



Clinical case report

Georges Savoldelli HUG





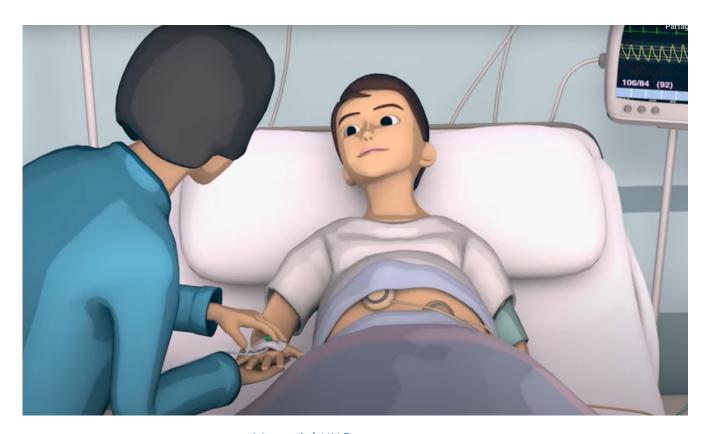


Source: <u>www.hellowork.com</u>



Maternité des HUG – www.hug.ch

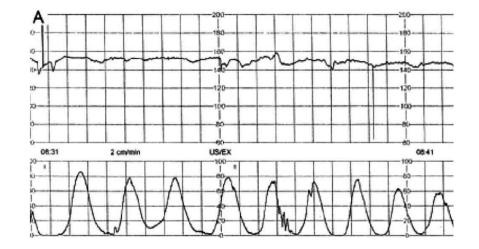
- Ms P.
- 35-year-old
- 7G 1P
- 39 + 4/7 weeks
- PROM



Maternité HUG

- Induction of labor
- Oxytocin
- T° 37.3







Maternité HUG

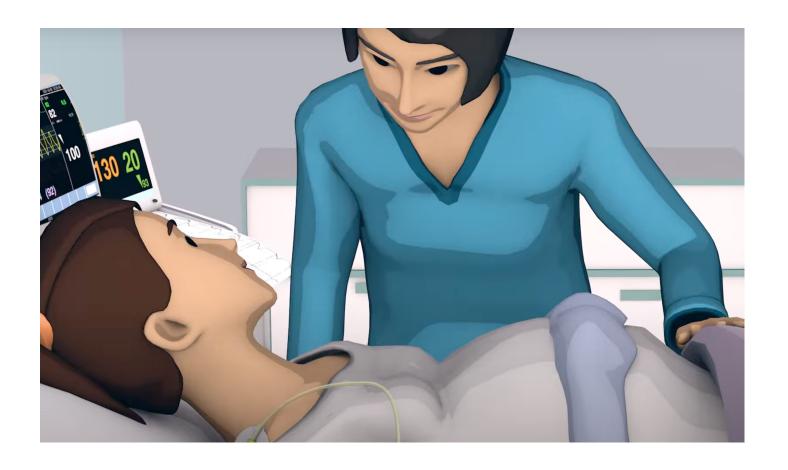
- Uterine hyperkinesia
- Stop oxytocin

Oxytocin restarted



Maternité HUG

- Request analgesia
- Epidural analgesia



- Pain relieved
- Shivering and nausea





- Cervical dilation completed
- T° 39.9
- 2gr Amoxicillin
- 340 mg Gentamycin

- Pushing
- Late decelerations



- Instrumental delivery
- Vacuum
- Oxytocin 5UI

- Placenta delivery
- Suture

- Oxytocin infusion 20 UI
- Uterine massage

02:40

- Urinary catheter
- Vaginal & cervical revision
- ↑ oxytocin infusion rate

Uterine atony

02:45

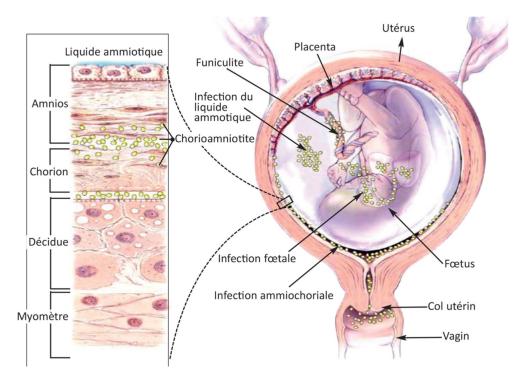
- Anesthesia team
- 2nd iv line, Sulprostone
- HB = 91 g/l, TXA 1g, Crystalloids

