

The Comparative study of Intravenous Tranexamic Acid with Intravenous Oxytocin in the Control of Bleeding during Hysteroscopic myomectomy in Women with Abnormal Uterine Bleeding

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Abstract

Introduction: Abnormal uterine bleeding is one of the most common causes of women who referring to gynecology clinics .One of the treatments approaches is removal of myoma by hysteroscopy. For reduction of bleeding volume during hysteroscopic myomectomy, several measures were performed. Therefore, the aim of this study was to compare the effects of tranexamic acid and oxytocin on bleeding during hysteroscopic myomectomy in women with abnormal uterine bleeding. **Materials and Methods:** This observer blinded clinical trial was conducted on patients undergoing operative hysteroscopy in Alzahra teaching hospital. By consideration of inclusion and exclusion criteria, 92 patients were classified into two groups. After general anesthesia, and upon insertion of the hysteroscope into the uterus, 46 patients in first group received 10 mg / kg of tranexamic acid in 500 ml of Ringer's serum at 10 ml per minute intravenous infusion, and for 46 patients in second group, 5 units of oxytocin were administered in 500 ml of ringer serum by 10 ml / min intravenous infusion. In both groups, dextrose solution 5% was used as a media for dilatation of the uterine cavity. The amount of bleeding, absorbed volume, the success rate of surgery, resolution of hysteroscopy image, side effects of two drugs, days of hospital stay, all were recorded in a pre-designed checklist and compared between 2 groups by SPSS 21. **Results:** In this clinical trial, 92 patients in both groups were matched for age, gravidity, parity and number of intrauterine myomas. Grade 0, 1 and 2 of intraoperative bleeding were observed in 6.9%, 3.9% and 0% Of patients in the Tranexamic acid 13% , 54.3% and 26.7% Of patients in Oxytocin group ,respectively (p=0.001, p=0.003,p=0.00). Patients treated with Tranexamic acid had significantly shorter operation time (11.5±7.24 minutes vs 21.23±11.7 minutes) and significantly hysteroscopic view (97.8% vs 65.2%) compared whit Oxytocin group. The hemoglobin and hematocrit changes, hospital stay duration, the mean absorbed volume were media, sodium and potassium changes and medications side effects were similar in the two groups. Myomectomy was done successfully in the two groups. **Conclusion:** Tranexamic acid was effective in reducing intraoperative bleeding, operation time and created bright hysteroscopic view.

Key words: Tranexamic acid, Uterine myoma, Hysteroscopy.

Introduction

Bleeding abnormalities can occur mostly in two reproductive spectrum, but it may also been observed at any age. One of the most important causes of uterine bleeding are the myomas (i.e. the most common benign tumors in women's reproductive life). In the United States, the annual incidence in the 25- 44 aged is 8.12 per 1,000 women over one year (Marshall et al., 1997). Estimated 70 to 80% of women with lymphoma are pre-menopausal (Baird et al., 2003), and approximately 30% of these patients have complain of menorrhagia (Lumsden and Wallace, 1998). The myomas are divided into three submucosal, intermoral, and sub-serous categories. The Association of European Endoscopic Gynecology categorized myoma as following:

Type 0 = Submucosal myoma that have pedicles and have not entered into myometrium.

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Type I = Myomas without pedicle that have penetrated into less than 50% of myometrium.

Type II = Myomas without pedicle that have penetrated into more than 50% of myometrium (Wamsteker K, Emanuel, 1993).

Submucosal Myomas are in contact with endometrial cavity or inside it, causing collapse, and these types of myomas cause severe and irregular menstrual bleeding, which can be well treated by hysteroscopy. While in the past, they were treated by hysterectomy or myomectomy (Clevenger-Hoeft et al., 1999; Emanuel et al., 1999). Hysteroscopy is a standard golden method for benign intrauterine diseases such as uterine septa and polyps, adhesions, and submucosal myomas. Removal of submucosal myomas by hysteroscopy in comparison with myomectomy by laparotomy is associated with advantages such as reduction of damage, shortening hospital stay, short recovery time and decreased intrauterine adhesion (Parker, 2007; Di Spiezio Sardo et al., 2007; Gutmann and Corson, 2005). Tranxamic acid is a synthetic derivative of lysine amino acid, which is in fact an anti-fibrinolytic agent, it reverses plasminogen activity and subsequently inhibits fibrinolysis and reduces bleeding. Tranxamic acid is used to reduce bleeding in cardiac surgery, liver transplantation, orthopedic surgeries, gynecologic procedures, as well as arthroplasty and knee joint replacements and bleeding after prostatectomy or tooth extraction. (Khezri et al., 2014) It is also used to treat idiopathic menorrhagia. By considering very few studies regarding the effect of intravenous tranxamic acid and oxytocin and comparison of effect of these two drugs on the amount of bleeding during hysteroscopic myomectomy, we aimed to conduction a study about this.

