Οργάνωση

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Ξενοδοχείο
Domotel Xenia
Volos, Βόλος

ΣΥΝΤΗΡΗΤΙΚΗ ΑΝΤΙΜΕΤΩΠΙΣΗ ΑΙΜΟΡΡΑΓΙΑΣ ΜΕΤΑ ΤΟΝ ΤΟΚΕΤΟ

ΠΑΝΑΓΙΩΤΗΣ ΠΕΪΤΣΙΔΗΣ MSC PHD
ΜΑΙΕΥΤΗΡΑΣ ΧΕΙΡΟΥΡΓΟΣ ΓΥΝΑΙΚΟΛΟΓΟΣ
ΔΙΔΑΚΤΩΡ ΠΑΝΕΠΙΣΤΗΜΙΟΥ ΑΘΗΝΩΝ

ΕΜΓΕ
Ελληνική Μαιευτική και Γυναικολογική Εταιρεία

Κατευθυντήρια Οδηγία Νο 24
Νοέμβριος 2014

Αιμορραγία μετά τον τοκετό

Αιμορραγία μετά τον τοκετό είναι η απώλεια αίματος σε τέτοια ποσότητα ώστε να προκαλέσει αιμοδυναμική αστάθεια. Η μέση απώλεια αίματος σε κολπικό τοκετό είναι 500ml και σε καισαρική τομή είναι 1000ml. Από το σύνολο των κολπικών τοκετών το 4% περιπλέκονται με απώλεια αίματος μεγαλύτερης των 500ml στις πρώτες 24 ώρες [1]

Ως ελάσσονα αιμορραγία ορίζουμε την απώλεια 500-1000 ml αίματος και ως μείζονα την απώλεια αίματος μεγαλύτερη από 1000 ml. Με τη σειρά της η μείζονα αιμορραγία μπορεί να διακριθεί σε μέτρια όταν η απώλεια είναι 1000- 2000ml και σοβαρή όταν είναι μεγαλύτερη από 2000ml.

Επίσης δευτεροπαθής ονομάζεται η αιμορραγία μετά τις 24 ώρες και 12 εβδομάδες μετά τον τοκετό [2].

Η μαιευτική αιμορραγία παραμένει μια από τις κύριες αιτίες μητρικής θνησιμότητας τόσο στις αναπτυσσόμενες όσο και στις αναπτυγμένες χώρες, προκαλώντας 125.000 θανάτους ετησίως επι συνόλου 125.000.000 γεννήσεων. Το ποσοστό αυτό αντιστοιχεί σε 1 θάνατο ανά 1000 γεννήσεις [3]. Στις ΗΠΑ ευθύνεται για 7,5 θανάτους ανά 100.000 γεννήσεις [4], ενώ στο Ηνωμένο Βασίλειο είναι η τρίτη αιτία μητρικής θνησιμότητας και ευθύνεται για 1 θάνατο ανά 100.000 γεννήσεις [5].

1. Combs, C.A., E.L. Murphy, and R.K. Laros, Jr., Factors associated with postpartum hemorrhage with vaginal birth. Obstet Gynecol, 1991. 77(1): p. 69-76.
2. Alexander, J., P. Thomas, and J. Sanghera, Treatments for secondary postpartum haemorrhage. Cochrane Database Syst Rev, 2002(1): p. CD002867.
3. Thaddeus, S. and D. Maine, Too far to walk: maternal mortality in context. Soc Sci Med, 1994. 38(8): p. 1091-110.
4. Berg, C.J., et al., Pregnancy-related mortality in the United States, 1987-1990. Obstet Gynecol, 1996. 88(2): p. 161-7.
5. Penney, G. and V. Brace, Near miss audit in obstetrics. Curr Opin Obstet Gynecol, 2007. 19(2): p. 145-50.

ΑΙΤΙΑ ΑΙΜΟΡΡΑΓΙΑΣ ΜΕΤΑ ΤΟΝ ΤΟΚΕΤΟ

4T's	Αίτια	Συχνότητα
Tone (Τόνος)	Ατονία μήτρας	70%
Trauma (Τραυματισμός)	Τραχηλικές, κολπικές και περινεϊκές κακώσεις, αιμάτωμα της πυέλου, εκτροφή-ρήξη μήτρας	20%
Tissue (Ιστός)	Παθολογική πρόσφυση πλακούντα, υπολείμματα πλακούντα	10 %
Thrombin (Πήξη)	Διαταραχές μηχανισμού πήξης	1%

- **Συντηρητική αντιμετώπιση Μαιευτικής αιμορραγίας**

ΧΟΡΗΓΗΣΗ ΥΓΡΩΝ

ΚΡΥΣΤΑΛΛΟΕΙΔΉ – ΚΟΛΛΟΕΙΔΉ ΑΠΑΙΤΕΊΤΑΙ ΙΔΙΑΊΤΕΡΗ ΠΡΟΣΟΧΉ ΣΤΗ ΧΟΡΉΓΗΣΗ ΥΓΡΏΝ ΓΙΑΤΊ ΕΙΔΙΚΆ ΜΕ ΤΑ ΚΟΛΛΟΕΙΔΉ ΠΡΟΚΎΠΤΕΙ ΣΗΜΑΝΤΙΚΉ ΑΙΜΟΑΡΑΊΩΣΗ ΜΕΊΩΣΗ ΠΑΡΑΓΌΝΤΩΝ ΠΗΚΤΙΚΌΤΗΤΑΣ ΚΑΙ ΔΕΥΤΕΡΟΓΕΝΕΊΣ ΔΙΑΤΑΡΑΧΈΣ ΠΗΚΤΙΚΌΤΗΤΑΣ

ΜΗΤΡΟΣΥΣΠΑΣΤΙΚΆ: ΩΚΥΤΟΚΊΝΗ, ΜΕΘΥΛΕΡΓΟΝΟΒΊΝΗ, ΠΡΟΣΤΑΓΛΑΝΔΊΝΕΣ, ΚΑΡΜΠΕΤΟΚΊΝΗ

BR J ANAEST 2008;100:307-314

- **Μετάγγιση παραγώγων αίματος: συνήθης τακτική** •
- Αναλογία RBCs: FFP:PLTS 1:1:1 ή 2:1 ή 1:3. Ανάλογα με την τιμή Hb στόχος >8mgr/dl • Ανάλογα με την κλινική εικόνα •
- **Μαλάξεις μήτρας και αμφίχειρη συμπίεση και τοποθέτηση ουροκαθετήρα.**

- Solomon C et al: BJA 2012;109(6):851-63 • Lange N et al: Obst & Gyn Survey 2012;67(7):426-436

ΝΕΟΤΕΡΑ ΔΕΔΟΜΕΝΑ

ΣΥΝΤΗΡΗΤΙΚΗ ΑΝΤΙΜΕΤΩΠΙΣΗ ΤΗΣ ΑΙΜΟΡΡΑΓΙΑΣ ΜΕΤΑ ΤΟΝ ΤΟΚΕΤΟ ΜΕ ΑΝΑΣΤΟΛΕΙΣ ΙΝΩΔΟΛΥΣΗΣ

- **Αναστολείς Ινωδόλυσης**

Ε-αμινοκαπροικό οξύ (EACA)
Τρανεξαμικό οξύ (ΤΧΑ)
Απροτινίνη (Νεφροτοξική)

UTAKO OKAMOTO 1918-2016

ΙΣΤΟΡΙΚΑ ΣΤΟΙΧΕΙΑ ΤΧΑ

ΑΝΑΚΑΛΥΦΘΗΚΕ ΤΟ 1950 ΑΠΌ ΤΗΝ ΕΡΕΥΝΗΤΙΚΗ ΟΜΑΔΑ ΤΗΣ **UTAKO OKAMOTO** ΣΤΟ ΠΑΝΕΠΙΣΤΗΜΙΟ ΚΕΙΟ ΤΟΥ ΤΟΚΥΟ ΜΕ ΣΚΟΠΟ ΤΗΝ ΑΝΤΙΜΕΤΩΠΙΣΗ ΤΗΣ ΑΙΜΟΡΡΑΓΙΑΣ ΜΕΤΑ ΤΟΝ ΤΟΚΕΤΟ.

Η ΟΚΑΜΟΤΟ ΜΕΛΕΤΗΣΕ ΑΡΧΙΚΑ ΤΟ **EACA** ΑΛΛΑ ΣΤΗΝ ΣΥΝΕΧΕΙΑ ΠΡΟΧΩΡΗΣΕ ΣΤΗΝ ΣΥΝΘΕΣΗ ΚΑΙ ΜΕΛΕΤΗ ΤΟΥ **ΤΧΑ** ΤΟ ΟΠΟΙΟ ΕΙΧΕ ΙΣΧΥΡΟΤΕΡΗ ΑΝΑΣΤΑΛΤΙΚΗ ΔΡΑΣΗ ΣΤΗΝ ΙΝΩΔΟΛΥΣΗ.

ΤΟ 1962 ΔΗΜΟΣΙΕΥΤΗΚΑΝ ΤΑ ΠΡΩΤΑ ΑΠΟΤΕΛΕΣΜΑΤΑ ΠΟΥ ΑΦΟΡΟΥΣΑΝ ΤΗΝ ΣΥΝΘΕΣΗ ΚΑΙ ΔΡΆΣΗ ΤΟΥ ΦΑΡΜΑΚΟΥ

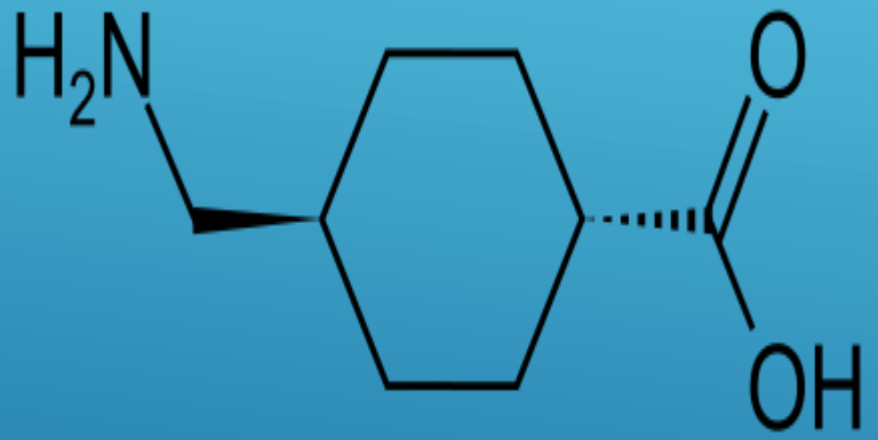
ΣΥΓΚΑΛΕΓΕΤΑΙ ΑΠΌ ΤΟ 2009 ΣΤΗ **WHO LIST OF ESSENTIAL DRUGS**

Bringing women to the forefront of science and medicine".
The Lancet. 10 March 2012.
Tranexamic acid. Keio Journal of Medicine.1962