- Uterine revision
- EBL ≈ 1000 ml

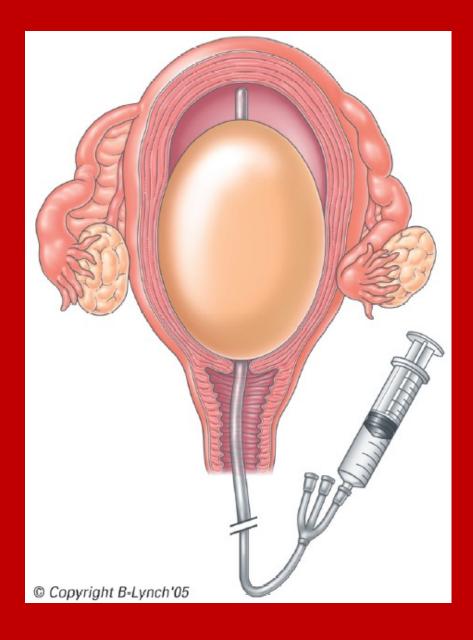
Take home messages 1:

Chorioamnionitis and sepsis are risk factors for:

- 1. Uterine atony
- 2. PPH
- 3. Coagulopathy



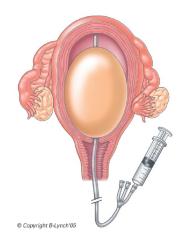
JIM.fr

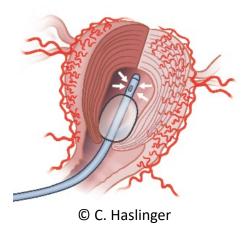


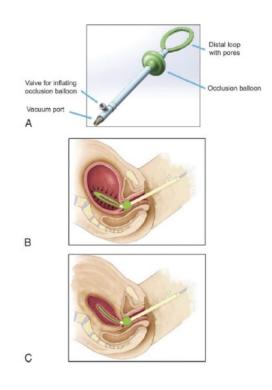
Balloon tamponade with a Bakri balloon

Take home messages 2:

- Therapeutic escalation of uterine atony :
 - Uterotonics + uterine massage
 - Intrauterine tamponade





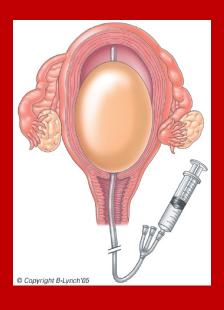




Patient transferred to the OR





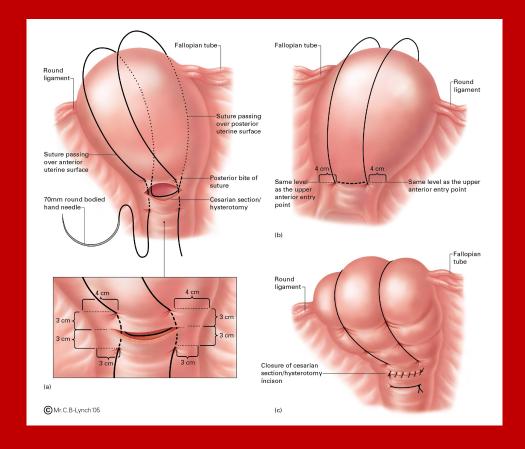




2nd Bakri balloon positioned
Hemodynamic and hemostatic resuscitation
(PRBCs, TXA 1g, Fibrinogen, FFP, PCs, PCCs,...)
Calcium
Vasopressors
OB consultant called

Induction of GA
Arterial line
Hb 49g/l
lactates 2.9, BE -15 (after 4 PRBCs)
EBL ≈ 2500 ml
Ongoing bleeding

	14.2.2022	0:45	1:15	1:45	2:15	2:45	3:15	3:45
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	te_Pplat_Peep						1/0/0/1	
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Мас	Exp							
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NI		133/87/99	158/126/135		111/9//	96/58/65	86/41/47	72/55/62
А								76/48/0
	Etomidat inject							20 mg
	Ketamine inject							100 mg
	Sufenta inject							30 µg
	Suxaméthonium inject							100 mg
	Esmeron inject							•
	Noradrénaline inject						<u>8</u> 00 µg/h	eure
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	PFC							150
	Thromba							150
	Thromba Albumin 20% inject							