Methods and Materials:

This randomized clinical trial study (IRCT 201105306563N2) was conducted in Tabriz Medical Sciences Center, Al-Zahra hospital after approval by ethic committee (95.3-4.15) and giving informed consent. Patients who were hospitalized for hysteroscopy and myomectomy from September 2016 until completing the volume of samples, were entered to study. Patients were randomly classified to two groups using the Randlist version 1, 2, Dattng CmbH, Tubingen Germany software, and with code 391836736. To determine the sample size, power and sample size calculation (PS) software was used. Considering $\alpha = 0.05$, the power of 90% and the difference of one unit in the level of hemoglobin change, 46 samples were taken for each group and 92 samples were evaluated. Uterus myoma, indication of hysteroscopy and myomectomy were inclusion criteria and patients with history of heart disease, liver, kidney, lung, hypertension, diabetes, hypertriglyceridemia, thromboembolism, uterine and periosteal cancer, submucosal myoma greater than 3 cm, acute genital infection, uterine septum, pregnant women requiring transfusion, severe hemorrhage and the consumption of anticoagulants and dissatisfaction of patients were excluded from study. Both groups were matched for age, gravidity, parity and number of myomas. Transvaginal ultrasound, Pop smear, pipelle endometrial biopsy, platelet count and PT (prothrombin time), PTT (partial thromboplastin time), INR (international ratio), Hb (hemoglobin), HCT (hematocrit), BG (blood grop), RH, U / A (urine analysis), U / C (urine culture), SGPT, SGOT, β HCG, urea, creatinine, FBS, K, Na was performed before surgery for all patients.

The patients were then sent to the operating room. After general anesthesia and on arrival time of the hysteroscope into the uterus, 46 patients (first group) received 10mg / kg of tranexamic acid 10 mg / kg intravenous in 500 ml of the intravenous infusion by rate of 10 ml / min, and for 46 patients (second group), 5 units of oxytocin in 500 ml Ringer serum by 10 ml / min intravenous was infused. In both groups, dextrose solution 5% was used as a mediator for dilatation of the uterine cavity. The amount of hemorrhage during surgery was evaluated using the Visual Analog Scale (VAS) as fpllows: Grade 0 (without bleeding), Grade 1 (mild bleeding), Grade 2 (Moderate bleeding), Grade 3 (partial severe bleeding), Grade 4 (Severe bleeding) was determined based on agreement of physician and nurse of the operating room. The agreement between the observers (physician and nurse) in measuring the amount of bleeding during surgery was evaluated by two observers in 10% of the sample size and the Kappa agreement agreement was calculated as 80%. In cases where the agreement between clinician and nurse was not available, in order to determine the definitive opinion, the opinion of the third person was considered as the auxiliary nurse of the operating room. In this study, hemoglobin changes were considered as a primary outcome. Hemoglobin and hematocrit levels were determined 6 hours after surgery in both groups and the amount of hemorrhage in the objective method was determined by HCT-Hb difference before surgery and 6 hours after the operation. Then, the rate of bleeding based on VAS and objective was compared between the two groups.