ΦΑΡΜΑΚΟΛΟΓΙΑ ΤΧΑ

- Το Τρανεξαμικό οξύ (ΤΧΑ) είναι συνθετικό παράγωγο του αμινοξέος λυσίνη το οποίο αναστέλλει την μετατροπή του πλασμινογόνου σε σερινική πρωτεάση πλασμίνη . Η αναστολή αυτή οφείλεται στην σύνδεση του ΤΧΑ στις θέσεις 4 και 5 των υποδοχέων λυσίνης του πλασμινογόνου . Με τον τρόπο αυτό επιτυγχάνεται η αναστολή του μηχανισμού της ινωδόλυσης.
- Έχει 8 φορές μεγαλύτερη αντιινωδολυτική δράση από το EACA
- Χρόνος ημίσειας ζωής 120 min.
- Συγκαταλέγεται σε Φάρμακό κατηγορίας Β όσον αφορά την κύηση (Δεν υπάρχουν ολοκληρωμένες μελέτες ότι προκαλεί τερατογένεση).
- Διαπερνά τον πλακούντα, παρατηρούνται ίδια επίπεδα ΤΧΑ στο πλάσμα και στον ομφάλιο λώρο σε έγκυες γυναίκες .
- Δεν αντενδείκνυται στον θηλασμό, 1 % ΤΧΑ ανευρίσκεται στο μητρικό γάλα.
- *British national formulary: BNF 69* (69 ed.). British Medical Association. 2015. p. 170

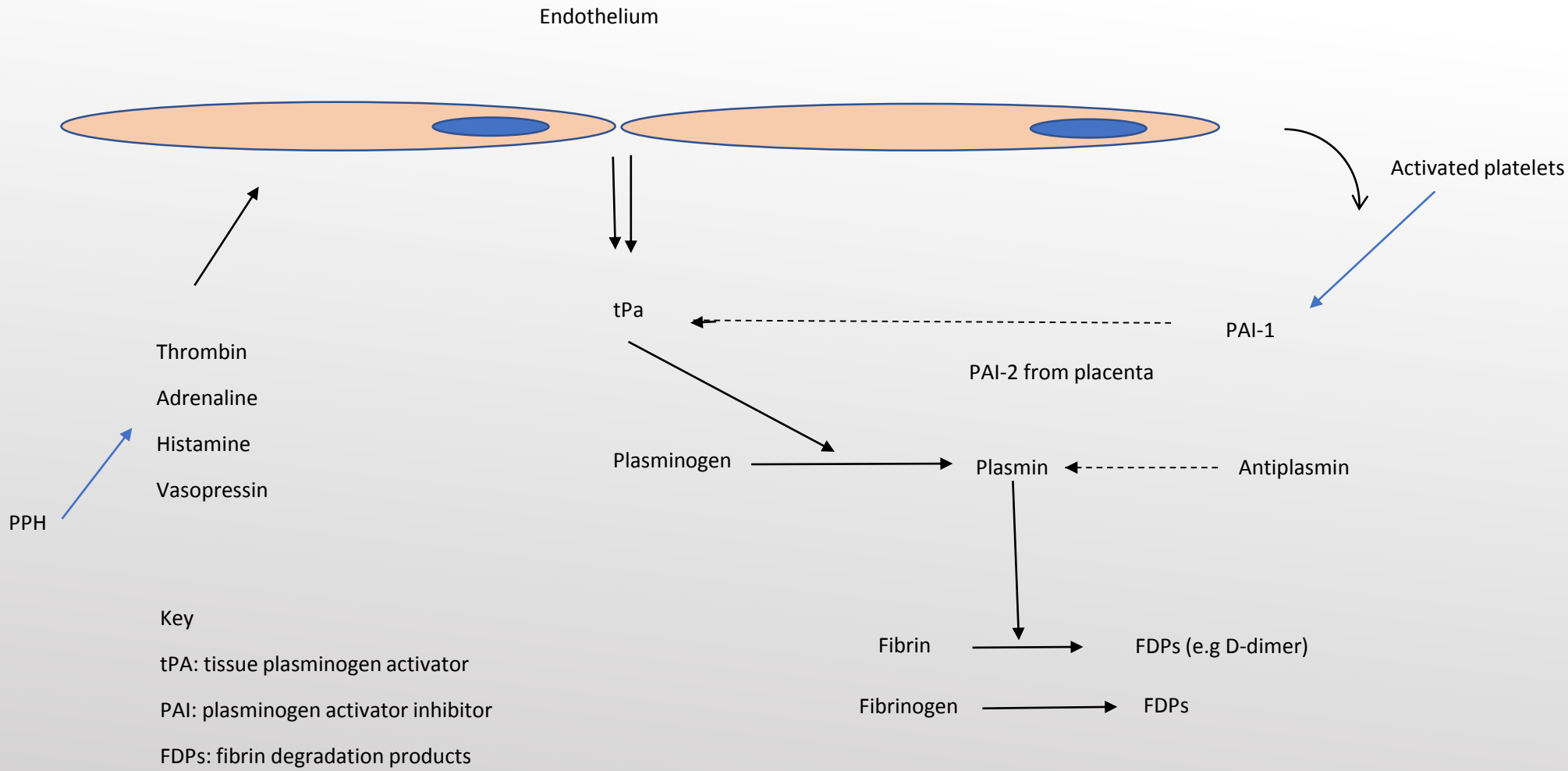
- ΤΡΑΝΕΞΑΜΙΚΟ ΟΞΥ (trans-4-(aminomethyl)cyclohexane-1-carboxylic acid) (TXA)



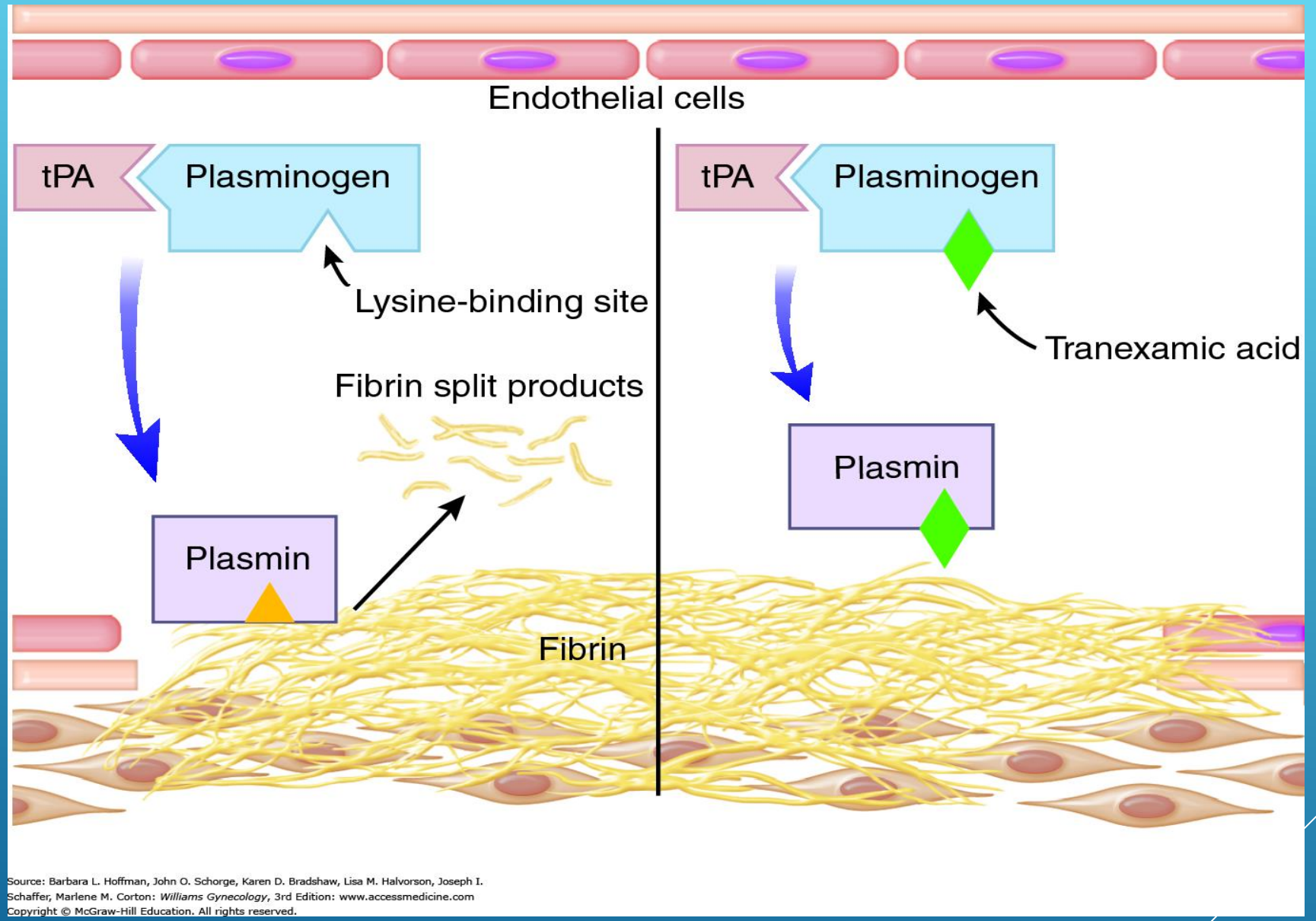
FORMULA C8H15NO2
MOLAR MASS 157.21 G/MOL

British national formulary: BNF 69 (69 ed.). British Medical Association. 2015

Fibrinolysis in post-partum haemorrhage (PPH)



