± 10.60	0.000

No significant difference was observed between the two groups before and after induction of anesthesia in the changes of arterial oxygen saturation SPO2 in minutes 10, 20and 30 after anesthesia (P value>0.05).

There was no significant difference in body temperature changes in the two groups before anesthesia induction and 10 minutes after anesthesia, but, in minutes 20 and 30 after anesthesia, body temperature in amino acid group was higher than control group (P value<0.05).

The mean shivering severity in two groups at minutes 10, 20 and 30 after anesthesia in amino acid group was lower than control group (P value<0.05).

Table 4: Comparing demographic variables between two groups, before anesthesia and at minutes 10, 20 and 30 after anesthesia.

Variable	Control group N = 40	Aminoacid group N = 40	P_{value}
	Mean ±Standard Deviation		
SPO2 (before anesthesia)	97.97 ± 1.98	97.97 ± 1.73	0.212
SPO2 (at minute 10)	95.87 ± 2.64	96.97 ± 2.23	0.726
SPO2 (at minute 20)	97.02 ± 2.16	97.00 ± 2.19	0.913
SPO2 (at minute 30)	96.60 ± 2.36	97.82 ± 1.59	0.101
TEMP (before anesthesia)	37.11 ± 0.20	37.39 ± 0.21	0.733

TEMP (at minute 10)	36.86 ± 0.11	37.49 ± 0.17	0.096
TEMP (at minute 20)	37.69 ± 0.09	37.36 ± 0.17	0.001
TEMP (at minute 30)	36.89 ± 0.11	37.40 ± 0.21	0.006
Shivering (at minute 10)	1.10 ± 1.05	0.30 ± 0.56	0.000
Shivering (at minute 20)	0.87 ± 0.91	0.25 ± 0.58	0.002
Shivering (at minute 30)	0.85 ± 0.86	0.20 ± 0.51	0.000

The frequency of shivering in minutes 10, 20 and 30 after anesthesia was 75, 82.5 and 72.5 percent (30, 33 and 29 patients) respectively. Patients had no shivering in amino acid group, while the rate of shivering in control group was 40, 42.5 and 42.5 percent (16, 17 and 17 patients) respectively. Thus, the frequency of patients without shivering in minutes 10, 20 and 30 after anesthesia in amino acid group was significantly higher than group Control.

The frequency of patients experiencing grade 1 severity of shivering in minutes 10, 20 and 30 after anesthesia was 20, 10 and 20 percent (8, 4 and 8 patients) in amino acid group respectively. The frequency of patients in control group experiencing grade 1 severity of shivering was 20, 32.5 and 20 percent (8, 13 and 8 patients) respectively. The frequency of patients with grade 1 severity in control group was 20 minutes after anesthesia, significantly more than amino acid group. But, it was equivalent to the amino acid group at minutes 10 and 30 after anesthesia.

The frequency of patients experiencing grade 2 severity of shivering in minutes 10, 20 and 30 after anesthesia in amino acid group was 5, 7.5 and 7.5 percent (2, 3 and 3 patients) respectively. The frequency of patients experiencing grade 2 severity of shivering in control group was 30, 20 and 37.5 percent (12, 8 and 11patients) respectively. Thus, the frequency of patients with grade 2 severity in control group was significantly higher than amino acid group.

Table 5: Frequency of patients based on severity and incidence of shivering in minutes 10, 20 and 30 after anesthesia.

Time	Grade of shivering	Control group Number (percent) N = 40	Aminoacid group Number (percent) N = 40
Minute 10	0	16 (40)	30 (75)
	1	8 (20)	8 (20)
	2	12 (30)	2 (5)
	3	0 (0)	0 (0)
Minute 20	0	17 (42.5)	33 (82.5)
	1	13 (32.5)	4 (10)
	2	8 (20)	3 (7.5)
	3	0 (0)	0 (0)
Minute 30	0	17 (42.5)	29 (72.5)
	1	8 (20)	8 (20)
	2	11 (27.5)	3 (7.5)
	3	0 (0)	0 (0)

DISCUSSION

The widespread use of amino acids infusion therapy is still unacceptable.[12] The effects of amino acid infusion have already been studied in both general anesthesia and epidural anesthesia and in various surgeries,[12,13] especially in pediatric age group.[14] In this study, the effects of amino acid infusion were studied only in female. We used amino acid infusion as a stimulant for energy consumption and heat generators to maintain neuromeremia during general anesthesia.

We searched the articles in MEDLINE (Pub Med) until 2017, but the article did not find out the effects of amino acid infusion on hemodynamic stability (blood pressure and heart rate) during anesthesia. However, the present study showed that infusion of amino acids prevents increasing systolic blood pressure and patient heart rate in recovery, so, it maintains hemodynamic stability of the patient during recovery.

Our study shows that infusing amino acid during general anesthesia, patient's body temperature maintains at higher rates in minutes 10, 20 and 30, and hence the severity and frequency of shivering after anesthesia reduces. These results are similar to the patient's body temperature pattern and shivering reduction in the study of Wu Q et al in 2015 (19), which indicates that infusion of amino acids during laparotomy for the stomach and intestine tumor leads to less shivering and postoperative hypothermia.

In a study by Sahin A. et al. the effects of Propofol and Isoflurane in control group compared with those receiving amino acid infusion in four groups,[16] and it

was determined that Propofol infusion with amino acid kept the central body temperature in higher degrees, but, the decrease in shivering intensity depends on the amino acid infusion. The results of this study are coincident with our findings, so that Propofol without amino acid infusion cannot reduce the intensity and frequency of shivering. Aminotransferase infusion is reduced the frequency of patients with grade 1 and 2 shivering and increased the frequency of patients without shivering.

In a study by Zhou P et al. it was shown that initiation of amino acid infusion in patients with grade 2 shivering and above, with central temperature less than 36 degrees during the first hour of exposure to PACU, can increase the body temperature (nasopharyngeal) and lead Shivering to definitive treatment.[17] In our study, with the onset of amino acid infusion during general anesthesia, similar effects were observed and, in addition to maintaining the central body temperature at higher levels, an obvious increase in the frequency of people without shivering was observed. Therefore, it is concluded that the onset of amino acid infusion simultaneously with the onset of shivering after anesthesia in the PACU has similar effects with amino acid infusion during general anesthesia.

CONCLUSION

Amino acid infusion during general anesthesia causes maintains body temperature at higher rates during recovery. Thus, the severity and frequency of shivering decrease in the first minutes after anesthesia. Also, amino acid infusion does not increase the systolic blood pressure and heart rate in patients during recovery. In addition, arterial oxygen saturation does not decrease during recovery.

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