During the surgery, after entering the hysteroscope, the amount of entered and shedded fluid into the uterus were measured ;and the amount of absorbed liquid was calculated by difference of these two value (in milliliters) after the completion of the myocardial resection. When the absorbed liquid reached 1500 ml, the surgery stopped. The complete resection of the myoma was referred when the myoma was separated from the endometrium to a depth of 1 to 2 mm below the lower layer of myometrium. The duration of hysteroscopy was calculated in minutes for both groups from entrance time of hysteroscope until exiting it from uterus. The brightness of image on monitor becomes bright and dark. To investigate the effects of oxytocin, blood pressure and heart rate was controlled during procedure, and decline of blood pressure of 90 mm and less, increased heart rate to 90 bpm or more were considered abnormal. One hour after the completion of procedure and ensuring of patient awareness, the side effects of tranexamic acid on nausea and vomiting, diarrhea and allergic dermatitis were recorded. The length of stay of each patient (i.e. day) in hospital was also recorded. Data analysis and statistical analysis were analyzed by descriptive statistics (mean \pm standard deviation, frequency, percentage) for comparing quantitative variables in two groups. The difference between mean of independent groups and of qualitative variables in two groups was performed

by Chi-square and Or Fisher's exact test if necessary, and analyzed using the Spss.21 statistical software. The p-value less than 5% was considered significant.

Results

This study was performed on 92 patients undergoing hysteroscopy and myomectomy. The first and second groups were treated by oxytocin and tranexamic acid. The mean age of first and second groups were 47.91 ± 9.14 (min: 31, max: 69 years) and 45.61 ± 8.67 (min:31 and max: 69 years) years, respectively. The minimum gravity was 0 in 2 cases (4.3%) and maximum was 8 in one case (2.2%) (mean: 3.46 ± 1.89) in tranexamic acid group and minimum gravity was 0 in 4 cases (8.7%) and maximum was 7 in one case (2.2%) (mean: 2.83 ± 1.84) in oxytocin group without significant differences between two groups (Table 1).

The mean parity of patients was 3.20 ± 1.83 in tranexamic acid and 2.61 ± 1.66 in oxytocin group without significant differences between two groups ($P = 0.853$). The mean value of endometrial thickness in first and second groups were 11.95 ± 4.4 mm and 11.63 ± 3.98 mm, respectively. Longitudinal dimension of uterus in first and second groups were 84 ± 27.39 mm and 85.75 ± 25.69 mm, respectively. The largest diameter of myoma in first and second groups were 19.05 ± 8.22 mm and 19.45 ± 11.01 mm, respectively. 35 patients (76.1%) and 39 patients (68.9%) in first and second groups had one myoma, respectively. It was also observed that all patients were discharged from the hospital on tomorrow of hysteroscopy. (Table 1).

Table 1: Patient characteristics in two groups of study

Variable	Tranexamic N=46 Mean± SD	Oxytocin N=46 Mean± SD	p-value
Age(year)	47.91±9.14	45.61±8.74	0.218
Gravity	3.46±1.89	2.83±1.84	0.109
Parity	3.20±1.83	2.61±1.66	0.112
Myoma	1.26±0.49	1.48±0.89	.134
Thickness of endometrium	11.95±4.4	11.63±3.98	0.711

The mean value of Hb levels before surgery were no significant differences in both groups. The mean value of Hb after surgery were no significant differences in both groups .The mean value of pre and post – operative Hb was 0.47 ± 0.16 mg/dL in first group and 0.80 ± 0.61 mg/dL in second group but there was not a significant difference.

The mean value of Hct levels before surgery were 36.62 ± 3.74 and 36.44 ± 3.22 mg/dL, respectively, there were no significant differences in both groups. The mean value of Hct after surgery were 34.9 ± 3.22 and 34.61 ± 3.17 mg/dL, respectively, there were no significant differences in both groups .The mean value of pre and post – operative Hct was 1.71 ± 1.36 mg/dL in first group and 1.83 ± 1.13 mg/dL in second group but there was not a significant difference .

Based on VAS, the results showed that 35 patients (76.1%), 11 cases (23.9%) and no case experienced no bleeding and mild bleeding, respectively. 6 patients (13%) had no bleeding during hysteroscopy in second group. There was significantly difference between two groups in grades 0,1 and 2 (Table 2).

