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Original Research Article

Comparison of intravenous tranexamic acid versus sublingual misoprostol in reducing blood loss in patients undergoing caesarean section-an analytical observational study

Deeksha Rao M., Munikrishna M.*

Department of Obstetrics and Gynaecology, Sri Devaraj URS Medical College, Kolar, Karnataka, India

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***Correspondence:**
Dr. Munikrishna M.,
E-mail: drmunikrishna_m@rediffmail.com

ABSTRACT

Background: Preventing postpartum haemorrhage using uterotonics or other antifibrinolytic drugs is need of the hour among women undergoing caesarean section (CS). This study is to compare the effectiveness of intravenous Tranexamic acid versus sublingual misoprostol in reducing blood loss by assessing intraoperative and postoperative blood loss in patients undergoing CS.

Methods: Analytical observational study was conducted in department of obstetrics and gynaecology at sri Devaraj URS medical college, among 118 pregnant women admitted for CS. Study was conducted between January 2020 to June 2021. The sample was divided equally into intravenous tranexamic acid and sublingual misoprostol groups. Number of mops, pads soaked, suction volume excluding the amniotic fluid, preoperative and post-operative haemoglobin, any complication were recorded.

Results: The mean of mops counts in the misoprostol, TXA group were noted as 4.73±1.27, 3.2±1.45 respectively. Around 8.47% of the participants in the misoprostol group required uterotonics, whereas, 15.25% in the TXA group required uterotonics. The preoperative and postoperative haemoglobin in misoprostol group were identified as 11.67±1.37, 10.78±1.12 respectively, whereas it was identified as 11.76±1.43, 11.17±1.4 in TXA group. The common side effects identified in the misoprostol group was chills, vomiting and fever with 47.46%, 13.56% and 11.86% while, it was 11.86%, 5.08% and 3.39% in the TXA group.

Conclusions: Both intravenous tranexamic acid, sublingual misoprostol could be prescribed as standard therapy to significantly control blood loss and increase the quality of surgery with better outcomes. But the use of TXA proved slightly better as there were lesser side effects and significantly lesser blood loss in uncomplicated cases.

Keywords: Haemorrhage, Uterotonics, CS, Postpartum, Anti-fibrinolytic agents

INTRODUCTION

Obstetric haemorrhage is the leading cause of maternal mortality worldwide, irrespective of the mode of delivery. CS is one of the most commonly performed major operations in women throughout the world, escalating between 20 and 30% in most developed countries over the past four decades.[1] India is representative of the magnitude of this problem. The increasing incidence of CS has contributed to postpartum haemorrhage (PPH), as the average blood loss during CS is twice that of vaginal delivery, which accounts for nearly 25% of maternal deaths.[2,3] Annually about 530000 women die in the world as a consequence of pregnancy or childbirth, and 14 million women suffer blood loss, with 2% of deaths occurring in 2-4 hours after blood loss starts.[4] Although there has been a remarkable improvement in the prevention and treatment of blood loss during CS in recent years, deaths due to blood loss remain relatively common in some parts of the world. To lower the occurrence rate of major morbidity and mortality due to blood loss during CS,

preventive measures should be taken to reduce intraoperative blood loss during CS.

Anti-fibrinolytic agents, such as tranexamic acid (TA), reduce the risk of death due to bleeding in trauma patients, and it has been suggested that TA administration reduces blood loss in females after vaginal or elective CS.[5] A recent systematic review and mathematical model estimated that almost 22,000 deaths per year could be averted worldwide if TXA were used prophylactically.[6] Misoprostol is a synthetic prostaglandin E1 analog, commonly used for the prevention and management of post-operative blood loss with potent uterotonic properties and fewer side effects at therapeutic doses and can be used in low-resource settings.[7] Youssef et al found preoperative administration of sublingual misoprostol (400 µg) during CS is better than postoperative administration, with reduced intraoperative and postoperative blood loss and drop in hemoglobin levels.[8]

Despite searching the available evidence, it was found that there is a dearth of literature regarding the efficacy of intravenous TA and sublingual misoprostol in reducing bleeding after CS, especially in developing countries like India. Sahhaf et al found no significant differences between misoprostol to TXA and suggested more studies with a greater population.[9] Therefore, this study was designed to evaluate and compare the efficacy of these two therapeutic options in controlling blood loss following CS.