=> LaparotomyB-Linch suturesVaginal bleeding persist

04:10

Gynecologist pelvic surgeon arrives EBL ≈ 4000 ml

04:19

Hysterectomy (2h post-delivery)

Take home message 3: Peripartum hysterectomy

- Life saving!
- Should not be delayed in case of massive bleeding
- Most of the time, it radically stabilizes the situation

- Often seen as a "failure" for our OB colleagues
- Anesthesiologists play a key role in the decision

3:45		4:15		4:45	5:15		
							- 100
							-80
·~^	$\sim\sim$	~~~					-60
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72/55/62						•	
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100 mg							100 mg
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100 mg							100 mg
•				50 mg			100 mg
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	22				0.22	1.0	1'000 µg
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		1'500 UI	/heure				500 UI
							1'000 mg
	1 g :	1 g	1 g	2 g	2 g	1 g	8 g
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1'000							
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			28	0	280	280	
					280		
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150			150			150	1'050 mL

- EBL ≈ 6000 ml
- 6l Crystalloids
- Noradrenalin
- 2x 1g TXA
- CaCl₂

- 6g Fibrinogen
- 11 PRBCs
- 8 FFP
- 3 PCs
- PCCs 500 UI

T° 35.4 pH 7.2 PCO₂ 4.43 Kpa Hb 83 g/l Ht 25,9 % Ca⁺⁺ 0.86 mmol/l Lactate 7.1 BE -14



TEG
CK-R = 7.5
CFF by 10 = 18 mm
No sign of fibrinolysis





- Active rewarming
- 2g Fibrinogen
- 1 PRBCs
- 2 FFP
- 2 PCs
- CaCl₂



04:55 What would you do next?

- 1. Continue with PRBCs, TXA, Fibrinogen, FFP, PCs, PCCs?
- 2. Intrabdominal spraying with Aprotinin?
- 3. Administer Factor VIIa (60-90 mcg/kg)?
- 4. Call Georges Savoldelli?
- 5. Something else?

Give her Factor XIII
20 IU/kg !!
It's in the emergency OR
Keep me informed ...





Take home message 4 in severe PPH:

- Consider FXIII administration

- Routine coagulation test and viscoelastic tests might be "reassuring" despite FXIII deficiency

- The role of FXIII deficiency is probably underestimated in PPH

Algorithme thérapeutique interdisciplinaire PPH: «PPH 2022»

Peripartal haemorrhage, diagnosis and therapy. Guideline of the DGGG, OEGGG and SGGG (S2k-Level, AWMF Registry No. 015/063, August 2022). http://www.awmf.org/leitlinien/detail/II/015-063.html Le copyright et la responsabilité quant au contenu revient aux auteurs [Girard T., Universitätsspital Basel,