Table 2: Variables which studied between two groups

Variable	Tranexamic N=46 Mean± SD	Oxytocin N=46 Mean± SD	p-value
Hemoglobin (mg / dl)			
Mean± SD			
Pre apportion	12.31±1.36	12.31±1.20	0.992
Post apportion	11.83±1.20	11.50±1.88	0.326
alteration	0.47±0.16	0.80±0.61	0.127
Hematocrit			
Mean± SD			
Pre apportion	36.62±3.74	36.44±3.22	0.812
Post apportion	34.9±3.56	34.61±3.17	0.683
alteration	1.71±1.36	1.83±1.13	0.797
Percentage of Bleeding during surgery N (%)			
Without bleeding	35(76.1)	6(13.0)	<0.001
Mild	11(23.9)	25(54.3)	0.003

Medium	0(0.0)	12(26.1)	<0.001
Severe	0(0.0)	3(6.5)	0.078

It was observed that the sodium and K level did not differ significantly between two groups pre – and post operatively. The duration of hysteroscopy was reported in first and second group were 11.5 ± 7.24 and 21.23 ± 11.7 minutes. (Table 3) The results showed that the mean of systolic blood pressure in first and second group was 125.08 ± 12.36 mmHg and in the oxytocin group was 121.91 ± 18.26 mmHg ($P = 0.332$). Heart rate was also detected, with an average of 74.43 ± 7.97 cm / min and an oxytocin group of 77.36 ± 8.01 per minute in first group ($P = 0.082$). It was demonstrated that mean value of absorbed volume in first and second group were 532.6 ± 510.03 and 620.39 ± 420.23 mL, respectively. 16 patients (43.8%) in second group had a dark hysteroscopy while in first group, only one case (2.2%) had a dark picture. This procedure was completely performed in first group, but in 3 patients of second group (6.5%), myomectomy was unsuccessful. The results of Pap smear showed that 8 patients (17.4%) and 3 patients (6.5%) had abnormal report. 6 patients (13.04%) experienced drug side effects in first group.

Table 3: Variables which studied between two groups

Variable Mean± SD	Tranexamic N=46	Oxytocin N=46	p-value
Sodium (meg / dl)			
Pre apportion	137.42±3.59	135.18±3.9	0.219
Post apportion	136.91±2.77	136.97±2.46	0.379
Alteration	1.14±0.98	2.87±1.22	0.134
Potassium(meg / dl)			
Pre apportion	3.98±0.54	3.55±0.3	0.164
Post apportion	3.66±0.53	3.62±0.18	0.826
Alteration	0.18±0.10	0.11±0.09	0.046
Duration of surgery (min)			
	11.5±7.24	21.23±11.7	<0.001
The interoperation absorbed volume	532.6±510.03	620.39±420.23	0.370
Resolution (%)			
Dark	1(2.2)	16(34.8)	
Bright	45(97.8)	30(65.2)	<0.001
Successful myomectomy			
Number(%)	43(93.5)	46(100)	0.078

Discussion

This study was conducted on 92 patients who undergoing hysteroscopy and myomectomy due to abnormal uterine bleeding. In evaluation of the severity of bleeding based on VAS, 76.1% of patients in tranexamic group and 13% of oxytocin group had not bleeding during hysteroscopy. In the other words, the incidence of hemorrhage in first group was significantly lower than in oxytocin group ($P=0.000$); hemoglobin and hematocrit alternation in two groups did not show any significant difference. In study of Pacheco et al. (2017), tranexamic acid, which was administered pre-emptively, it reduced the amount of bleeding during labor and need for blood transfusions. Mayur et al.(2007) reported that bleeding from labor to 2 hours after cesarean delivery was 472.79 ml in tranexamic acid recipients and 472.79 ml in placebo group, and tranexamic could reduce bleeding significantly. Shaaban et al. (2016), suggested mean value of hemoglobin and hematocrit in group did not differ significantly and postoperative hemoglobin and hematocrit levels were 9.09g/dL(29%) and 8.23g/dL (26.77%) in first and second groups, respectively; which showed a significant difference. Also, the amount of bleeding during and after surgery were 346.67 ml and 60.36 ml in first group, respectively, and in control group were 60.56 and 36.116 ml, which was reported higher bleeding rate in control group (i.e. the difference was significant). In the study Gobbur et al.(2017), the rate of bleeding during cesarean section was 289 ml in tranexamic acid group and 328 ml in control group ($P = 0.004$). Also, the rate of bleeding after cesarean delivery up to 2 hours was 360 mL in tranexamic acid group and 443 ml in control group ($P = 0.0008$), and it was able to reduce the amount of bleeding during and after C/S cesarean section. Sekhvat et al.(2009) reported that bleeding from the end of C/S was 28 ml in tranexamic group and 37 ml in control group ($P = 0.000$) up to 2 hours later, and Hb level was reported 12.5 in tranexamic acid group and 11.74 g/dL in placebo group ($P = 0.002$). The results showed that tranexamic acid could reduce the amount of bleeding after C/S and, on the other hand, it could maintain Hb levels at higher rates. Opoku-Anane et al.(2015), reported hemoglobin level was not significantly different with start of study. Mean value of hemorrhage was reported in tranexamic acid group 133.3 and in placebo group 180 ml ($P < 0.05$), however, the Hb level did not change significantly. The results of Wang et al.(2017) showed that transaxamic acid could lead to an insignificant decrease in postoperative hemoglobin ($P = 0.035$). Also, the amount of postoperative hemorrhage in tranexamic acid group was significantly lower than placebo group ($P = 0.016$). In survey and comparison with our study,