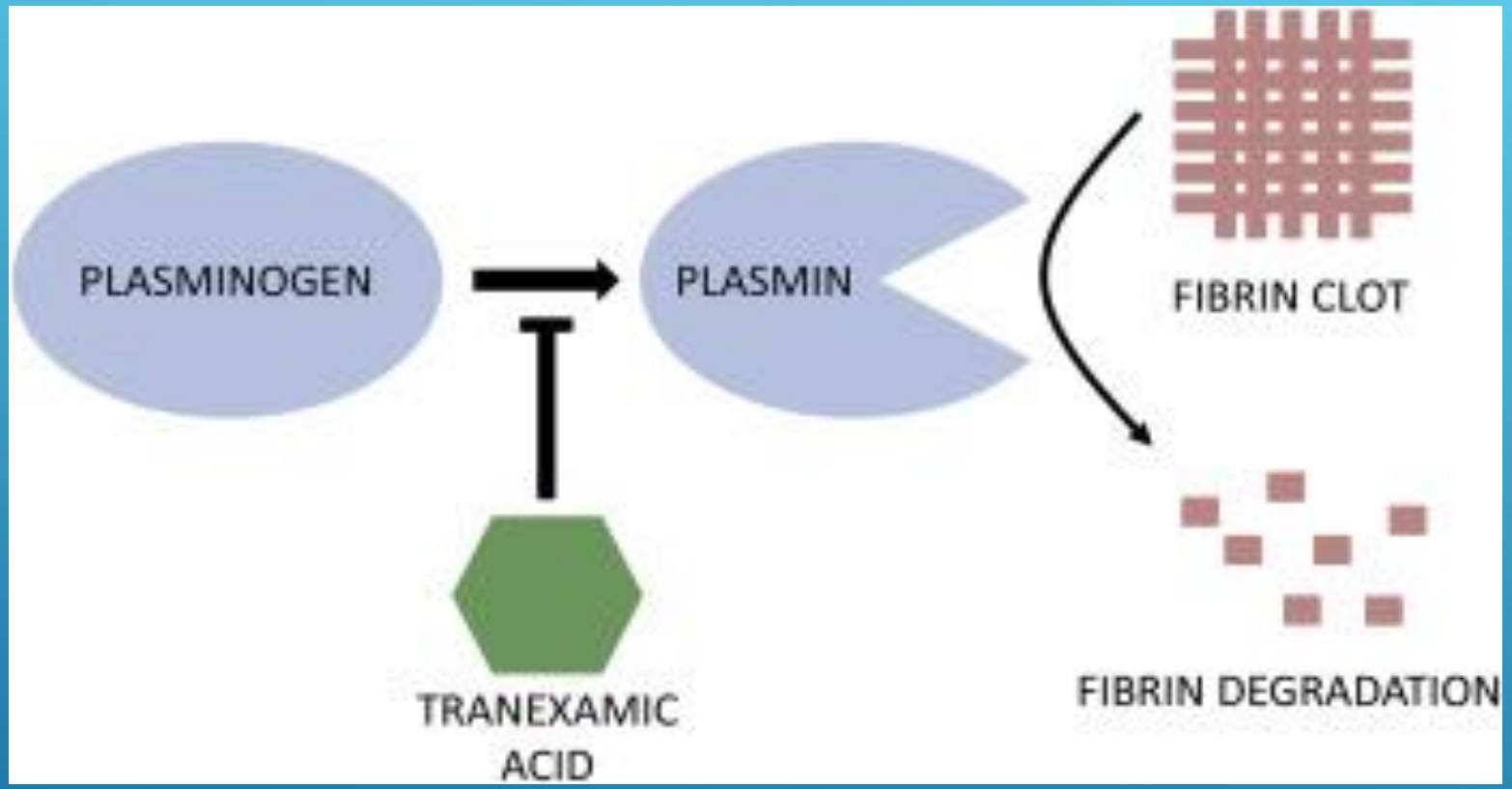
Higgs et al BJH 2017



Source: Barbara L. Hoffman, John O. Schorge, Karen D. Bradshaw, Lisa M. Halvorson, Joseph I. Schaffer, Marlene M. Corton: *Williams Gynecology*, 3rd Edition: www.accessmedicine.com

TPA (TISSUE PLASMINOGEN ACTIVATOR)-ενζυμο καταλύτης μετατροπής Πλασμινογόνου σε Πλασμίνη)

ΜΗΧΑΝΙΣΜΟΣ ΔΡΑΣΗΣ ΤΟΥ ΤΧΑ



ΤΟ ΤΧΑ ΕΊΝΑΙ ΣΥΝΘΕΤΙΚΟ ΠΑΡΑΓΩΓΟ ΤΟΥ ΑΜΙΝΟΞΕΟΣ ΛΥΣΙΝΗ. ΑΝΑΣΤΕΛΛΕΙ ΤΗΝ ΜΕΤΑΤΡΟΠΗ ΤΟΥ ΠΛΑΣΜΙΝΟΓΟΝΟΥ ΣΕ ΣΕΡΙΝΙΚΗ ΠΡΩΤΕΑΣΗ (ΠΛΑΣΜΙΝΗ). Η ΑΝΑΣΤΟΛΗ ΑΥΤΉ ΕΠΙΤΥΓΧΑΝΕΤΑΙ ΜΕ ΤΗΝ ΣΥΝΔΕΣΗ ΤΟΥ ΤΧΑ ΣΤΙΣ ΘΕΣΕΙΣ 4 ΚΑΙ 5 ΤΩΝ ΥΠΟΔΟΧΕΩΝ ΤΗΣ ΛΥΣΙΝΗΣ ΤΟΥ ΠΛΑΣΜΙΝΟΓΟΝΟΥ, ΜΕ ΑΠΟΤΕΛΕΣΜΑ ΝΑ ΑΝΑΣΤΑΛΛΕΙ Η ΙΝΩΔΟΛΥΣΗ.

British national formulary: BNF 69 (69 ed.). British Medical Association. 2015

ΦΑΡΜΑΚΕΥΤΙΚΕΣ ΜΟΡΦΕΣ ΤΧΑ

- **TRANSAMIN CAPS 250MG**
  CAP BTx50 CAPS (BLIST 5x10) (BLIST 5x10)

TRANSAMIN INJ.SOL 500MG/5ML AMP BTx10AMPx5ML IV+IM INJ_SOL100MG/ML

ΑΝΤΕΝΔΕΊΞΕΙΣ ΧΟΡΉΓΗΣΗΣ : ΑΛΛΕΡΓΊΑ, ΙΣΤΟΡΙΚΌ ΘΡΟΜΒΟΕΜΒΟΛΙΚΉΣ ΝΌΣΟΥ, ΔΙΆΧΥΤΗ ΕΝΔΟΑΓΓΕΙΑΚΉ ΠΉΞΗ, ΠΡΟΕΚΛΑΜΨΙΑ-ΕΚΛΑΜΨΙΑ, ΙΣΤΟΡΙΚΟ ΣΠΑΣΜΩΝ.

ΠΑΡΕΝΈΡΓΕΙΕΣ : ΝΑΥΤΙΑ, ΔΙΆΡΡΟΙΑ, ΚΟΙΛΙΑΚΆ ΆΛΓΗ, ΖΆΛΗ, ΕΜΒΟΊΕΣ, ΡΙΝΙΚΉ ΣΥΜΦΌΡΗΣΗ, ΚΕΦΑΛΑΛΓΊΑ, ΕΞΑΝΘΉΜΑΤΑ, ΜΥΑΛΓΙΕΣ, ΔΙΑΤΑΡΑΧΈΣ ΟΡΆΣΕΩΣ.

ΙΔΙΑΊΤΕΡΗ ΠΡΟΣΟΧΉ ΣΤΗΝ ΧΟΡΉΓΗΣΗ ΣΕ ΠΕΡΙΣΤΑΤΙΚΆ ΜΕ ΚΑΡΔΙΑΚΗ-ΝΕΦΡΙΚΗ-ΗΠΑΤΙΚΗ ΔΥΣΛΕΙΤΟΥΡΓΙΑ.

ΠΗΓΉ: ΓΑΛΗΝΌΣ ΟΔΗΓΌΣ ΦΑΡΜΆΚΩΝ

Πρώτη δημοσίευση χρήσης ΤΧΑ σε κύηση BMJ 1978

Recurrent abruptio placentae treated with the fibrinolytic inhibitor tranexamic acid

Abruptio placentae occurs in about 0·5 % of all deliveries[1]; the risk is even higher in women who have had abruptio once or twice before—17 % and 25 % respectively.[2] In such cases the coagulation mechanism might be activated by mainly thromboplastic substances from the placenta or by amniotic fluid and the fibrinolytic system by mainly fibrinolytic activators from the endothelium of uterine vessels entering the maternal blood stream.

We describe here a patient whose previous pregnancies had been affected by abruptio placentae and who received a fibrinolytic inhibitor, tranexamic acid, during her third pregnancy.

Case report

This woman's first pregnancy in 1973 resulted in premature delivery with suspected abruptio placentae. The child did not survive. During the second pregnancy in 1974 abruptio placentae was diagnosed. At delivery the blood loss was massive, and the child was stillborn. Fibrinogen concentrations were barely measurable, and fibrinogen-fibrin degradation products (FDP) were found in the serum.

In 1976 the patient became pregnant again and was sent to our hospital in the 26th week of pregnancy. Analysis of the coagulation factors and components of the fibrinolytic system before admission had shown nothing abnormal, but bleeding occurred on the day of admission. Gynaecological and ultrasonic examination suggested abruptio placentae. Laboratory analysis (see figure) showed low concentrations of fibrinogen, factor V, and factor VIII and the presence of FDP. The platelet count and P and P complex (factors II, VII, and X)[3] were normal. The ethanol gelation test gave a negative result. The analysis indicated pathological proteolysis with activation mainly of the fibrinolytic system. The patient was therefore treated with the fibrinolytic inhibitor tranexamic acid (Cyklokapron), which is related to epsilon-aminocaproic acid, in a dose of 1 g intravenously every fourth hour. The bleeding stopped and her coagulation status became normal. After three days of intravenous administration tranexamic acid was given by

Astedt B, Nilsson IM. Recurrent abruptio placentae treated with the fibrinolytic inhibitor tranexamic acid. Br Med J. 1978 Mar 25;1(6115):756-7.

Πρώτη δημοσίευση χρήσης ΤΧΑ σε αιμορραγία μετά τον τοκετό BJOG 1996

British Journal of Obstetrics and Gynaecology
December 1996, Vol. 103, pp. 1250–1251

CASE REPORTS

Tranexamic acid in the management of postpartum haemorrhage

***Alok K. As** *Clinical Lecturer*, ****Phillip Hagen** *Registrar*, *****J. B. Webb** *Consultant (Obstetrics and Gynaecology)*

**University Department of Obstetrics and Gynaecology, Rosie Maternity Hospital, Cambridge;*
***Obstetrics and Gynaecology, King's College Hospital, London; ***Lister Hospital, Stevenage*

Case report

A 39 year old woman became pregnant by *in vitro* fertilisation having had a right salpingectomy for ectopic pregnancy and a blocked left tube. A first trimester ultrasound scan at King's College Hospital, London, performed to estimate an increased risk of Down's syndrome by nuchal translucency, was reassuring. An anomaly scan at 19 weeks of gestation detected no structural abnormality of the fetus, but the placenta was covering the internal cervical os. All routine antenatal investigations were normal.

In her first pregnancy she had had a fresh stillbirth secondary to placental abruption at 39 weeks of gestation. In her second pregnancy a salpingectomy was performed for a ruptured ectopic pregnancy in the right tube. She had two first trimester miscarriages in her third and fifth pregnancies in 1990 and 1991, respectively. Her only live child was born by an emergency caesarean section at 35 weeks of gestation for recurrent antepartum haemorrhage from a central placenta praevia.

