



HAE Australasia

hope • advocacy • education

Australasian Patient Organisation for Hereditary Angioedema

Patient and Carer Webinar Series 2024

HAE In Women and Pregnancy

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Acknowledgement of Country

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We would like to begin by acknowledging the Traditional Owners of the land on which we meet today. We would also like to pay respects to Elders past and present.



LIVING WITH HAE AS A WOMAN

PROF CH KATELARI

CAMPBELLTOWN HOSPITAL AND WESTERN SYDNEY UNIVERSITY

HAE in Women-overview

Female sex hormones appear to play an important role in the onset of HAE and the frequency of attacks:

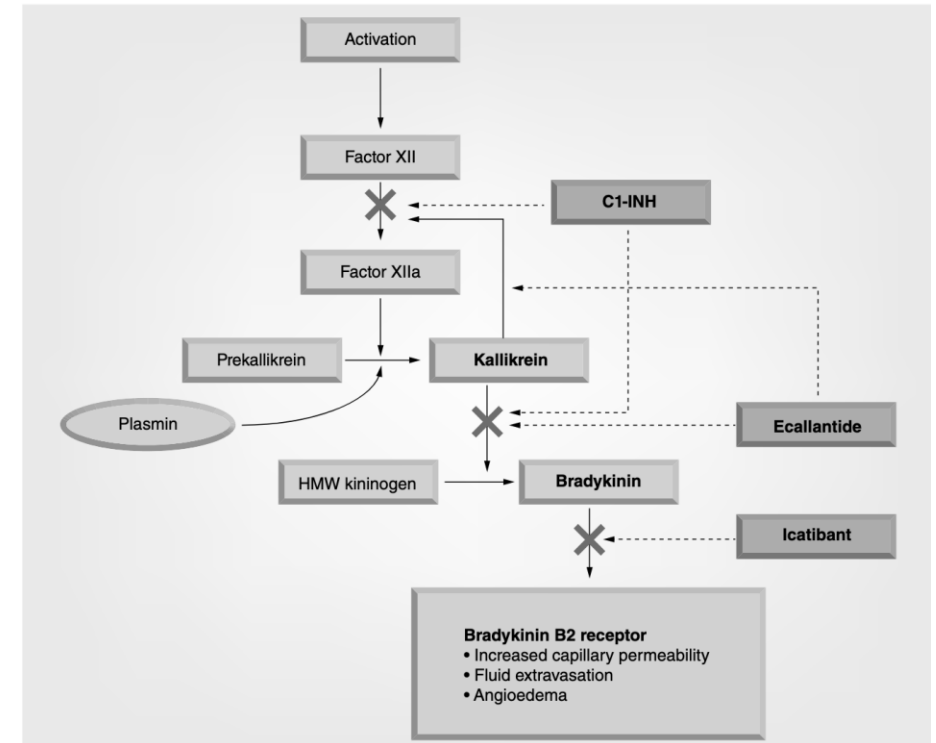
- Women have more frequent attacks of HAE than men
- Women often have more severe HAE symptoms than men and require hospitalisation for attacks more often
- In a survey of 150 women with HAE:
 - 62% reported that the disease worsened during puberty
 - 80% that it worsened while taking oestrogen containing oral contraceptives
- Menstruation and ovulation have been found to trigger HAE attacks
 - use of progestin-only OCs has been reported to reduce the frequency of attacks
- Initiation of oestrogen replacement during menopause has been reported to exacerbate HAE

HAE-nC1INH

- A high proportion of women report that their symptoms began when
 - they initiated oestrogen-containing oral contraceptives
 - became pregnant for the first time
 - their symptoms are exacerbated by OC use or pregnancy
- In 29% of HAE -nC1INH patients, symptoms occur only during periods of increased exposure to oestrogen

Female sex hormones in HAE

- Role not fully understood
- Various physiologic associations have been observed, particularly with regard to the kallikrein–kinin system
- Women treated with oestrogens have increased plasma levels of coagulation factor XII, bradykinin and kallikrein
- Oestrogen has been shown in animal studies to regulate bradykinin B2-receptor gene expression and function



Menstruation

- HAE attacks are reported to be triggered by menses in 35% and by ovulation in 14%
- Diagnosing an abdominal HAE attack during menses is difficult
 - Eg. Pain may be due to pelvic endometriosis
- With severe abdominal pain or intestinal swelling, improvement after administration of an HAE treatment suggests HAE