it can be seen that tranexamic acid is a drug that can be used in gynecologic surgeries and significantly reduced maternal hemorrhage in women who undergoing C/S as well as myomectomy.

In present study, the duration of hysteroscopy from the beginning until exitance of hysteroscope in tranexamic acid group was 11.5 minutes and in oxytocin group was 21.23 minutes, and the significance relationship between time of hysteroscopy and study group was observed ($P = 0.000$). Shaaban et al.(2016), suggested duration of myomectomy in group receiving tranexamic acid and in control group were 75.9 min, 86.7 min, respectively. This difference was statistically significant. Caglar et al. (2008), stated duration of myomectomy was 73 minutes in tranexamic group and 84 minutes in normal saline group, and it was observed that tranexamic acid ($P = 0.03$) significantly reduced duration of procedure. Wang et al. (2017) reported that tranexamic acid significantly reduced the duration of surgery ($P = 0.000$). We observed that tranexamic acid could significantly reduce the duration of surgery, and this reduction was also significant in present study.

In this study, hemodynamic changes in two groups did not show any significant difference. Also, the incidence of drug side effects in two groups did not show any significant difference. Pacheco et al. (2017) stated that tranexamic acid is safe and reliable in treatment of childbirth bleeding, and has very few side effects. In another study by Dunn and Goa (1999), was suggested tranexamic acid was able to reduce the incidence of bleeding in women with menorrhagia who compared to control group by 34-9.9%. It was also reported that drug could have remarkable effects on the rate of reduction bleeding in pediatric, postpartum hemorrhage, and post cervical conization. Mayur et al. (2007), showed heart rate, respiratory rate, systolic and diastolic blood pressure prior to labor, 1 and 2 hours after labor, did not show any changes in two groups. Shaaban et al. (2016),reported 12.1% nausea and 9.1% vomiting in case group and 1.5% nausea and vomiting in control ,there were noted the incidence of these complications was statistically significant. Caglar et al. (2008) showed need for blood transfusion was similar in two groups and did not show a significant difference. It was also stated in this study that the proposed protocol was easily tolerated in patients and the drug side effects were very uncommon (e.g. mainly digestive) and it did not differ significantly from placebo. No thrombotic events were observed in this study. Gobbur et al. (2017) also reported no significant complication in tranexamic group and there was no significant difference in incidence of side effectes in comparing with control group. Sekhvat et al. (2009), demonstrated no complication in two groups. In a study by Wang et al. (2017) the incidence of DVT ($P = 0.999$) and pulmonary embolism ($P = 0.617$) was not significantly different in studies compared with placebo group. The present study shows that used doses in gynecologic surgeries did not have any serious complications. There were no significant differences in gastrointestinal and neurological complications in placebo group. So you can use without stress in such patients.

Conclusion:

Our results showed tranexamic acid is a safe drug which could results in reduction of bleeding during surgery, shorter duration of surgery, and high resolution of hystereoscopy image in myomectomy.

Conflict of interest:

The authors stated that they have no conflict of interest.

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Limitation:

The low number of cases, we require to studies with higher number cases for definite recommendations.