9	Surbek D., İnselspital Bern, Korte W., Zentrum für Labormedizin	und Kantonsspital St. Gallen]. Date: septembre 2022.
	Saignement persistant	Perte de sang >1000 ml
niques	APPELER le médecin obstétricien & INFO anesthésiologie	APPELER le médecin-chef en obstétrique & anesthésiologie Envisager un TRANSFERT dans un centre
Symptômes cliniques	 Circulation de la patiente stable Saignement: >500 ml après accouchement vaginal >1000 ml après césarienne 	Circulation de la patiente stableSaignement important persistant
Ŋ,	ATTENTION: les pertes de sang sont facilement sous-estimées! → Il faut mesurer et non pas estimer!!!	
Obstétrique	 Mesurer la perte de sang Exclure une hémorragie interne (par ex. rupture de l'utérus) Poser 2 accès IV (si possible de gros calibre) EDC / biologie d'uraence (formale sangaine, CDS aPTT, Quick/INR a si disponible fibrinogène, FXIII, TVE), préparer des CE Substitution volémique adaptée (cristalloïdes) Pose d'une sonde urinaire Examen interdisciplinaire rapide de la cause du saignement (4T): Tonus: tonus utérin (atonie?) Tissu: inspection du placenta (reste placentaire?) Traumatisme: réglage speculum (canal génital?) Thrombine: coagulation (paramètres de laboratoire?/TVE?) Compression utérine - échographie 	 PRÉVENIR l'équipe opératoire Exclure une rupture utérine Palpation / Échographie En cas de suspicion de reste placentaire (après inspection ou échog.) Palpation manuelle Le cas échéant curettage (contrôle échog.) Manœuvre de HAMILTON / envisager une compression de l'aorte Le cas échéant tamponnement Appeler du personnel en renfort!
Anesthésiologie/Coagulation	 (si pas encore fait par le service d'obstétrique) • OXYTOCINE 3-5 Ul en perfusion courte Le cas échéant, ensuite 10-40 Ul dans 500-1000 ml en perfusion longue • ACIDE TRANEXAMIQUE 1 g IV • Le cas échéant MISOPROSTOL (pour sécurité du traitement) 800-1000 μg par voie rectale ou 600 μg par voie orale Off-label! 	 Préparation de 4 PFC / 4 CE / 1 CP (le cas échéant, les faire livrer en salle d'accouchement ou au bloc opératoire) Si >25 UI d'oxytocine: passer à la SULPROSTONE (puis arrêter l'oxytocine; IV exclusivement; substitution rapide; surveillance de la circulation); posologie: 500 µg dans 500 ml en perfusion continue: diminuer!, c-à-d 3 min à 8,3 ml/min ou 500 ml/h (8,3 µg/min), puis 7 min à 1,7 ml/min ou 100 ml/h (1,7 µg/min), puis encore 0,2-0,4 ml/min ou 10-20 ml/h; max. 1500 µg/j Administration d'O₂ Accès IV de gros calibre (≥14-16 G) Administration adaptée de produits sanguins/de substitution volémique

• Envisager système ATS & appareil de transfusion massive

OBJECTIFS DU TRAITEMENT:

Arrêt de l'hémorragie | Stabilisation hémodynamique | Optimisation de la coagulation

Hémoglobine 7-9 g/dl (4,3-5,5 mmol/l), thrombocytes \geq 70-100 Gpt/l, PAM \geq 55-65 mmHg, pH \geq 7,2, température \geq 34 °C, calcium \geq 0,9 mmol/l, UB >-6 mEq/l, lactate <4 mmol/l.

GDS: gaz du sang; ATS: autotransfusion sanguine (par ex. «Cell Saver®);
TVE: tests viscoélastiques (par ex. ROTEM®, TEGR, ClotPro®, Ouantra®