Aims and objectives

Aim and Objectives were to compare the effectiveness of intravenous tranexamic acid versus sublingual misoprostol in reducing blood loss by assessing intraoperative and postoperative blood loss in patients undergoing CS.

METHODS

Study design

Analytical observational study was used.

Study setting

This study was conducted in the department of obstetrics and gynaecology at sri Devaraj URS medical, Tamaka, Kolar.

Source population

Pregnant women visiting the department of obstetrics and gynaecology at sri Devaraj URS medical, Tamaka, Kolar.

Study population

All the eligible patients admitted for CS in the department of obstetrics and gynaecology at sri Devaraj URS medical college were considered as the study population.

Study period

The study conducted between January 2020 to June 2021.

Sample size

The sample size was calculated based on the mean suction blood loss in both tranexamic acid and misoprostol groups in a previous study by Pakhniat et al.[10] Thus considering a 90% power and an alpha error of 1%, a sample size of 59 was taken in each group.

Group A (59)-Intravenous tranexamic acid will be given. (A dose of 1 gram slowly over 2 minutes, at least 10 minutes before the start of the procedure). Group B (59)-Sublingual misoprostol of 400 mcg as soon as the baby was born. In both groups, 20 units of oxytocin were administered in 1 L of RL with the rate of 1000 CC/h.

Sampling technique

All eligible subjects recruited into study consecutively by convenient sampling for feasibility of study.

Ethics statement

The study was approved by the institutional human ethics committee and institutional review board [Reference: SDUMC/KLR/IEC/147/2019-20]. Data confidentiality was maintained. Written informed consent was obtained from the patients.

Inclusion criteria

Woman aged between completed 18 and 40 years, gestational age between 37 weeks and 42 weeks, singleton pregnancy and patients undergoing lower segment CS under spinal anesthesia were included in the study.

Exclusion criteria

Antepartum hemorrhage, pre-eclampsia and eclampsia, any underlying disease (heart, liver, kidney, pulmonary), allergic to tranexamic acid (allergy, thromboembolic events during pregnancy) and misoprostol. Coagulation disorders, intrauterine fetal demise, polyhydramnios, fibroid, DIC, anticoagulant therapy and previous history of uterine rupture were excluded.

Data collection

All the relevant parameters were documented in a structured study proforma. All the routine investigations required for preoperative evaluation were done for the proposed surgery. In the operating room, the IV line was secured, and the patient was shifted to the OT room under aseptic precaution. The patient was painted and draped. Spinal anesthesia was given, and a CS was done. Intraoperatively, the vitals were recorded.

Parameters observed

Number of mops, pads soaked, suction volume excluding the amniotic fluid. Preoperative and postoperative hemoglobin and the presence of any complication in the preoperative and postoperative periods was noted, particularly in relation to respiratory or cardiovascular problems, nausea or vomiting, and headache.

Operational definitions

Primary PPH is defined as a blood loss of more than 1000 ml during the first 24 hours after delivery, and it is the most common cause of maternal mortality worldwide.[11]

Study variables

Mops, suction volume, preoperative HB, and postoperative HB were considered as primary outcome variables.

Statistical analysis

Descriptive analysis was carried out by mean and standard deviation for quantitative variables, frequency, and proportion for categorical variables. Categorical outcomes were compared between study groups using the Chi-square test /Fisher's Exact test. For normally distributed Quantitative parameters, the mean values were compared between study groups using an independent sample t-test. The change in the quantitative parameters before and after the intervention was assessed by paired t-test. P<0.05 was considered statistically significant. IBM SPSS version 22 was used for statistical analysis.[12]

RESULTS

A total of 118 subjects were included in the final analysis. Mean age of women in tranexamic acid group was 24.12±3.3 years and in misoprostol group it was 23.81±3.64 years. Mean age difference between 2 groups was not statistically significant (p=0.634). The 43 (72.88%) in tranexamic acid group and 42 (71.19%) in misoprostol group in between 37-40 weeks gestational age. Difference in terms of gestational age not statistically significant (p=0.837). The 38 (64.41%) in tranexamic acid group, and 35 (59.32%) in misoprostol group had emergency CS and difference of groups in terms of type of CS was not statistically significant (p=0.57) (Table 1).