In the current pregnancy the placental position was found to be unchanged at a repeat ultrasound scan at 32 weeks of gestation. Pregnancy progressed uneventfully until 35 weeks when she presented to the delivery suite with massive vaginal bleeding estimated to be about 1·5 L. Active resuscitation was commenced involving a consultant obstetrician, a haematologist and an anaesthetist. Two intravenous lines were sited, one in each arm, with a colloid infusion (Gelofusine®, Braun Medical Ltd, Aylesbury, UK) in one line and a crystalloid (Hartmann's solution) in the other. Six units of blood were requested initially. The cardiotocograph was still normal, and an immediate lower segment caesarean section was performed under general anaesthetic. At operation the placenta was under the lower segment incision. Rapid attempts were made to negotiate its upper edge, but it was too high. An attempt to go round the lower edge was not possible as it was on the posterior aspect of the lower segment. Therefore the placenta was transected to deliver her of a live male infant. Although the placenta was morbidly adherent (accreta), as much placental tissue as could be was removed piecemeal, and the uterine cavity swabbed clean. Bleeding from the lower segment was observed for 5 min and found to be satisfactory. The rest of the operation was completed in the usual way.

The estimated blood loss at operation was 1000 mL. She had a transfusion of four units of blood and 500 μg of ergometrine was administered intravenously to help uterine contraction and retraction. A continuous syntocinon infusion was started (40 units in 500 mL of normal saline running at the rate of 60 mL/h) and prophylactic antibiotic (1·2 g of co-amoxyclav 1000/200 intravenously) was administered. An indwelling Foley catheter was left *in situ* for free drainage. A central venous line was sited to monitor her fluid replacement and balance, and she was transferred to the intensive therapy unit for her post-operative care. The haematological indices, fluid balance, cardiopulmonary and renal functions were constantly monitored according to the protocol of the intensive therapy unit.

She continued bleeding per vaginum at a rate of about 300 mL/h. Despite having four additional units of blood, 1 L of Hartmann's solution, continuous syntocinon infusion and a repeat intravenous injection of 500 μg of ergometrine, her blood pressure was hovering around 74–85/45–50 mmHg over the first 4 h post-operatively, and the average hourly urine output was 20 mL during that period. The upper segment of the uterus was well contracted, with the bleeding assumed to be coming from the lower segment. As the rate of per vaginum blood loss overwhelmed the rate of replacement, a choice had to be made between continuation of conservative medical treatment and surgical options, including hysterectomy. Before

Correspondence: Mr A. K. As, University Department of Obstetrics and Gynaecology, Rosie Maternity Hospital, Robinson Way, Cambridge CB2 2SW, UK.

As AK, Hagen P, Webb JB. Tranexamic acid in the management of postpartum

haemorrhage. Br J Obstet Gynaecol. 1996 Dec;103(12):1250-1.

1η Συστηματική ανασκόπηση και μετανάλυση.

Ferrer P, Roberts I, Sydenham E, Blackhall K, Shakur H. Anti-fibrinolytic agents in post partum haemorrhage: a systematic review. BMC Pregnancy Childbirth. 2009 Jul 15;9:29. doi: 10.1186/1471-2393-9-29. Review.

BioMed Central

Research article

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Anti-fibrinolytic agents in post partum haemorrhage: a systematic review

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Email: Pili Ferrer - piliferrer@eresmas.com; Ian Roberts* - ian.roberts@lshtm.ac.uk; Emma Sydenham - emma.sydenham@lshtm.ac.uk; Karen Blackhall - karen.blackhall@lshtm.ac.uk; Haleema Shakur - haleema.shakur@lshtm.ac.uk

* Corresponding author

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1η Μαζική συστηματική ανασκόπηση (Case reports and RCTS) και 2η Μετανάλυση για χρήση ΤΧΑ στην κύηση.

Peitsidis P, Kadir RA. Antifibrinolytic therapy with tranexamic acid in pregnancy and postpartum.
Expert Opin Pharmacother. 2011 Mar; 12(4):503-16

Expert Opinion

Antifibrinolytic therapy with tranexamic acid in pregnancy and postpartum

Panagiotis Peitsidis† & Rezan A Kadir
The Royal Free Hospital, Haemophilia Centre & Thrombosis Unit, Department of Obstetrics and Gynaecology, London, UK

Objective: The aim of this study is critically to review the available evidence regarding the use, efficacy and safety of tranexamic acid in the management of hemorrhage during pregnancy and for prevention and treatment of postpartum hemorrhage.

Research design and methods: We performed a systematic search of electronic literature (PubMed, Embase, CINAHL, Scopus, Cochrane, DARE) to review all studies looking at the use of tranexamic acid during pregnancy and puerperium. We did a metanalysis on three randomized controlled trials that evaluated reduction in blood loss in women undergoing cesarean sections with the use of tranexamic acid.

Results: An electronic search yielded 34 articles, the studies dating from 1976 to 2010, five randomized controlled trials, seven observational studies, and twenty-two case reports. Meta-analysis showed that the estimate of the combined effect of tranexamic acid compared with placebo was a difference of 32.5 ml reduction in blood loss (95% CI -4.1 -- 69.13; p = 0.08). Tranexamic acid was also used successfully to prevent and treat bleeding in observation studies and case reports. Pulmonary embolism was reported in two cases; however, the possible involvement of tranexamic acid in these thrombotic episodes could neither be confirmed nor excluded.

Conclusions: The clinical studies suggest that tranexamic acid reduces the amount of blood loss after delivery during cesarean sections and vaginal deliveries, and reduces the requirement for blood transfusion. Tranexamic acid seems to be safe and effective in the prevention and management of bleeding during pregnancy. Further investigation and larger clinical trials with better design and methodological quality are required to confirm these findings.

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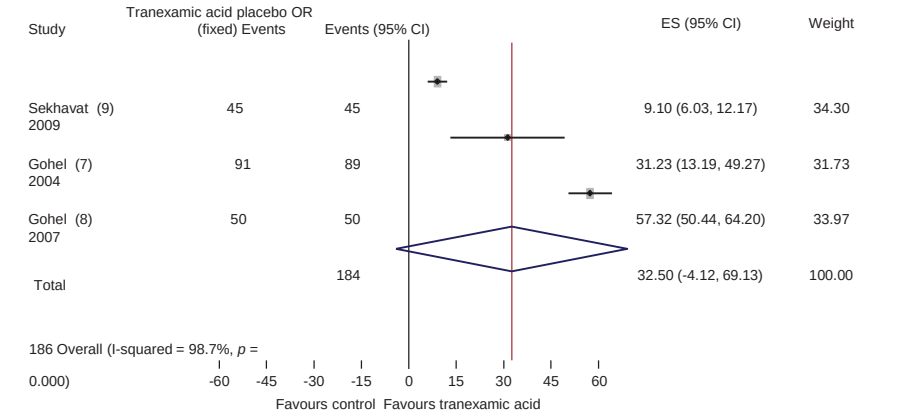

Figure 2. Meta-analysis of randomized controlled trials of tranexamic acid versus placebo during cesarean section for reduction of postpartum blood loss.

CI: Confidence interval; ES: Effect size; OR: Odds ratio.

Metanalysis showed a 32.5 ml reduction of blood loss In patients receiving TXA 1gr IV 10-20 min before CS. However the studies had poor methodological quality (Randomisation). Tranexamic acid is safe . Larger studies are required to reach to safer conclusions.Reduces the need for Transfusions.

Mild adverse effects (Nausea) were observed.

Peitsidis P, Kadir RA. Antifibrinolytic therapy with tranexamic acid in pregnancy and postpartum. Expert Opin Pharmacother. 2011 Mar;12(4):503-16

PROF. IAN ROBERTS LONDON SCHOOL OF TROPICAL MEDICINE AND HYGIENE-DESIGNER OF WOMAN **(WORLD MATERNAL ANTIFIBRINOLYTIC TRIAL) AND CRASH-2 TRIAL.**

Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial

*CRASH-2 trial collaborators**

Lancet 2010; 376: 23–32

Published Online June 15, 2010
DOI:10.1016/S0140- 6736(10)60835-5

See Comment page 3

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crash@lshtm.ac.uk

Summary

Background Tranexamic acid can reduce bleeding in patients undergoing elective surgery. We assessed the effects of early administration of a short course of tranexamic acid on death, vascular occlusive events, and the receipt of blood transfusion in trauma patients.

Methods This randomised controlled trial was undertaken in 274 hospitals in 40 countries. 20 211 adult trauma patients with, or at risk of, significant bleeding were randomly assigned within 8 h of injury to either tranexamic acid (loading dose 1 g over 10 min then infusion of 1 g over 8 h) or matching placebo. Randomisation was balanced by centre, with an allocation sequence based on a block size of eight, generated with a computer random number generator. Both participants and study staff (site investigators and trial coordinating centre staff) were masked to treatment allocation. The primary outcome was death in hospital within 4 weeks of injury, and was described with the following categories: bleeding, vascular occlusion (myocardial infarction, stroke and pulmonary embolism), multiorgan failure, head injury, and other. All analyses were by intention to treat. This study is registered as ISRCTN86750102, Clinicaltrials.gov NCT00375258, and South African Clinical Trial Register DOH-27-0607-1919.

Findings 10 096 patients were allocated to tranexamic acid and 10 115 to placebo, of whom 10 060 and 10 067, respectively, were analysed. All-cause mortality was significantly reduced with tranexamic acid (1463 [14·5%] tranexamic acid group *vs* 1613 [16·0%] placebo group; relative risk 0·91, 95% CI 0·85–0·97; p=0·0035). The risk of death due to bleeding was significantly reduced (489 [4·9%] *vs* 574 [5·7%]; relative risk 0·85, 95% CI 0·76–0·96; p=0·0077).

Interpretation Tranexamic acid safely reduced the risk of death in bleeding trauma patients in this study. On the basis of these results, tranexamic acid should be considered for use in bleeding trauma patients.

Funding UK NIHR Health Technology Assessment programme, Pfizer, BUPA Foundation, and J P Moulton Charitable Foundation.