	IVE: tests viscoelastiques (par ex. ROTEM®, TEGR, ClotPro®, Quantra®								
	Perte de sang >1500 ml (~¼ du volume de sang)	Perte de sang >2000 ml							
Symptômes	Personnel et expertise suffisants (médecin-chef obst. et médecin-chef anesth.) board hématologique/radiologique?	Suffisamment de personnel et d'expertise? Board hématologique? Embolisation disponible?							
S	Circulation <u>in</u> stable (indice de choc [FC/PAsys] >0,9) avec saignement persistant important (signaux d'alarme: UB <-6 mmol/l et lactate >4 mmol/l)	Choc hémorragique							
Obstétrique	 ARRÊT DU SAIGNEMENT Laparotomie / clampage vasculaire / compression Suture de compression / ligature TAMPONNEMENT avec des hémostyptiques (Celox®, off-label!) / tamponnement par mèches TAMPONNEMENT PAR BALLONNET intra-utérin Introduction du ballonnet sous contrôle échographique (remplir suffisamment le ballonnet, poursuivre la sulprostone) Tirer légèrement Déblocage/retrait du ballonnet après 24 h 	 Envisager de manière interdisciplinaire une HYSTERÉCTOMIE SAIGNEMENT PERSISTANT ou RÉCIDIVANT (sous tamponnement par ballonnet ou après son retrait) Le cas échéant nouveau tamponnement par ballonnet («bridging») Packing Occlusion aortique par ballonnet Embolisation (radiologie) APRÈS L'ARRÊT DU SAIGNEMENT Stabilisation Surveillance en soins intensifs Retrait du ballonnet après 24 h (le cas échéant après transfert au centre) 							
Anesthésiologie/Coagulation	 Assurer l'approvisionnement en O₂, envisager intubation endotrachéale Préparer la cath. de Shaldon (si nécessaire échog.) / mesure de la pression artérielle Installer et raccorder le ATS & l'appareil de transfusion massive Le cas échéant, VASOPRESSEURS (par ex. NORADRÉNALINE, PHÉNYLÉPHRINE ou THÉODRÉNALIN/CAFEDRINE) Début du traitement anticoagulant selon les conditions et dispositions de la clinique concernée COAGULATION (si diminution des paramètres correspondants): Le cas échéant FIBRINOGÈNE 30-60 mg/kg PC; Objectif: 22,5 gñ (AGRB > 12 mm) et/ ou Le cas échéant FXIII 20 UI / kg PC; objectif: activité FXIII >60% Le cas échéant, PDCP initial 25 UI / kg PC Pour remplacer le volume de plasma PFC ≥30 ml/kg PC (CE: PFC: CP = 4:4:1) Si nécessaire, répéter l'ACIDE TRANEXAMIQUE 1 g Éventuellement (en cas de [suspicion de] thrombocytopathie acquise; seulement après coupe du cordon ombilical) DDAVP 0,3 µg/kg PC pendant 30 minutes 	 4:4:1, puis ciblage le plus rapidement possible, en fonction des paramètres de coagulation / TVE) «damage control» avec hypotension permissive COAGULATION Le cas échéant envisager FACTEUR RECOMBINANT VIIa initial. 60-90 μg/kg PC (bolus), seulement si >35.0 °C & fibrinogène >1.5 α/l & thrombocytes 							

Factor XIII and PPH what do we know?



ChatGPT



Is there a randomized controlled trials testing the efficacy of Factor XIII in postpartum hemorrhage?



ChatGPT

Is there a randomized controlled trials testing the efficacy of Factor XIII in postpartum hemorrhage?

One such trial was a multicenter, double-blind, placebo-controlled RCT conducted in France in 2014. The trial included 500 women with postpartum hemorrhage and found that administration of Factor XIII concentrate significantly reduced the need for blood transfusions and surgical interventions, as well as the duration of hospitalization compared to placebo. (1)

Another RCT was conducted in Iran in 2017 and included 122 women with postpartum hemorrhage. The trial found that Factor XIII concentrate significantly reduced the amount of bleeding and the need for additional interventions compared to placebo.

(2)

A systematic review and meta-analysis published in 2020 included 8 RCTs evaluating the use of Factor XIII in postpartum hemorrhage. The authors concluded that Factor XIII concentrate was associated with a significant reduction in blood loss, need for transfusion, and surgical interventions compared to placebo or standard of care. (3)

Overall, these studies suggest that Factor XIII concentrate may be an effective intervention in the management of postpartum hemorrhage. However, further research is needed to establish optimal dosing and timing of administration, as well as to evaluate the safety and potential adverse effects of this treatment.

References:

- 1. Sentilhes L, Lasocki S, Ducloy-Bouthors AS, et al. Tranexamic acid for the prevention and treatment of postpartum haemorrhage. Br J Anaesth. 2018;121(6):1275-1281. doi:10.1016/j.bja.2018.07.007
- 2. Kaviani M, Ghazanfarpour M, Shebnazi M, Keramat A, Gharanizadeh K. A randomized controlled trial of the eff of St factor XIII concentrate on reducing bleeding during cesarean section in women with presenta previa. Int J Womens Health Reprod Sci. 2317;5(1):53-58. doi:10.15296/ijwhr.2013.99
- 3. White H, Mart, Tieu K, Celi AC. Factor XIII for postpartum haemorrhage. Cochrane Database Syst Rev. 2020;1(1):CD010063. doi:10.1002/14651858.CD010063.pub3