The mean of mops count was 3.2±1.45 in tranexamic acid group, and 4.73±1.27 in misoprostol group. The difference in mops count between study groups was statistically significant (p<0.001). In tranexamic acid group, 6 (10.17%) participants suction volume was less than 200 ml, for 26 (44.07%) it was between 200 to 400 ml and 27 (45.76%) had between 400 to 600 ml. In misoprostol group, 8 (13.56%) had suction volume less than 200 ml, 29 (49.15%) had between 200 to 400 ml and 22 (37.29%) had between 400 to 600 ml and difference in proportions between the groups was statistically not significant (p=0.619). Nine (15.25%) participants in tranexamic acid group and 5 (8.47%) in misoprostol group needed uterotonics and difference in proportions between groups was statistically not significant (p=0.255). Only 1(1.69%) participant needed additional procedure (bilateral internal iliac artery ligation) to control intraoperative bleeding and 2 (3.39%) participants needed blood transfusion in tranexamic acid group (Table 2).

Table 1: Comparison of baseline and maternal parameters between study groups, (n=118).

Parameters	Study groups (Mean± SD)		P value
	Tranexamic acid, (n=59) (%)	Misoprostol, (n=59) (%)	
Age (Years)	24.12±3.3	23.81±3.64	0.634
Gestational age (weeks)			
37-40	43 (72.88)	42 (71.19)	0.837
40+1-42	16 (27.1)	17 (28.81)	
Type of CS			
Elective	21(35.59)	24 (40.68)	0.57
Emergency	38 (64.41)	35 (59.32)	

Table 2: Comparison of baseline and maternal parameters between study groups, (n=118).

Parameters	Study groups (Mean ± SD)		P value
	Tranexamic acid, (n=59) (%)	Misoprostol, (n=59) (%)	
Mops count	3.2±1.45	4.73±1.27	<0.001
Suction volume (ml)			
<200	6 (10.17)	8 (13.56)	0.619
200-400	26 (44.07)	29 (49.15)	
400-600	27 (45.76)	22 (37.29)	
Need for uterotonics	9 (15.25)	5 (8.47)	0.255
Additional procedure required	1 (1.69)	0 (0)	*
Blood transfusion	2 (3.39)	0 (0)	*

*No statistical test was applied- due to 0 subjects in the cells.

There is reduction in post-op hemoglobin in both groups when compared to preoperative hemoglobin, however, the mean difference was high in misoprostol group (Table 3).

Out of 59 participants in tranexamic acid group, 7 (11.86%) participants had chills, 3 (5.08%) participants had vomiting, 2 (3.39%) participants had fever and 5 (8.47%) participants had headache. Out of 59 participants in misoprostol group, 28 (47.46%) participants had chills, 8 (13.56%) participants had vomiting, 7 (11.86%) participants had fever and 4 (6.78%) participants had headache. The difference between two groups was statistically significant (p<0.001) (Figure 1).