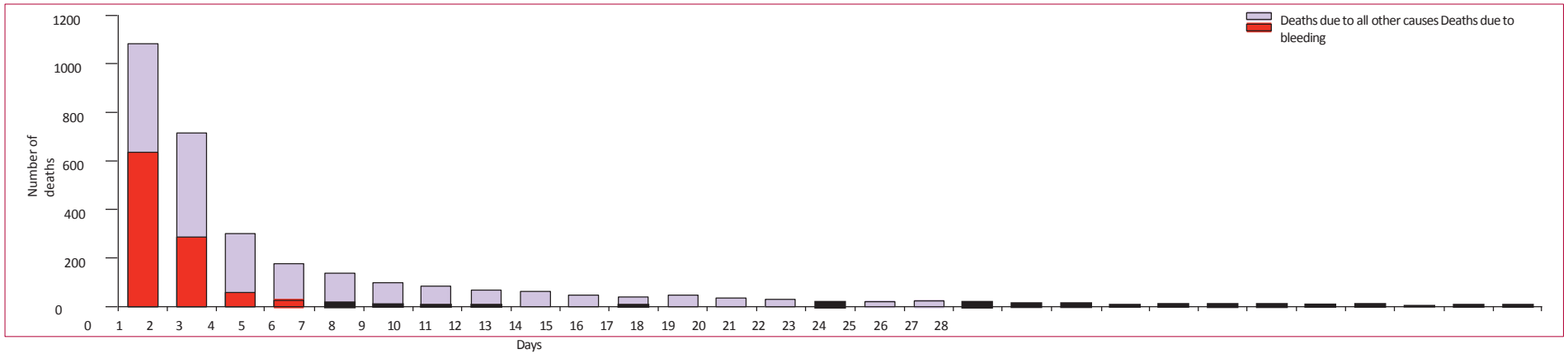

***Figure 2*: Mortality by days from randomisation**

Στατιστικά σημαντική μείωση του αριθμού των θανάτων από αιμορραγία 489 vs 574 p=0.0077

CRASH-2 trial collaborators, Shakur H, Roberts I, Effects of tranexamic acid on death, vascular occlusiveevents, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. Lancet. 2010 Jul 3;376(9734):23-32.

Πρωτόκολλο μελέτης
WOMAN TRIAL
TRIALS 2010

Shakur *et al. Trials* 2010, **11**:40
http://www.trialsjournal.com/content/11/1/40

TRIALS

STUDY PROTOCOL Open Access

The WOMAN Trial (World Maternal Antifibrinolytic Trial): tranexamic acid for the treatment of postpartum haemorrhage: an international randomised, double blind placebo controlled trial

Haleema Shakur*[1], Diana Elbourne[4], Metin Gülmezoglu[2], Zarko Alfirevic[3], Carine Ronsmans[5], Elizabeth Allen[4] and Ian Roberts[1]

Abstract

Background: Each year, worldwide about 530,000 women die from causes related to pregnancy and childbirth. Of the deaths 99% are in low and middle income countries. Obstetric haemorrhage is the leading cause of maternal mortality, most occurring in the postpartum period. Systemic antifibrinolytic agents are widely used in surgery to prevent clot breakdown (fibrinolysis) in order to reduce surgical blood loss. At present there is little reliable evidence from randomised trials on the effectiveness of tranexamic acid in the treatment of postpartum haemorrhage.

Methods: The Trial aims to determine the effect of early administration of tranexamic acid on mortality, hysterectomy and other morbidities (surgical interventions, blood transfusion, risk of non-fatal vascular events) in women with clinically diagnosed postpartum haemorrhage. The use of health services and safety, especially thromboembolic effect, on breastfed babies will also be assessed. The trial will be a large, pragmatic, randomised, double blind, placebo controlled trial among 15,000 women with a clinical diagnosis of postpartum haemorrhage. All legally adult women with clinically diagnosed postpartum haemorrhage following vaginal delivery of a baby or caesarean section will potentially be eligible. The fundamental eligibility criterion is the responsible clinician's 'uncertainty' as to whether or not to use an antifibrinolytic agent in a particular woman with postpartum haemorrhage. Treatment will entail a dose of tranexamic acid (1 gram by intravenous injection) or placebo (sodium chloride 0.9%) will be given as soon as possible after randomisation. A second dose may be given if after 30 minutes bleeding continues, or if it stops and restarts within 24 hours after the first dose.

The main analyses will be on an 'intention to treat' basis, irrespective of whether the allocated treatment was received or not. Subgroup analyses for the primary outcome will be based on type of delivery; administration or not of prophylactic uterotonics; and on whether the clinical decision to consider trial entry was based primarily on estimated blood loss alone or on haemodynamic instability. A study with 15,000 women will have over 90% power to detect a 25% reduction from 4% to 3% in the primary endpoint of mortality or hysterectomy.

Trial registration: Current Controlled Trials: ISRCTN76912190 and Clinicaltrials.gov ID: NCT00872469

Background

Each year, worldwide, about 530,000 women die from causes related to pregnancy and childbirth. Nearly all (99%) of these deaths are in low and middle income countries[1]. Haemorrhage, which usually occurs in the postpartum period, is responsible for between one quarter and one third of obstetric deaths[2]. Postpartum haemorrhage (PPH) is commonly defined as blood loss of ≥ 500 mL after vaginal delivery of a baby, or ≥ 1000 mL after caesarean section. However, these thresholds do not take into account pre-existing health status, and blood loss of

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Shakur H, Roberts I, Edwards P, Elbourne D, Alfirevic Z, Ronsmans C. The effect of tranexamic acid on the risk of death and hysterectomy in women with post-partum haemorrhage: statistical analysis plan for the WOMAN trial. Trials. 2016 May 17;17(1):249.

Δημοσίευση αποτελεσμάτων **WOMAN TRIAL** LANCET 2017

Effect of early tranexamic acid administration on mortality, hysterectomy, and other morbidities in women with post-partum haemorrhage (WOMAN): an international, randomised, double-blind, placebo-controlled trial

*WOMAN Trial Collaborators**

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See Editorial page 2081
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thewomantrial@LSHTM.AC.UK

Summary

Background Post-partum haemorrhage is the leading cause of maternal death worldwide. Early administration of tranexamic acid reduces deaths due to bleeding in trauma patients. We aimed to assess the effects of early administration of tranexamic acid on death, hysterectomy, and other relevant outcomes in women with post-partum haemorrhage.

Methods In this randomised, double-blind, placebo-controlled trial, we recruited women aged 16 years and older with a clinical diagnosis of post-partum haemorrhage after a vaginal birth or caesarean section from 193 hospitals in 21 countries. We randomly assigned women to receive either 1 g intravenous tranexamic acid or matching placebo in addition to usual care. If bleeding continued after 30 min, or stopped and restarted within 24 h of the first dose, a second dose of 1 g of tranexamic acid or placebo could be given. Patients were assigned by selection of a numbered treatment pack from a box containing eight numbered packs that were identical apart from the pack number. Participants, care givers, and those assessing outcomes were masked to allocation. We originally planned to enrol 15 000 women with a composite primary endpoint of death from all causes or hysterectomy within 42 days of giving birth. However, during the trial it became apparent that the decision to conduct a hysterectomy was often made at the same time as randomisation. Although tranexamic acid could influence the risk of death in these cases, it could not affect the risk of hysterectomy. We therefore increased the sample size from 15 000 to 20 000 women in order to estimate the effect of tranexamic acid on the risk of death from post-partum haemorrhage. All analyses were done on an intention-to-treat basis. This trial is registered with ISRCTN76912190 (Dec 8, 2008); ClinicalTrials.gov, number NCT00872469; and PACTR201007000192283.

Findings Between March, 2010, and April, 2016, 20 060 women were enrolled and randomly assigned to receive tranexamic acid (n=10 051) or placebo (n=10 009), of whom 10 036 and 9985, respectively, were included in the analysis. Death due to bleeding was significantly reduced in women given tranexamic acid (155 [1·5%] of 10 036 patients *vs* 191 [1·9%] of 9985 in the placebo group, risk ratio [RR] 0·81, 95% CI 0·65–1·00; p=0·045), especially in women given treatment within 3 h of giving birth (89 [1·2%] in the tranexamic acid group *vs* 127 [1·7%] in the placebo group, RR 0·69, 95% CI 0·52–0·91; p=0·008). All other causes of death did not differ significantly by group. Hysterectomy was not reduced with tranexamic acid (358 [3·6%] patients in the tranexamic acid group *vs* 351 [3·5%] in the placebo group, RR 1·02, 95% CI 0·88–1·07; p=0·84). The composite primary endpoint of death from all causes or hysterectomy was not reduced with tranexamic acid (534 [5·3%] deaths or hysterectomies in the tranexamic acid group *vs* 546 [5·5%] in the placebo group, RR 0·97, 95% CI 0·87–1·09; p=0·65). Adverse events (including thromboembolic events) did not differ significantly in the tranexamic acid versus placebo group.

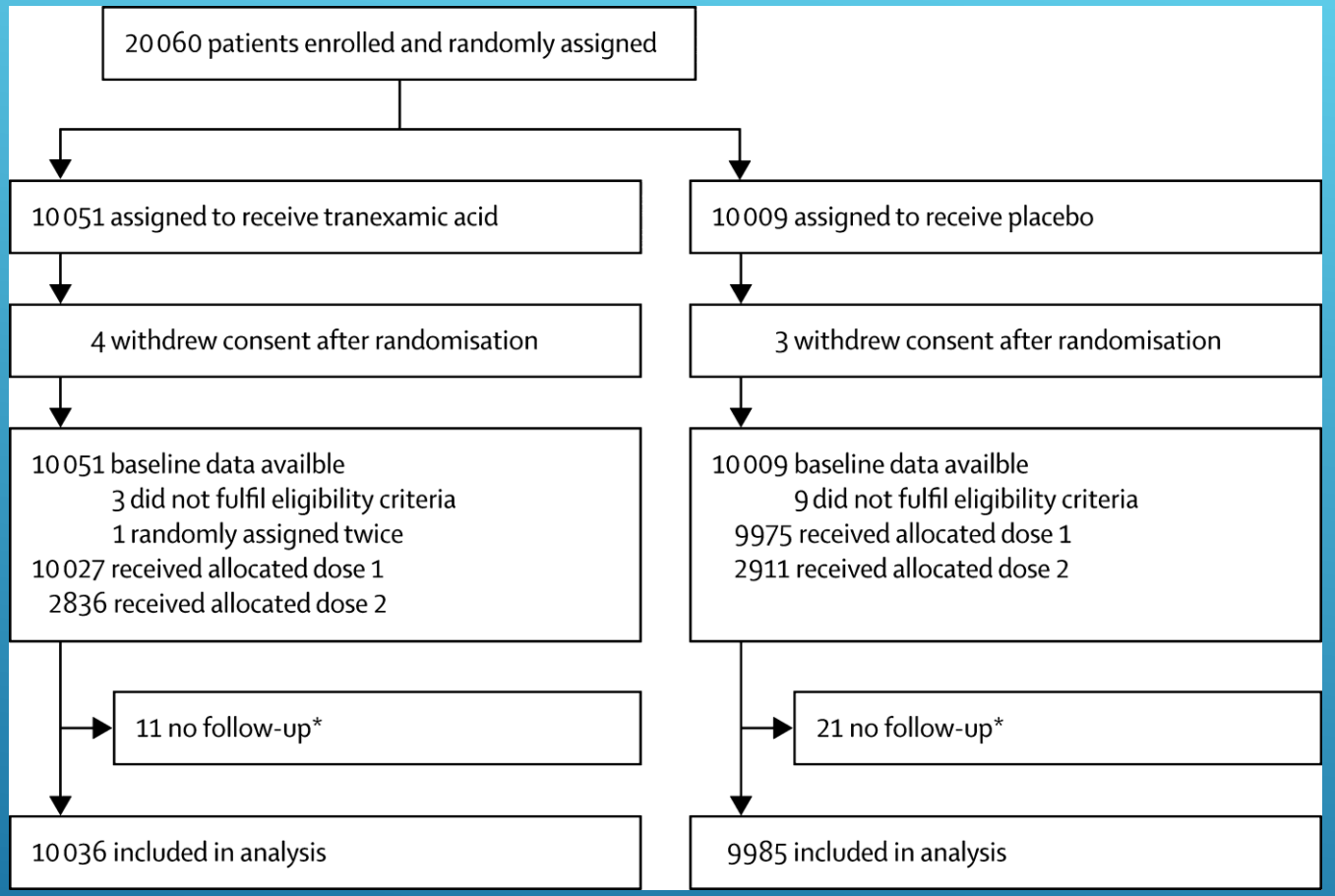
Interpretation Tranexamic acid reduces death due to bleeding in women with post-partum haemorrhage with no adverse effects. When used as a treatment for postpartum haemorrhage, tranexamic acid should be given as soon as possible after bleeding onset.