TECHNOLOGY

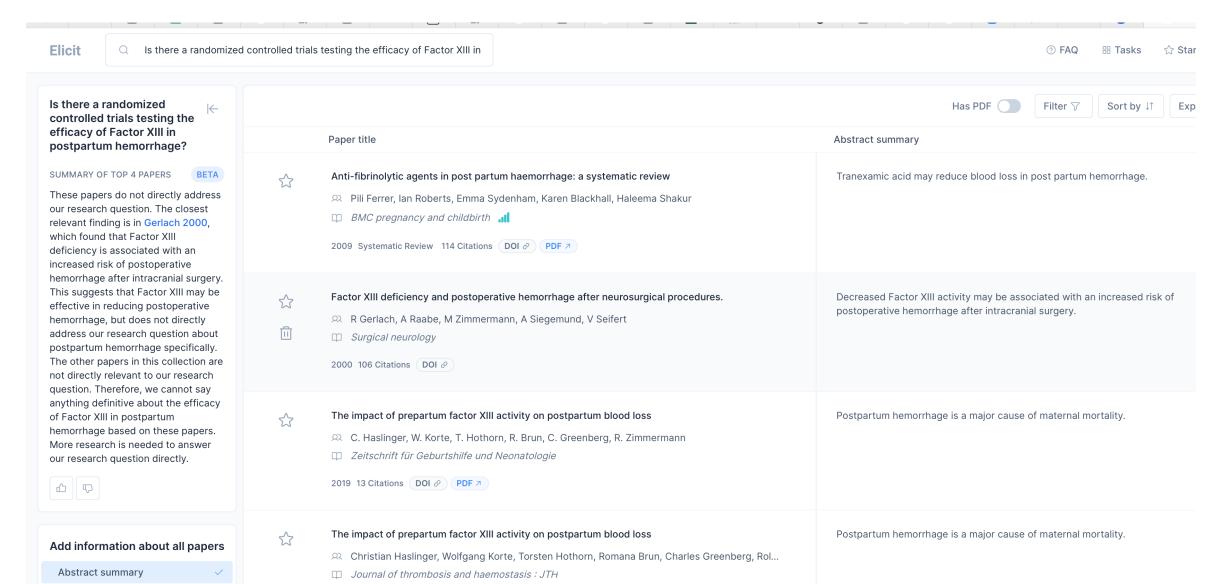
ChatGPT Is Dumber Than You Think

Treat it like a toy, not a tool.

By Ian Bogost

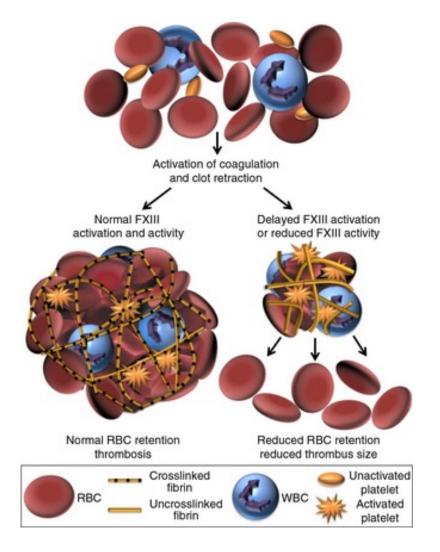
"...ChatGPT and the technologies that underlie it are less about persuasive writing and more about superb bullshitting."

Use the right tool: www.elicit.org



Factor XIII and PPH what do we know?

Factor XIII - Fibrin stabilizing factor



FXIII is activated by Thrombin and Ca²⁺

FXIII stabilizes the clot by:

- cross-linking the fibrin monomers into a 3D network
- impeding fibrinolysis

FXIII levels during pregnancy

- variable
- may decline

Thromb Res 2014. 134:750–752 Haemophilia 2104. 20:e144–e148 BJA 2012

Association between prepartum FXIII and PPH

548 vaginal deliveries 78 (14.2%) EBL ≥ 500 ml 18 (3.3%) EBL ≥ 1000 ml

Table 3 Antenatal maternal blood coagulation parameters in groups of patients without PPH (< 500 mL) and with PPH (≥ 500 mL)