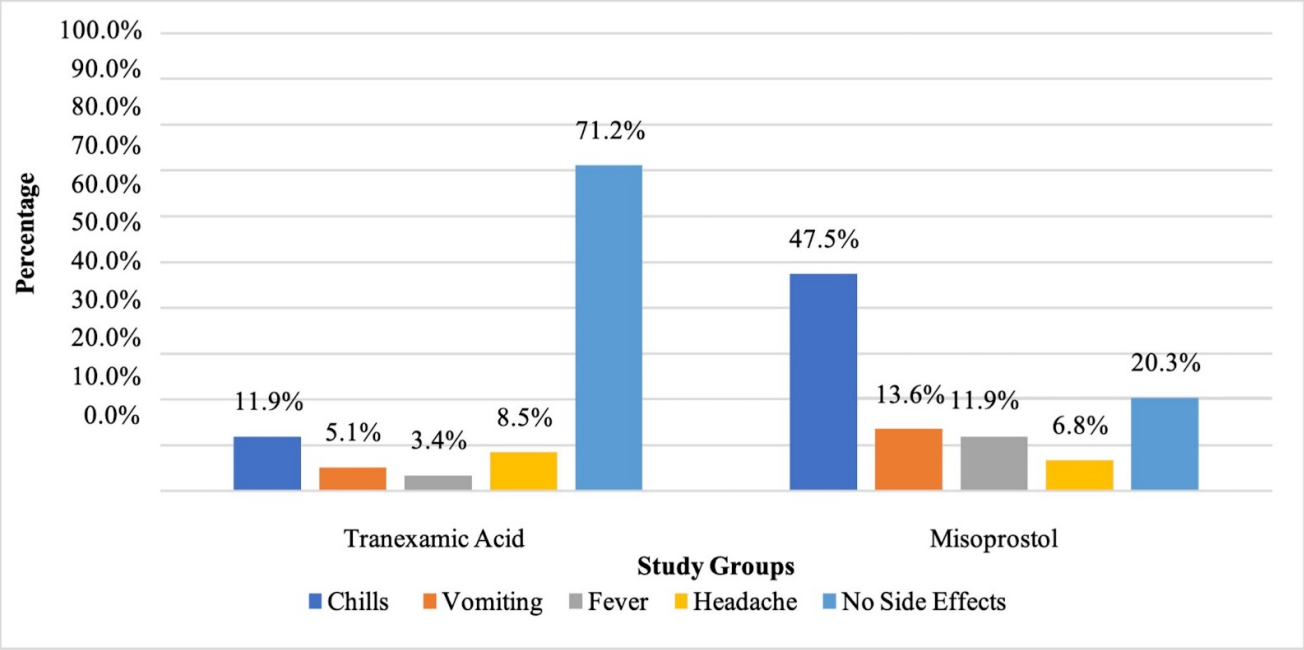

Figure 1: Cluster bar chart of comparison of side effects between study groups, (n=118).

Out of 118 participants in total, 25 patients underwent elective CS, 24 patients underwent emergency CS in view of fetal distress, 16 in view of previous CS and 16 in view of maternal desire (Table 4).

Table 3: Comparison of hemoglobin pre to post in 2 groups individually, (n=118).

HB (g/dl)	Mean ± SD	Mean difference	P value
Tranexamic acid			
Pre-operative	11.76±1.43	0.59	<0.001
Post-operative	11.17±1.4		
Misoprostol			
Pre-operative	11.67±1.37	0.89	<0.001
Post-operative	10.78±1.12		

Table 4: Descriptive analysis of indication in the study groups, (n=118).

Indication	N	Percentages (%)
Previous LSCS (Elective)	25	21.19
Fetal distress	24	20.34
CDMR	16	13.56
Previous LSCS (Emergency)	16	13.56
CPD	8	6.78
Oligohydramnios	7	5.93
Contracted pelvis	6	5.08
Failed induction	5	4.24
Malpresentation	4	3.39
Deep transverse arrest	4	3.39
Malpresentation	3	2.54

DISCUSSION

According to the results, there was a significant reduction in postoperative haemoglobin in both groups when compared to the preoperative haemoglobin. However, the mean difference was high in the Misoprostol group (p<0.001). There are various studies regarding drugs used to control blood loss during CS. However, authors could not come across many published studies that compared the efficacy of misoprostol and TXA during CS to prevent post-operative blood loss. Hence, authors had to analyse results with existing data comparing misoprostol and oxytocin, and those between TXA and oxytocin infusion. Pakniat et al found significantly lower total bleeding in sublingual misoprostol compared to the tranexamic acid group.[10] Hemodynamic variables were stabilized greater in the misoprostol group than in the tranexamic acid group. Sahhaf et al found no significant differences between misoprostol and tranexamic acid group in haemorrhage during labour, postpartum haemoglobin level, and discharge haemoglobin level, and stated that Misoprostol has no specific preferences to TXA.[9] The differences in results may be due to the type and dosage of administered drugs. Bose et al found statistically insignificant reduction in blood loss in the TXA group compared with the misoprostol group, irrespective of the presence or absence of high-risk factors (470.30 vs 491.74 mL, p=0.487).[2]

One (1.69%) participant needed an additional procedure to control intraoperative bleeding, and 2 (3.39%) participants needed a blood transfusion in the tranexamic acid group in the present study. Li et al in their systematic review and meta-analysis found the lesser risk of blood transfusions with tranexamic acid, which contrast with the present study finding.[13] Chaudhuri et al compared Misoprostol and oxytocin versus oxytocin and placebo in reduction of

blood loss during and after CS.[14] The mean postoperative blood loss was lower in the misoprostol group than in the placebo group, but the difference was not statistically significant (p=0.07). In the present study, sublingual Misoprostol of 400mcg was given as soon as the baby was born, and 20 units of oxytocin were administered in 1 L of RL at the rate of 1000 CC/h.