Funding London School of Hygiene & Tropical Medicine, Pfizer, UK Department of Health, Wellcome Trust, and Bill & Melinda Gates Foundation.

Introduction

Primary post-partum haemorrhage, usually defined as a blood loss of more than 500 mL within 24 h of giving birth, is the leading cause of maternal death worldwide, responsible for about 100 000 deaths every year.[1–3] Most of the deaths occur soon after giving birth and almost all (99%) occur in low-income and middle-income countries.[4,5]

Tranexamic acid reduces bleeding by inhibiting the enzymatic breakdown of fibrinogen and fibrin by plasmin.[6] Findings of a systematic review of clinical trials of tranexamic acid in surgery showed that the drug



T v *he Lancet* 2017 389, 2105-2116DOI: (10.1016/S0140-6736(17)30638-4)

ΑΠΟΤΕΛΈΣΜΑΤΑ ΜΕΛΈΤΗΣ **WOMAN- (WORLD MATERNAL ANTIFIBRINOLYTIC TRIAL)**

- Διπλή τυχαιοποιημένη μελέτη **2010-2016** με συμμετοχή **20.060** γυναικών με αιμορραγία μετά τον τοκετό από 21 χωρές αναπτυγμένες η αναπτυσσόμενες σε σύνολο **193** νοσοκομείων.
- **Μεθοδολογία.**
- **Πληθυσμός : 10.051** γυναίκες έλαβαν IV **1 γρ**. TXA VS **10009** γυναίκες Placebo.
- (Δεύτερη δόση 1 γρ στα πλαίσια επανεναρξης αιμορραγίας στα 30 min η στις 24 ωρες). Ταχύτητα Χορήγησης 1 mL per min.
- **Πρωτογενή αποτελέσματα : Αριθμός των Θανάτων από όλες τις αιτίες (Mortality).**
- **Δευτερογενή αποτελέσματα-νοσηρότητα (Morbidity)** –Αριθμός Θρομβοεμβολικων επεισόδιων εγκεφαλικών,εμφραγμάτων,χειρουργικές παρεμβάσεις (Υστερεκτομία, απολίνωση μητριαίων αρτηριών, αιμοστατικές ραφές,παθολογικές επιπλοκές (νεφρική, καρδιακή,αναπνευστική ανεπάρκεια.

- Woman trial collaborators. Lancet. 2017 May 27; 389(10084): 2105–2116.

	Tranexamic acid group (n=10 036)	Placebo group (n=9985)	RR (95% CI)	p value (two-sided)
Bleeding	155 (1·5%)	191 (1·9 %)	0·81 (0·65–1·00)	0·045
Pulmonary embolism	10 (0·1%)	11 (0·1)	0·90 (0·38–2·13)	0·82
Organ failure	25 (0·3%)	18 (0·2%)	1·38 (0·75–2·53)	0·29
Sepsis	15 (0·2%)	8 (0·1%)	1·87 (0·79–4·40)	0·15
Eclampsia	2 (0·02%)	8 (0·1%)	0·25 (0·05–1·17)	0·057
Other	20 (0·2%)	20 (0·2%)	0·99 (0·54–1·85)	0·99
Any cause of death	227 (2·3%)	256 (2·6%)	0·88 (0·74–1·05)	0·16

Data are n (%), unless otherwise indicated. RR=risk ratio.

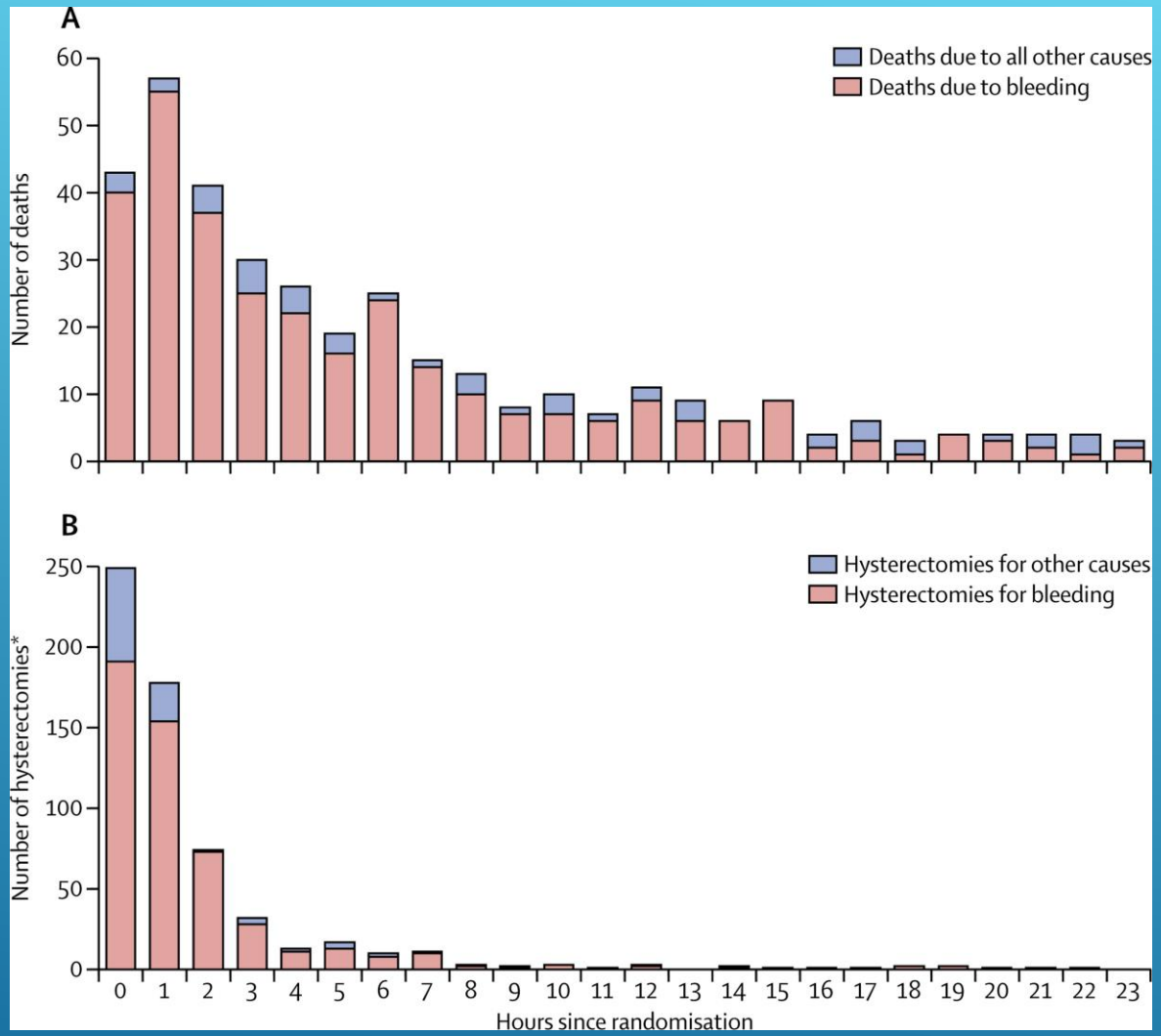
Table 2: **Effect of tranexamic acid on maternal death**

ΘΆΝΑΤΟΙ 483- 100 %
374 (77%) ΕΝΤΌΣ 24 ΩΡΏΝ ΑΠΌ ΤΥΧΑΙΟΠΟΊΗΣΗ
43 (9%) ΕΝΤΟΣ ΜΙΑΣ ΏΡΑΣ ΑΠΌ ΤΥΧΑΙΟΠΟΊΗΣΗ
155 (1.5 %) TXA VS 191 (1.9 %)PLACEBO P VALUE 0.045 SS

WOMAN TRIAL COLLABORATORS. LANCET. 2017 MAY 27; 389(10084): 2105–2116.

Διακύμανσείς του αριθμού θανατών ανα ώρα λόγω Αιμορραγίας ή άλλων αίτιών

Διακυμάνσεις του αριθμού υστερεκτομιών ανά ωρα λόγω αιμορραγίας η άλλων αιτιών



Woman trial collaborators. Lancet. 2017 May 27; 389(10084): 2105–2116.

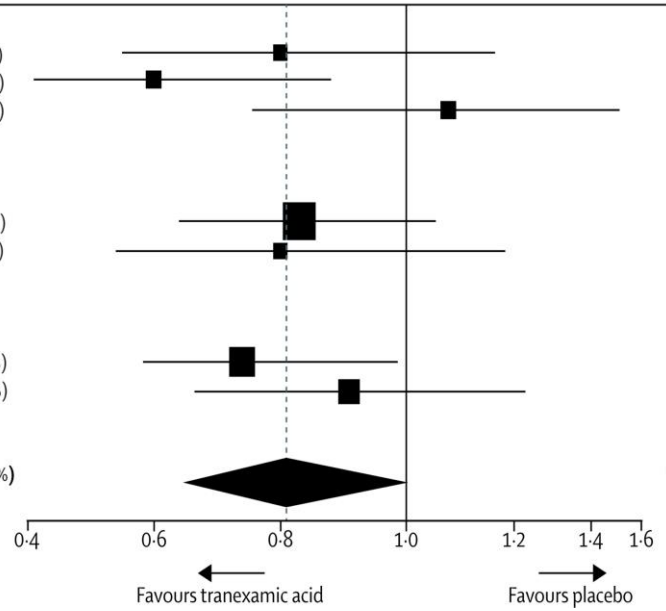
Παρατηρήθηκε μείωση των θανάτων από αιμορραγία σε περιπτώσεις ενδοφλέβιας χορήγησης ΤΧΑ εντός 3 ωρών από την έναρξη της αιμορραγίας 89 vs 121 p=0.008

- Σημαντική μείωση του αριθμού των λαπαροτομιών 82 (0.8%) vs 127 (1.3%) 0.002
- σε γυναίκες που έλαβαν ΤΧΑ έναντι PLACEBO.