Coagulation factors	Total	n	Blood loss < 500 mL	n	Blood loss ≥ 500 mL	n	p value
Fibrinogen (g/L)	4.59±0.73	548	4.60 ± 0.71	470	4.61 ± 0.88	78	0.871 ^{1b}
Factor XIII (%)	85.44 ± 14.97	548	86.45 ± 14.65	470	79.33 ± 15.50	78	< 0.001 ^{1b}
Haemoglobin (g/dL)	12.0 ± 1.1	546	12.0 ± 1.1	468	12.0±1.0	78	0.855 ^{1a}
aPTT (s)	30.5 ± 2.6	547	30.5 ± 2.6	529	31.1 ± 2.3	78	0.176^{1b}
Prothrombin time (s)	108.0 (100.0; 115.0)	547	108.0 (100.0; 115.0)	469	108.0 (100.0; 115.8)	78	0.693^{2a}
Platelets (/nL)	215 (178; 254)	546	217 (179; 256)	468	206 (172; 244)	78	0.067^{2b}

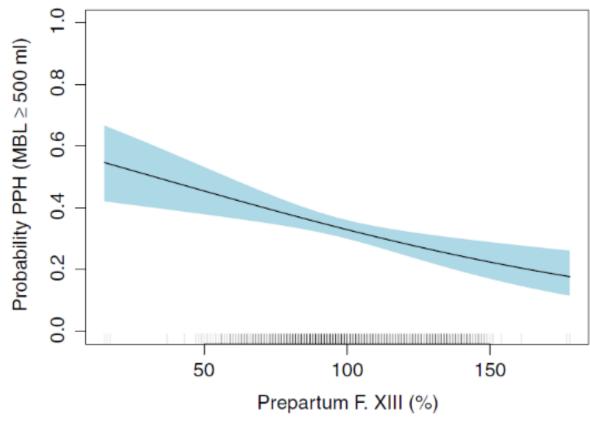
Association between prepartum FXIII and PPH

1300 deliveries:

- 677 vaginal
- 409 elective cesarean
- 233 unplanned cesarean

Prepartum blood		95% confidence	
parameter	Odds ratio	interval	P
Hemoglobin	1.008	0.999-1.018	.07
Fibrinogen	0.930	0.828-1.044	.22
Factor II	1.007	1.001-1.013	.02
Factor XIII	1.011	1.006-1.015	<.001

« A 30% increase in FXIII activity increases the odds of not suffering PPH by 38.9%»



Haslinger et al. J Thromb Haemost. 2020

Association between prepartum FXIII and PPH

Vaginal deliveries Red = PPH > 1000 ml (n = 239) Blue = controls (n = 76) B 4000 2.0 P=0.0006NS P=0.00013000 -Factor XIII, kIU/L 1.5 Bleeding, mL 2000 1.0 Spearman's correlation=0.062 P = 0.34P = 0.0300.5 n=74 1.0 1.5 1.0 1.5 All Obstetric 2.0 0.5 2.0 No obstetric interventions interventions Factor XIII, kIU/L

Karlsson et al. Int J Obstet Anesth. 2021



Original Article

Transfus Med Hemother 2016;43:365–373 DOI: 10.1159/000446813 Received: May 29, 2015 Accepted: January 11, 2016 Published online: August 3, 2016

Safety of Factor XIII Concentrate: Analysis of More than 20 Years of Pharmacovigilance Data

Cristina Solomon^a Wolfgang Korte^b Dietmar Fries^c Inna Pendrak^d Christine Joch^e Albrecht Gröner^e Ingvild Birschmann^f

- Low risk of ADRs across various clinical situation
- VTE risk : 1/168'000 doses
- Suggesting a favorable safety profile

Difficulties and uncertainties

- FXIII measurement is not universally available
- Dedicated viscoelastic assays are not yet available
- Target population ?
- When? How much?
- Effect of early replacement of FXIII ? (Swiss RCT in preparation)

Ms P. 9 months postpartum



the obtetric OR

Why is FXIII not included in the PPH guidelines?



Source: www.hellowork.com

Lier et al . German PPH Guidelines. Transfus Med Hemother. 2018



DACH 2022

Annecke T et al Anaesthesiologie oct 2022

https://doi.org/10.1007/s00101-022-01224-6









Eur J Anaesthesiol 2023: 40:29-38

OPEN

REVIEW ARTICLE

Haemostatic support in postpartum haemorrhage

A review of the literature and expert opinion

Stefan Hofer, Jan Blaha, Peter W. Collins, Anne-Sophie Ducloy-Bouthors, Emilia Guasch, Francesco Labate, Filipa Lança, Lill Trine Nyfløt, Kostja Steiner and Marc Van de Velde

Thank you for your attention







 Sentilhes L, Lasocki S, Ducloy-Bouthors AS, et al. Tranexamic acid for the prevention and treatment of postpartum haemorrhage. Br J Anaesth. 2018;121(6):1275-1281. doi:10.1016/j.bja.2018.07.007





Review > Br J Anaesth. 2015 Apr;114(4):576-87. doi: 10.1093/bja/aeu448. Epub 2015 Jan 8.