In present study, misoprostol group had higher side effects, with 28 (47.46%) participants having chills, 8 (13.56%) having vomiting, and 7 (11.86%) having fever. Similarly, Othman et al found more frequent temporary side effects, including shivering and metallic taste, with use of sublingual misoprostol.[15] Tabatabaie et al found no side effects, as nausea and diarrhoea with tranexamic acid, and also no complications of misoprostol, as headache, nausea, uterine cramps, stomach ache, diarrhoea, flatulence, and fever, or serious complications, such as uterine rupture, coagulation disorders, as well as severe and abnormal vaginal bleeding.[16] Okonofua et al reported to include additional uterotonics and other ancillary treatments for ineffective reduction of blood loss due to PPH.[17]

Most reported studies used sublingual misoprostol to manage post-operative blood loss; nevertheless, a few studies used it as a preventive measure, as the current study. Our study supports the fact that sublingual misoprostol is effective in reducing postpartum blood loss and required less additional oxytocic drugs but without statistical significance. In comparison to the oral and rectal route, sublingual administration is more convenient, leads to rapid absorption, and effects are comparable.[15]

A CS is the most common major operation performed on women worldwide. Despite routine use of oxytocin during caesarean delivery, a number of women, especially those at high risk, may develop uterine atony and haemorrhage either during surgery or in the immediate postoperative period, with serious consequences. Any modality of treatment, which helps in its prevention, will be useful in reducing maternal mortality and morbidity. Misoprostol is an evidence-based alternative to other uterotonic agents due to its wide availability, low cost, stability at room temperature, and ease of use. Intra-venous administration of TXA has been routinely used for many years to reduce haemorrhage during and after many surgical procedures. And it's use has been increasing in recent years as it has shown to be effective and safe in women undergoing CS.[18]

The council on patient safety in women's health care outlined essential steps that delivery units should take to decrease the incidence and severity of postpartum hemorrhage.[19] The creation of a haemorrhage cart with supplies and the use of huddles, rapid response teams, and massive transfusion protocols are among the recommendations. Advanced life support in obstetrics (ALSO) training can be part of a systems approach to improving patient care. The use of interdisciplinary team training with, *in situ* simulations, available through the ALSO program and from team STEPPS (Team strategies and tools to enhance performance and patient safety), has been shown to improve perinatal safety.[20]

Limitations

The study was conducted in a single center, and findings cannot be applied to general community. The dose response or the effects of multiple dose therapy were not evaluated in present study. Accuracy in estimating blood loss cannot be ensured. the relationship between the causes of CS and the level of bleeding was not assessed in the current study. Further multicentric studies with large sample are recommended to support the findings of present study.

CONCLUSION

Both intravenous tranexamic acid and sublingual misoprostol could be prescribed as standard therapy to significantly control blood loss and increase the quality of surgery with better outcomes. But the use of TXA proved slightly better as there were lesser side effects and significantly lesser blood loss in uncomplicated cases.

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REFERENCES

1. Martin JA, Hamilton BE, Sutton PD, Ventura SJ, Mathews TJ, Kirmeyer S et al. Births: final data for 2007. Natl vital Stat. 2010;58(24):1-85.
2. Bose D, Beegum R. Sublingual Misoprostol vs Intravenous Tranexamic Acid in reducing Blood Loss during Cesarean Section: A Prospective Randomized Study. J South Asian Fed Obstet Gynaecol. 2017;9(1):9-13.
3. Mirghafourvand M, Mohammad-Alizadeh S, Abbasalizadeh F, Shirdel M. The effect of prophylactic intravenous tranexamic acid on blood loss after vaginal delivery in women at low risk of postpartum haemorrhage: A double-blind randomised controlled trial. Aust N Zeal J Obstet Gynaecol. 2015;55(1):53-58.
4. Quantin C, Benzenine E, Ferdynus C, Sediki M, Auverlot B, Abrahamowicz M et al. Advantages and limitations of using national administrative data on obstetric blood transfusions to estimate the frequency of obstetric hemorrhages. J Public Heal (United Kingdom). 2013;35(1):147-56.
5. Alam A, Choi S. Prophylactic Use of Tranexamic Acid for Postpartum Bleeding Outcomes: A Systematic Review and Meta-Analysis of Randomized Controlled Trials. Transfus Med Rev. 2015;29(4):231-41.
6. McClure EM, Jones B, Rouse DJ, Griffin JB, Kamath-Rayne BD, Downs A et al. Tranexamic acid to reduce postpartum hemorrhage: A MANDATE systematic