- Δεν υπήρξε καμία στατιστικά σημαντική διαφορά όσον αφορά
- το ποσοστό των υστερεκτομιών ,το ποσοστό των επιπλοκών
- (Χειρουργικών) και Παθολογικών-Εμφραγμα,Σήψη,Εμβολή,Καταπληξία, Νεφρική,Καρδιακή,Αναπνευστική δυσχέρεια κλπ.).
- Επίσης δεν παρατηρήθηκε στατιστικά σημαντικα διαφορά στον αριθμό των μεταγγίσεων
- μεταξύ των 2 ομάδων καθώς και των παρενεργειών από την χρήση του ΤΧΑ.

Woman trial collaborators. Lancet. 2017 May 27; 389(10084): 2105–2116.

	Tranexamic acid group	Placebo group†	Risk ratio (95% CI)
Time from delivery (h)			
≤1	49/4846 (1·0%)	60/4726 (1·3%)	0·80 (0·55–1·16)
>1–3	40/2674 (1·5%)	67/2682 (2·5%)	0·60 (0·41–0·88)
>3	66/2514 (2·6%)	63/2569 (2·5%)	1·07 (0·76–1·51)
p=0·085*			
Type of delivery			
Vaginal	110/7083 (1·6%)	135/7108 (1·9%)	0·82 (0·64–1·05)
Caesarean section	45/2952 (1·5%)	55/2871 (1·9%)	0·80 (0·54–1·18)
p=0·91*			
Primary cause of haemorrhage			
Uterine atony	77/6428 (1·2%)	103/6333 (1·6%)	0·74 (0·55–0·99)
Other/unknown	78/3608 (2·2%)	88/3652 (2·4%)	0·90 (0·66–1·21)
p=0·36*			
All patients	**155/10036 (1·5%)**	**191/9985 (1·9%)**	**0·81 (0·65–1·00)**
Two-sided p=0·045			



Στατιστικά σημαντική μείωση των θανάτων από αιμορραγία στις περιπτώσεις ενδοφλέβιας χορήγησης ΤΧΑ <1 h , 1-3 h .
Η χορήγηση ΤΧΑ > 3 h δεν παρουσίασε στατιστικά σημαντική μείωση θανάτων. Woman trial collaborators. Lancet. 2017 May 27; 389(10084): 2105–2116.

Updated WHO Recommendation on Tranexamic Acid for the Treatment of Postpartum Haemorrhage

Highlights and Key Messages from the World Health Organization's 2017 Global Recommendation

October 2017

www.mcsprogram.org

	Indication	Timing	Dosing
WHO 2012 TXA Recommendation	Use of TXA is recommended for the treatment of PPH **if oxytocin and other uterotonics fail to stop the bleeding or if it is thought that the bleeding may be partly due to trauma.**	For atonic uterus, use TXA **if oxytocin and other uterotonics fail to stop the bleeding.**	**IV (slowly): 1g** **Repeat after 30 minutes if bleeding continues.**
WHO 2017 TXA Recommendation (updated)	Use TXA **in all casesof PPH, regardless of whether the bleeding is due to genital tract trauma or other causes.**	Use TXA **within 3 hours and as early as possible after onset of PPH. Do not initiate TXA more than 3 hours after birth,** unless being used for bleeding that restarts within 24 hours of completing the first dose (see dosing).	Fixed dose of **1 g in 10 mL (100 mg/mL) IV at 1 mL per minute (i.e., administered over 10minutes)** **Second dose** of 1 g IV **if bleeding continues after30 minutes or if bleeding restarts within 24 hours of completing the firstdose**

Effect of treatment delay on the effectiveness and safety of antifibrinolytics in acute severe haemorrhage: a meta-analysis of individual patient-level data from 40 138 bleeding patients

*Angèle Gayet-Ageron, David Prieto-Merino, Katharine Ker, Haleema Shakur, François-Xavier Ageron, Ian Roberts, for the Antifibrinolytic Trials Collaboration**

Summary

Background Antifibrinolytics reduce death from bleeding in trauma and post-partum haemorrhage. We examined the effect of treatment delay on the effectiveness of antifibrinolytics.

Methods We did an individual patient-level data meta-analysis of randomised trials done with more than 1000 patients that assessed antifibrinolytics in acute severe bleeding. We identified trials done between Jan 1, 1946, and April 7, 2017, from MEDLINE, Embase, the Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science, PubMed, Popline, and the WHO International Clinical Trials Registry Platform. The primary measure of treatment benefit was absence of death from bleeding. We examined the effect of treatment delay on treatment effectiveness using logistic regression models. We investigated the effect of measurement error (misclassification) in sensitivity analyses. This study is registered with PROSPERO, number 42016052155.

Findings We obtained data for 40 138 patients from two randomised trials of tranexamic acid in acute severe bleeding (traumatic and post-partum haemorrhage). Overall, there were 3558 deaths, of which 1408 (40%) were from bleeding. Most (884 [63%] of 1408) bleeding deaths occurred within 12 h of onset. Deaths from post-partum haemorrhage peaked 2–3 h after childbirth. Tranexamic acid significantly increased overall survival from bleeding (odds ratio [OR] 1·20, 95% CI 1·08–1·33; p=0·001), with no heterogeneity by site of bleeding (interaction p=0·7243). Treatment delay reduced the treatment benefit (p<0·0001). Immediate treatment improved survival by more than 70% (OR 1·72, 95% CI 1·42–2·10; p<0·0001). Thereafter, the survival benefit decreased by 10% for every 15 min of treatment delay until 3 h, after which there was no benefit. There was no increase in vascular occlusive events with tranexamic acid, with no heterogeneity by site of bleeding (p=0·5956). Treatment delay did not modify the effect of tranexamic acid on vascular occlusive events.

Interpretation Death from bleeding occurs soon after onset and even a short delay in treatment reduces the benefit of tranexamic acid administration. Patients must be treated immediately. Further research is needed to deepen our understanding of the mechanism of action of tranexamic acid.

Funding UK NIHR Health Technology Assessment programme, Pfizer, BUPA Foundation, and JP Moulton Charitable Foundation (CRASH-2 trial). London School of Hygiene & Tropical Medicine, Pfizer, UK Department of Health, Wellcome Trust, and Bill & Melinda Gates Foundation (WOMAN trial).

Introduction

Acute severe bleeding is a leading cause of death.[1] Traumatic extracranial haemorrhage, often the consequence of road traffic crashes or violence, is responsible for more than two million deaths each year.[2] Traumatic and spontaneous intracranial bleeding are common causes of death and disability.[3] Severe surgical haemorrhage strongly predicts adverse patient outcomes and is associated with an increase in the odds of death by eight times.[4] Thousands of patients are admitted to hospital with gastrointestinal bleeding each year in the UK, with a case fatality of about 10% for upper gastrointestinal bleeding and 3% for lower gastrointestinal bleeding.[5,6] Postpartum haemorrhage accounts for about 100 000 maternal deaths each year worldwide, with the majority occurring in less developed countries.[7]

Antifibrinolytic drugs (tranexamic acid, aminocaproic acid, aprotinin, and aminomethylbenzoic acid) reduce bleeding by inhibiting the breakdown of fibrin clots.[8,9] Antifibrinolytics reduce surgical bleeding and the need for transfusion by about a third, irrespective of the site of surgery.[10] Administration of tranexamic acid within 3 h of bleeding onset reduces deaths from bleeding in patients with trauma and post partum haemorrhage.[11–13] We sought to quantify the effect of treatment delay on the effectiveness of antifibrinolytics in acute severe bleeding by analysing individual patientlevel data from randomised placebo controlled trials.

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See Comment page 97

*Members of the Antifibrinolytic Trials Collaboration are listed at the end of the Article

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ian.roberts@lshtm.ac.uk

Μετανάλυση 2 RCT WOMAN+CRASH-2 TRIALS

Επι συνόλου 40.138 ασθενών.

Στατιστικά σημαντική μείωση κατά 10% του ποσοστού επιβίωσης για κάθε 15 λεπτά καθυστέρησης στην χορήγηση του TXA iv . Μετά το πέρας των 3 h δεν υπάρχει όφελος από την χορήγηση TXA στην αντιμετώπιση της αιμορραγίας.

Gayet-Ageron A, Prieto-Merino D, Ker K, Shakur H, Ageron FX, Roberts I; Antifibrinolytic Trials Collaboration. Effect of treatment delay on the effectiveness and safety of antifibrinolytics in acute severe haemorrhage: a meta-analysis of individual patient-level data from 40 138 bleeding patients. Lancet. 2018 Jan 13;391(10116):125-132.

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Antifibrinolytic drugs for treating primary postpartum haemorrhage (Review)

Shakur H, Beaumont D, Pavord S, Gayet-Ageron A, Ker K, Mousa HA

Shakur H, Beaumont D, Pavord S, Gayet-Ageron A, Ker K, Mousa HA.
Antifibrinolytic drugs for treating primary postpartum haemorrhage.
Cochrane Database of Systematic Reviews 2018, Issue 2. Art. No.: CD012964.
DOI: 10.1002/14651858.CD012964.

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Antifibrinolytic drugs for treating primary postpartum haemorrhage (Review)

ΣΥΜΠΕΡΑΣΜΑΤΑ COCHRANE REVIEW

Μετανάλυση 3 RCT.
20412 Ασθενών .
ΤΧΑ μειώνει τον αριθμό θανάτων σε ΦΤ και ΚΤ .
Δεν παρατηρείται αύξηση θρομβοεμβολικων επεισοδίων
Η χορήγηση πρέπει να γίνει όσο το δυνατόν ταχύτερα εντός τριώρου.
Εναλλακτικές μέθοδοι χορήγησης (Per os) Είναι σημαντικοι ειδικά σε καταστάσεις όπου η νοσοκομειακή υποδομή είναι ανεπαρκής.

