

The obstetric and gynaecological experience of women with congenital prothrombin deficiency: a systematic review of literature.

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INTRODUCTION:

- Congenital prothrombin deficiency is a rare, autosomal recessive bleeding disorder with an estimated worldwide incidence of around 1 in 2,000,000. Prothrombin is a vitamin-K-dependent polypeptide synthesised in the liver.
- Prothrombin deficiency can manifest as a hypoprothrombinemia (a true deficiency of normal prothrombin), as dysprothrombinemia (where a dysfunctional prothrombin exists) or as a combination of the two, depending on the specific mutation involved. The bleeding diatheses often present in childhood with varying degrees of severity.
- The aim of this systematic review was to determine the optimal management of the specific challenges posed to obstetrics and gynaecology in those women of a reproductive age.

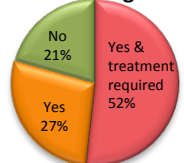
METHOD:

- The existing literature was systematically reviewed online via Medline, Embase, MIDIRS and Cochrane using the appropriate MeSH terms, including 'prothrombin deficiency', 'hypoprothrombinemia', 'dysprothrombinemia', 'clotting factor ii', or 'coagulation factor ii'.
- The search was limited to cases in humans with an isolated congenital prothrombin deficiency and articles published in English, however case series where it was not possible to confirm gender nor extract the data for an individual were excluded. There was no time limitation on the cases collected.
- 29 relevant articles were identified, comprising 15 case reviews and 14 case series. This included 32 women of a childbearing age with 26 pregnancies occurring in 10 of these women.

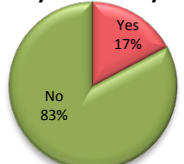
Prothrombin Deficiency in Gynaecology

- **Menorrhagia** was reported in 79% (23/29).
 - Treatment was required in 52% (15/29) of these patients. In the acute setting, treatment included transfusion support (blood, FFP and prothrombin complex concentrate) and aminocaproic acid. Longer term prophylaxis included the oral contraceptive pill in 28% (8/29) or monthly prothrombin complex concentrate in one case.
 - One patient who did not have menorrhagia had been on regular FFP prophylaxis since childhood for a severe bleeding tendency.
- **Hysterectomy** was reported in 17% (5/29) women.
 - 4 of these (80%) were elective for patients with a history of severe menorrhagia.
 - 1 was performed as an emergency following unabated bleeding at miscarriage.
- **Haemoperitoneum** was reported in 10% (3/29).
 - They were thought to be related to ovulation bleeding or corpus luteal haemorrhage. 2 of 3 cases were recurrent and bleeding usually resolved with transfusion support, though 1 case eventually ended in bilateral oophorectomy.

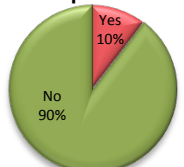
Menorrhagia?



Hysterectomy?



Haemoperitoneum?



Prothrombin Deficiency in Obstetrics

- 23 pregnancies in 9 patients were reviewed, resulting in 18 live births and 5 (22%) miscarriages. 2 were delivered by Caesarean (indication not specified), 2 were confirmed spontaneous vaginal deliveries and the remaining 14 were not otherwise specified.
- **Surgical management of miscarriage** was successfully performed on 3 separate occasions in the same patient using PCC prophylaxis. The management of one case was not specified and one case ended in emergency hysterectomy.
- **Maternal intracerebral haemorrhage** was documented in two separate women. One occurred at 24 weeks' gestation without any lasting maternal morbidity and resulted in a normal delivery at term. The other case occurred two weeks postpartum resulting in a maternal death.
- **Prothrombin Complex Concentrate prophylaxis** were documented in 6 uneventful deliveries, including one Caesarean. No PPH was sustained in these cases. 4 further deliveries (including 1 other Caesarean) were documented with no mention of prophylaxis at all; all 4 patients were known to normally be free from bleeding tendencies.
- **Postpartum haemorrhage** was documented in 8 cases. All were reported as "severe" and requiring transfusion support. No pharmaceutical, mechanical nor surgical methods of PPH management were detailed. 6 of these cases had no mention of transfusion prophylaxis prior to delivery, 1 case used only FFP for prophylaxis and another only reported "adequate protection".

RECOMMENDATIONS:

- Anticipation of menorrhagia and consideration to prophylaxis with the oral contraceptive pill, levonorgestrel-releasing intrauterine system, or regular prothrombin complex concentrate injections can dramatically alter the quality of life for these women.
- Women with prothrombin deficiency of a childbearing age should be counselled pre-conceptually. Planning a pregnancy with a multidisciplinary team in a tertiary unit with experience in managing women with rare bleeding disorders is recommended. Partner testing may be necessary.
- Prothrombin complex concentrates given in the 24 hours prior to delivery with an active third stage should provide adequate cover, though acute bleeds may be managed with further PCC, FFP and/or blood. Early recourse to uterotonic medication and mechanical methods such as intrauterine balloons should be considered.