References

- Ahonen J. The role of recombinant activated factor VII in obstetric hemorrhage. *Current Opinion in Anesthesiology*. 2012;25(3):309-14.
- Baird DD, Dunson DB, Hill MC, Cousins D, Schectman JM. High cumulative incidence of uterine leiomyoma in black and white women: ultrasound evidence. *American Journal of Obstetrics & Gynecology*. 2003;188(1):100-7.
- Caglar G, Tasci Y, Kayikcioglu F, Haberal A. Intravenous tranexamic acid use in myomectomy: a prospective randomized double-blind placebo controlled study. *European Journal of Obstetrics and Gynecology and Reproductive Biology*. 2008;137(2):227-31.
- Clevenger-Hoeft M, Syrop CH, Stovall DW, Van Voorhis BJ. Sonohysterography in premenopausal women with and without abnormal bleeding. *Obstetrics & Gynecology*. 1999;94(4):516-20.

- Di Spiezio Sardo A, Mazzon I, Bramante S, Bettocchi S, Bifulco G, Guida M, et al. Hysteroscopic myomectomy: a comprehensive review of surgical techniques. *Human Reproduction Update*. 2007;14(2):101-19.
- Dunn CJ, Goa KL. Fibrin sealant. *Drugs*. 1999;58(5):863-86.
- Emanuel MH, Wamsteker K, Hart AA, Metz G, Lammes FB. Long-term results of hysteroscopic myomectomy for abnormal uterine bleeding. *Obstetrics & Gynecology*. 1999;93(5):743-8.
- Gobbur VR, Shiragur SS, Jhanwar UR, Tehalia MJ. Efficacy of tranexamic acid in reducing blood loss during lower segment caesarean section. *International Journal of Reproduction, Contraception, Obstetrics and Gynecology*. 2017;3(2):414-7.
- Gutmann JN, Corson SL. GnRH agonist therapy before myomectomy or hysterectomy. *Journal of minimally invasive gynecology*. 2005;12(6):529-37.
- Khezri MB, Faraji-Soleimani F, Naseh N, Oveisi S. The effects of the combination of tranexamic acid and diclofenac on pain and post-operative bleeding in patients undergoing spinal anesthesia for cesarean. *KAUMS Journal (FEYZ)*. 2014;18(4):376-82.
- Lumsden MA, Wallace EM. 2 Clinical presentation of uterine fibroids. *Baillière's clinical obstetrics and gynaecology*. 1998;12(2):177-95.
- Marshall LM, Spiegelman D, Barbieri RL, Goldman MB, Manson JE, Colditz GA, et al. Variation in the incidence of uterine leiomyoma among premenopausal women by age and race. *Obstetrics & Gynecology*. 1997;90(6):967-73.
- Mayure G, Purvi P, Ashoo G, Pankaj D. Efficacy of tranexamic acid in decreasing blood loss during and after cesarean section: a randomized case controlled prospective study. *Jobstet gynecol india*, 2016;57(3):227-30.
- Opoku-Anane J, Vargas M, Moawad G, Cherie M, Robinson J. Use of intravenous tranexamic acid during myomectomy: a randomized double-blind placebo controlled trial. *Journal of minimally invasive gynecology*. 2015;22(6):S197.
- Pacheco LD, Hankins GD, Saad AF, Costantine MM, Chiossi G, Saade GR. Tranexamic acid for the management of obstetric hemorrhage. *Obstetrics & Gynecology*. 2017;130(4):765-9.
- Parker WH. Uterine myomas: management. *Fertility and sterility*. 2007;88(2):255-71.
- Sekhavat L, Tabatabaai A, Dalili M, Farajkhoda T, Tafti AD. Efficacy of tranexamic acid in reducing blood loss after cesarean section. *The Journal of Maternal-Fetal & Neonatal Medicine*. 2009;22(1):72-5.
- Shaaban MM, Ahmed MR, Farhan RE, Dardeer HH. Efficacy of tranexamic acid on myomectomy-associated blood loss in patients with multiple myomas: a randomized controlled clinical trial. *Reproductive Sciences*. 2016;23(7):908-12.
- Wamsteker K, Emanuel MH. Transcervical hysteroscopic resection of submucous fibroids for abnormal uterine bleeding: results regarding the degree of intramural extension. *Obstetrics and Gynecology*. 1993;82(5):736-40.
- Wang D, Wang L, Wang Y, Lin X. The efficiency and safety of tranexamic acid for reducing blood loss in open myomectomy: A meta-analysis of randomized controlled trials. *Medicine*. 2017;96(23).