Contraception

- In 80% of women, use of oestrogen containing oral contraceptives precipitates the onset of HAE attacks in a previously healthy patient or worsens previously diagnosed HAE- discontinuing use usually relieves or reduces symptoms
- Oestrogen-progestin contraceptives as patch or vaginal ring expected to have effects similar to those of oestrogen-containing OCs
- Use of progestin only OCs reduced the frequency of attacks in 45 (81.8%) of 55 women with HAE
- IUDs are generally well tolerated by women with HAE
 - Short-term prophylaxis before insertion is not considered necessary, but treatment for an attack should be available.
- For emergency contraception, a progestin-only agent should be used, and oestrogen containing agents should be avoided
- Barrier methods of contraception have not been found to have any effect on occurrence of HAE symptoms

Studies on management of pregnancy in HAE patients



EU

Disease expression in women with HAE

107 patients/227 pregnancies¹



Brazil

Pregnancy and postpartum in HAE with C1-INH deficit in women who have no access to therapy

13 patients/22 pregnancies²



Italy

Pregnancy in women with HAE due to C1-INH deficiency: Results from the ITACA cohort study on outcome of mothers and children with in utero exposure to pdC1-INH

87 patients/168 pregnancies³



Hungary

The natural history of HAE and the impact of treatment with human C1-INH concentrate during pregnancy: a long-term survey

41 patients/118 pregnancies⁴



Spain

Management of pregnancy and delivery in patients with HAE due to C1-INH deficiency

61 patients/143 pregnancies⁵



India

Management of pregnancy in HAE in a resource-constrained setting: our experience at Chandigarh, North India

4 patients/9 pregnancies⁶



Germany

Characterization of acute HAE attacks during pregnancy and breast-feeding and their treatment with C1-INH concentrate

22 patients/35 pregnancies⁷



Czech Republic

Treatment of HAE attacks with icatibant and recombinant C1-INH during pregnancy

6 patients/6 pregnancies⁸



Australia

HAE and pregnancy

7 patients/16 pregnancies⁹

HAE and Pregnancy

- Clinical presentations of HAE varies among pregnant patients
- Clinical presentations vary among pregnancies in the same woman
- Attacks may increase, decrease or stay the same
- Attacks increase in 48%-83% of pregnancies
- All three trimesters may be impacted
- Some studies report higher attack rate in 1st trimester; others in 3rd trimester –
These patterns likely reflect the most active changes in oestrogen levels especially in relation to progesterone levels, which occur during the first and third trimesters
- Abdominal attacks most frequently reported
- Attacks may increase post partum and during lactation
- The only guideline recommended treatment in pregnancy is pdC1INH concentrate (Berinert)



Long-term prophylaxis with Berinert in pregnancy

- Expert guidelines support use as needed during pregnancy
- Long-term prophylaxis should be considered for women with histories of miscarriage, high-risk pregnancies and those with frequent, severe attacks



Termination of Pregnancy

- Short-term prophylaxis before procedure is recommended
- Alternatively, the procedure may be carried out without prophylaxis, provided that acute treatment is immediately available

Labor & Delivery

- Vaginal delivery is preferred for patients with HAE because surgery or general anesthesia with endotracheal intubation may provoke an attack
- Surprisingly, HAE attacks are uncommon during vaginal delivery, occurring at a rate of 6–8%, therefore routine prophylaxis against an HAE attack is not recommended
- In case an attack does occur, acute treatment (preferably pdC1-INH) should be available
- Administration of pdC1-INH is recommended before forceps delivery or vacuum extraction

Caesarian section



- Before cesarean delivery, pdC1-INH should be administered to reduce the risk of an HAE attack
- Epidural anesthesia is preferred because intubation for general anesthesia might trigger a laryngeal attack
- Emergency procedures should not be delayed if pdC1-INH is not immediately available
- Patients may experience an increased frequency of HAE attacks during the postpartum period
- Close follow-up for 72 h after delivery is necessary
 - staff to be familiar with the management of HAE

Lactation

- May be associated with an increased frequency of HAE attacks, possibly associated with increased serum prolactin levels
- Discontinuing lactation might reduce the frequency of attacks
- Tranexamic acid is excreted into breast milk and **should not be used in patients who are breastfeeding**
- Avoid Danazol during lactation
- Berinert recommended for on-demand or prophylactic therapy of HAE in lactating women

Menopause

- In a survey of women with HAE, 32% reported symptom worsening, 13% reported improvement and 55% reported no change
- Oestrogen replacement therapy (including phytoestrogens) is contraindicated in women with HAE
- Progesterone and progestins are alternatives for treatment of hot flushes
- Non-hormonal treatments for the symptoms of menopause are not known to trigger HAE attacks
- Tibolone (Livial) may be well tolerated

Infertility

Fertility is unaffected by HAE

Short-term prophylaxis is recommended before investigations for infertility

If intrauterine insemination or IVF is attempted, oestrogen induced by injectable gonadotropins may trigger an HAE attack

Short-term prophylaxis with pdC1-INH should be provided before procedures that might trigger an attack, and should be used in the event of an attack



Questions???