Shakure et al .Antifibrinolytic drugs for treating primary postpartum haemorrhage.Cochrane 2018

ΣΥΣΤΆΣΕΙΣ ΤΗΣ WHO ΓΙΑ ΤΗ ΧΡΉΣΗ ΤΟΥ TRANEXAMIC ACID ΣΤΗΝ ΑΝΤΙΜΕΤΩΠΙΣΗ ΤΗΣ ΑΙΜΟΡΡΑΓΊΑΣ ΜΕΤΆ ΤΟΝ ΤΟΚΕΤΟ

- **Το ΤΧΑ μπορεί να χρησιμοποιηθεί σε όλες τις περιπτώσεις αιμορραγίας μετά το τοκετό ανεξαρτήτου αίτιας που την προκάλεσε .**
- **Το ΤΧΑ θα πρέπει να ενταχτεί στα πρωτοκολλά συντηρητικής όπως και χειρουργικής αντιμετώπισης της αιμορραγίας μετα τον τοκετό .**

- **Το ΤΧΑ θα πρέπει να είναι διαθέσιμο πάντα στην αίθουσα τοκετού και στα τμήματα οπού εμφανίζονται περιπτώσεις με επείγουσα αιμορραγία.**

- **Το ΤΧΑ έχει χαμηλό κόστος και διάρκεια 3 έτη σε συσκευασία με θερμοκρασία δωματίου 15-30 C ˚**
- **Η χορήγηση ΤΧΑ πρέπει να γίνεται μετα την περάτωση του τοκετού και αμέσως μετα την έναρξη της αιμορραγίας εντός του χρονικού πλαισίου των 3 ωρών.**

Updated WHO recommendation on Tranexamic Acid for the treatment of Postpartum Haemorrhage 2017.

Συστάσεις της WHO για τη χρήση του tranexamic acid στην αντιμετώπιση της αιμορραγίας μετά τον τοκετό

- **Η καθυστέρηση στην έναρξη της χρήσης του ΤΧΑ μειώνει σημαντικά το όφελος του καθώς η καθυστέρηση 15 λεπ. μειώνει το ποσοστό επιβίωσης κατά 10%.**
- **Το ΤΧΑ χορηγείται σε σταθερή δόση ενός γρ. (1γρ. σε 10 ml IV) . Χορηγείται αργά με ρυθμό 1 ml ανά λεπτό). Εάν η αιμορραγία συνεχίζετε και στα επόμενα 30 λεπτά η δόση επαναλαμβάνετε με τον ίδιο τρόπο. Η επαναλαμβανομένη δόση μπορεί να εφαρμοστεί επίσης για αντιμετώπιση της αιμορραγία μέσα σε 24 ώρες μετά την πρώτη δόση.**
- **Η ενδοφλέβια χορήγηση του ΤΧΑ μπορεί να γίνει στα περισσότερα υγρά έγχυσης, τα οποία περιέχουν και οκυτωκίνη . Δεν χορηγείται μαζί με αίμα πενικιλίνη και μανιτόλη.**
- **Το ΤΧΑ δεν χορηγείται σε περιστατικά που έχουν αλλεργία στο φάρμακο , ιστορικό θρομβώσεων πριν ή κατά την διάρκεια της κύησης καθώς και περιστατικά με ενεργό ενδοαγγειακή θρόμβωση και ιστορικό σπασμών.**

Updated WHO recommendation on Tranexamic Acid for the treatment of Postpartum Haemorrhage 2017.

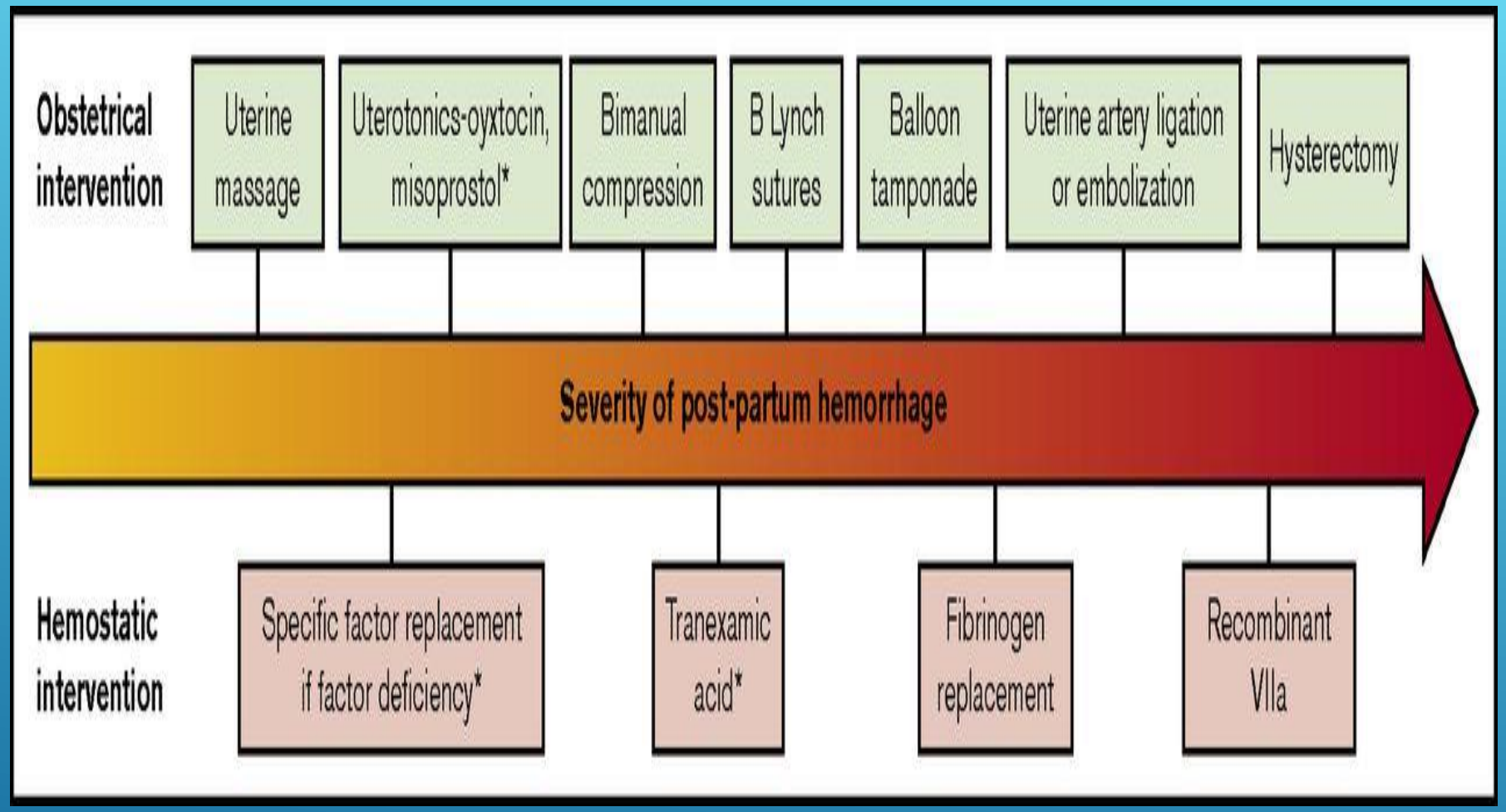
- **ΑΠΑΡΑΊΤΗΤΑ ΜΕΤΡΑ ΑΝΤΙΜΕΤΩΠΙΣΗΣ ΑΙΜΟΡΡΑΓΙΑΣ WHO GUIDELINES**
- **(STANDARD TREATMENT PACKAGE) WHO GUIDELINES**
- 1.ΧΟΡΗΓΗΣΗ **ΥΓΡΩΝ**
- 2.ΧΟΡΗΓΗΣΗ ΜΗΤΡΟΣΥΣΠΑΣΤΙΚΩΝ (**ΩΚΥΤΟΚΙΝΗ,ΚΑΡΒΕΤΟΣΙΝΗ,ΜΕΘΕΡΓΟΤΑΜΙΝΗ,ΜΙΣΟΠΡΟΣΤΟΛΗ**)
- 3.ΧΟΡΗΓΗΣΗ **ΤΡΑΝΕΞΑΜΙΚΟΥ ΟΞΕΟΣ (ΑΜΕΣΑ ΚΑΙ ΌΧΙ ΠΕΡΑ ΤΩΝ ΤΡΙΩΝ ΩΡΩΝ)**
- 4.MONITORING **ΖΩΤΙΚΩΝ ΣΗΜΕΙΩΝ.**
- 5.ΜΗ ΧΕΙΡΟΥΡΓΙΚΟΙ ΧΕΙΡΙΣΜΟΙ (**ΑΜΦΙΧΕΙΡΗ ΣΥΜΠΙΕΣΗ ΜΗΤΡΑΣ,ΜΑΛΑΞΕΙΣ ΜΗΤΡΑΣ, ΜΠΑΛΟΝΙ ΕΠΙΠΩΜΑΤΙΣΜΟΥ, ΕΞΩΤΕΡΙΚΗ ΣΥΜΠΙΕΣΗ ΑΟΡΤΗΣ**)
- 6.ΧΕΙΡΟΥΡΓΙΚΟΙ ΧΕΙΡΙΣΜΟΙ (**ΑΙΜΟΣΤΑΤΙΚΕΣ ΡΑΦΕΣ, ΑΠΟΛΙΝΩΣΗ ΕΣΩ ΛΑΓΟΝΙΟΥ, ΑΓΓΕΙΑΚΟΣ ΕΜΒΟΛΙΣΜΟΣ, ΥΣΤΕΡΕΚΤΟΜΙΑ**).

VOGEL JP, OLADAPO OT, DOWSWELL T, GÜLMEZOGLU AM. UPDATED WHO RECOMMENDATION ON INTRAVENOUS TRANEXAMIC ACID FOR THE TREATMENT OF POST-PARTUM HAEMORRHAGE. LANCET GLOB HEALTH. 2018 JAN;6(1)

Δυνητικά οφέλη και παρενέργειες από την χρήση του ΤΧΑ

ΟΦΕΛΗ	ΠΑΡΕΝΕΡΓΕΙΕΣ
Μείωση της αιμορραγίας μετά τον τοκετό	Ελάσσονες παρενέργειες Ναυτία,έμετοι,κεφαλαλγία,αλλεργία
Μείωση του ποσοστού μεταγγίσεων	Αρτηριακή θρόμβωση
Μείωση της χρήσης μητροσυσπαστικών	Φλεβική θρόμβωση
Μείωση της ενδοφλέβιας χορήγησης σιδήρου	Νεφρική ανεπάρκεια, οξεία σωληναριακή νέκρωση.
Μείωση του χρόνου νοσηλείας	Σπασμοί. (Αναστολή υποδοχέων λυσίνης σε συνάψεις στο ΚΝΣ)

KOUIDES PA. ANTIFIBRINOLYTIC THERAPY FOR PREVENTING VWD-RELATED POSTPARTUM HEMORRHAGE: INDICATIONS AND LIMITATIONS. BLOOD ADV. 2017 APR 25;1(11):699-702.



Kouides PA. Antifibrinolytic therapy for preventing VWD-related postpartum hemorrhage: indications and limitations. Blood Adv. 2017 Apr 25;1(11):699-702.

Χρήσιμοι σύνδεσμοι.

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Σας ευχαριστώ