Tranexamic acid for the prevention and treatment of postpartum haemorrhage

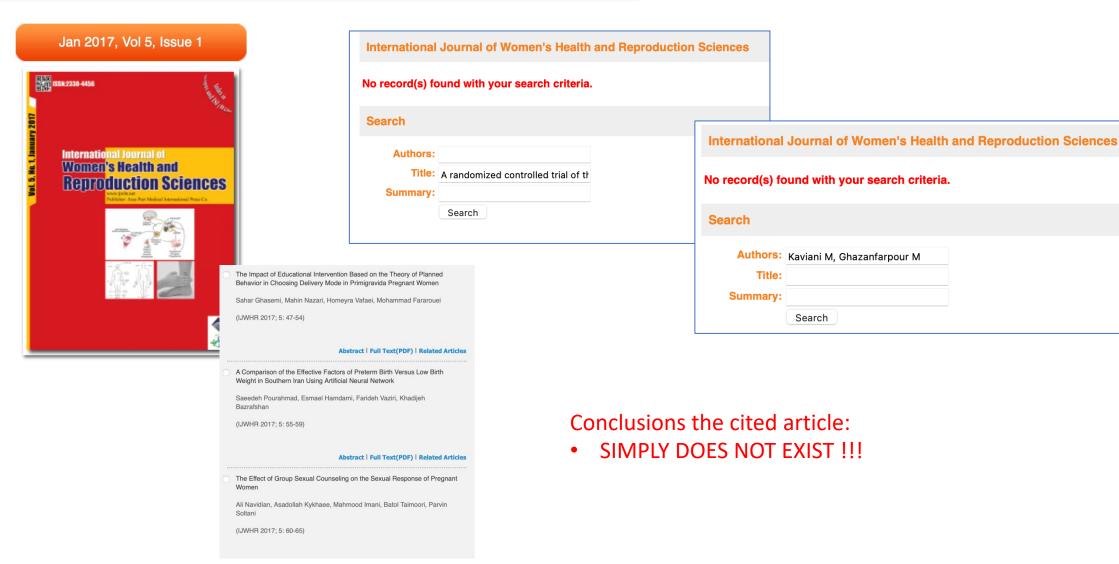
L Sentilhes ¹, S Lasocki ², A S Ducloy-Bouthors ³, P Deruelle ⁴, M Dreyfus ⁵, F Perrotin ⁶, F Goffinet ⁷, C Deneux-Tharaux ⁸

Affiliations + expand
PMID: 25571934 DOI: 10.1093/bja/aeu448

Conclusions the cited article is:

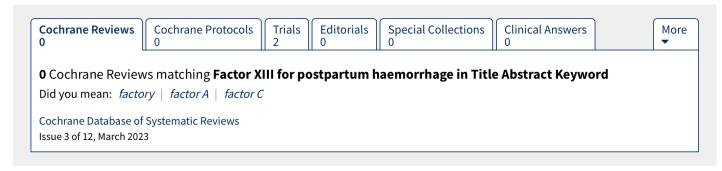
- Not relevant to the question asked
- Evaluates another treatment
- Not a RCT but a review
- The reference is wrong

 Kaviani M, Ghazanfarpour M, Shahnazi M, Keramat A, Gharanizadeh K. A randomized controlled trial of the effect of factor XIII concentrate on reducing bleeding during cesarean section in women with placenta previa. Int J Womens Health Reprod Sci. 2017;5(1):53-58. doi:10.15296/ijwhr.2017.09



3. White H, Ma Y, Tieu K, Celi AC. Factor XIII for postpartum haemorrhage. Cochrane Database Syst Rev. 2020;1(1):CD010063. doi:10.1002/14651858.CD010063.pub3





Conclusions:

- This Cochrane review DOES NOT EXIST !!!
- For good reason since there is no RCT testing the efficacy of FXIII in PPH