review and analyses of impact on maternal mortality. Am J Perinatol. 2015;32(5):469-74.
7. Bahadur A, Khoiwal K, Bhattacharya N, Chaturvedi J, Kumari R. The effect of intrauterine misoprostol on blood loss during caesarean section. J Obstet Gynaecol (Lahore). 2019;39(6):753-6.
8. Youssef AEA, Khalifa MA, Bahaa M, Abbas AM. Comparison between Preoperative and Postoperative Sublingual Misoprostol for Prevention of Postpartum Hemorrhage during Cesarean Section: A Randomized Clinical Trial. Open J Obstet Gynecol. 2019;09(04):529-38.
9. Sahhaf, Abbasalizadeh S, Ghojazadeh M, Velayati A, Khandanloo R, Saleh P et al. Comparison effect of intravenous tranexamic acid and misoprostol for postpartum haemorrhage. Niger Med J. 2014;55(4):348.
10. Pakniat H, Chegini V, Shojaei A, Khezri MB, Ansari I. Comparison of the Effect of Intravenous Tranexamic Acid and Sublingual Misoprostol on Reducing Bleeding After Cesarean Section: A Double-Blind Randomized Clinical Trial. J Obstet Gynecol India. 2019;69(3):239-45.
11. American College of Obstetricians and Gynecologists. ACOG Practice Bulletin No. 76: Postpartum Hemorrhage. Obstet Gynecol. 2006;108(4):1039-48.
12. IBM Corp. IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp. 2013.
13. Li C, Gong Y, Dong L, Xie B, Dai Z. Is prophylactic tranexamic acid administration effective and safe for postpartum hemorrhage prevention? A systematic review and meta-analysis. Med (United States). 2017;96(1):1-11.
14. Chaudhuri P, Mandi S, Mazumdar A. Rectally administrated misoprostol as an alternative to intravenous oxytocin infusion for preventing post-partum hemorrhage after cesarean delivery. J Obstet Gynaecol Res. 2014;40(9):2023-30.
15. Othman ER, Fayez MF, El Aal DEMA, El-Dine Mohamed HS, Abbas AM, Ali MK. Sublingual misoprostol versus intravenous oxytocin in reducing bleeding during and after cesarean delivery: A randomized clinical trial. Taiwan J Obstet Gynecol. 2016;55(6):791-5.
16. Tabatabaie SS, Alavi A, Bazaz M. Comparison of the effect of tranexamic acid and misoprostol on blood loss during and after cesarean section: A randomized clinical trial. Razavi Int J Med. 2021;9(1):e811.
17. Okonofua FE, Ogu RN, Akuse JT, Ujah IAO, Galadanci HS, Fabamwo AO. Assessment of sublingual misoprostol as first-line treatment for primary post-partum hemorrhage: Results of a multicenter trial. J Obstet Gynaecol Res. 2014;40(3):718-22.
18. Hua J, Chen G, Xing F, Scott M, Li Q. Effect of misoprostol versus oxytocin during caesarean section: a systematic review and meta-analysis. BJOG An Int J Obstet Gynaecol. 2013;120(5):531-40.
19. Main EK, Goffman D, Scavone BM, Low LK, Bingham D, Fontaine P et al. National Partnership for Maternal Safety: Consensus Bundle on Obstetric Hemorrhage. Obs Gynecol. 2015;126(1):155-62.
20. Evensen A, Anderson JM, Fontaine P. Postpartum Hemorrhage: Prevention and Treatment. Am Fam Physician. 2017;95(7):442-9.

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