

Non-gynaecological issues in women with bleeding disorders

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Iron deficiency/anaemia and periodontal disease are among the non-gynaecological issues that may present a challenge in women with bleeding disorders. Anaemia is a global health problem, affecting around 32.5% of non-pregnant women under 50 and over 40% of pregnant women. It causes fatigue, shortness of breath and dizziness. Anaemia is usually diagnosed by a low serum level of ferritin. Ferritin may be normal in a person who is taking an iron supplement or in the presence of inflammation, in which case the diagnosis can be confirmed by a low transferrin saturation level. A low level of iron should be corrected in a woman with a bleeding disorder, and women must recognise the importance of doing so. If a healthy diet alone does not avoid iron deficiency, oral supplementation is indicated on a low dose regimen to reduce adverse effects; intravenous administration should be used when rapid restoration of iron is indicated. Failure to respond to iron supplementation is an indication for further investigation. Periodontal disease has only recently been recognised as a modern-day epidemic and can have a major impact on quality of life. Oral

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health has long been ignored in people with a bleeding disorder as bleeding gums secondary to periodontitis are often attributed to the underlying condition. People with a bleeding disorder may therefore feel they can do nothing to improve their oral health. However, healthy gums do not bleed, even in people with a bleeding disorder. While bleeding gums are often accepted as a consequence of having a bleeding disorder, effective cleaning has been shown to reduce gingivitis and bleeding. Regular contact with a dentist should start at a young age and continue throughout life.

Keywords: *Women with bleeding disorders, iron deficiency, anaemia, oral health, dental care, von Willebrand disease*

DETECTION AND MANAGEMENT OF IRON DEFICIENCY AND ANAEMIA IN WOMEN WITH BLEEDING DISORDERS

Anaemia is a low blood level of haemoglobin. In cases of anaemia, oxygen delivery to all parts of the body is reduced, causing fatigue, shortness of breath and dizziness; a person with anaemia may have a pale skin. It is a global health problem, which in 2016 had a prevalence of around 32.5% among non-pregnant women aged 15–49, and

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over 40% of pregnant women^[1,2]. Prevalence varies widely between communities and countries due to differences in economic status and nutritional status; no country is exempt. The World Health Organization has committed to reducing the prevalence of anaemia by 50% by 2025^[3].

Anaemia may be due to insufficient production of haemoglobin (associated with genetic disorders such as thalassemia, sickle cell disease or iron deficiency) or excessive destruction (due to blood loss and haemolysis). Iron deficiency can result from increased demand (pregnancy, growth), reduced intake (nutritional problem, malabsorption) or loss (infection, bleeding). Anaemia is often due to iron deficiency but other causes must be excluded.

Dietary iron may be heme iron obtained from meat and fish or non-heme iron, a less available form obtained from vegetables. Its absorption is regulated and is increased in the presence of anaemia. Absorption can be reduced by some medicines, including acid-blocking drugs.

Iron is essential for cellular respiration. After absorption (mainly from the duodenum), iron is stored in cells in combination with the protein ferritin. It is released from duodenal cells into the circulation via the transporter protein ferroportin, a process regulated by hepcidin. Uptake by cells is facilitated by transferrin. Anaemia can be diagnosed by a low serum level of ferritin. However, ferritin may be normal in a person

who is taking an iron supplement or in the presence of inflammation, in which case the diagnosis can be confirmed by a low transferrin saturation level.

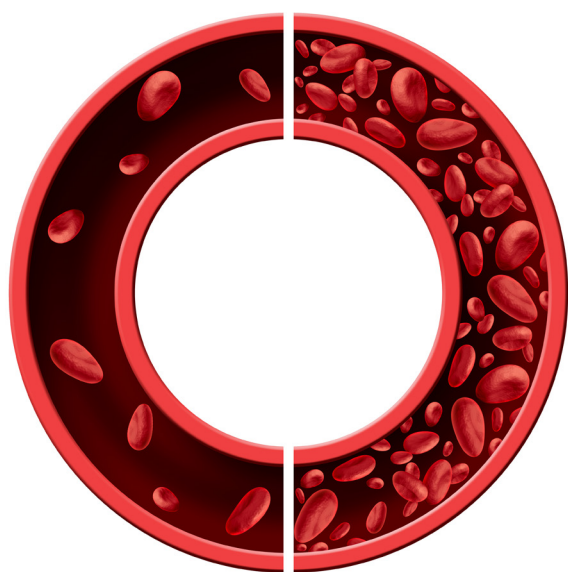
There is debate about whether iron deficiency alone (without anaemia) can cause chronic fatigue, but clinicians agree that a low level of iron should be corrected in a woman with a bleeding disorder, even when it might be expected (as in pregnancy). If a healthy diet alone does not avoid iron deficiency, oral supplementation is indicated and it is essential that women understand its importance. In women without anaemia, the recommended dose is 40–60mg on alternate days; this low-dose regimen is associated with a fewer gastro-intestinal effects but raises questions about whether adherence can be maintained when the dose is not taken every day. In women with anaemia, the usual dose is 100–200mg once or twice daily; once iron stores are replenished (which takes at least three months), the dose can be reduced. The effectiveness of oral iron supplementation should be evaluated with a full blood count, including reticulocytes, and a clinical evaluation. Oral iron is not effective in the presence of some concomitant drugs, partial or total gastrectomy, or bariatric obesity, helicobacter pylori infection or coeliac disease. Iron-refractory iron-deficient anaemia is a rare autosomal recessive disorder accounting for <1% of cases of iron-deficient anaemia. This may be suspected if there is no increase in haemoglobin after four to six weeks of oral iron therapy.

When oral supplementation is ineffective despite good adherence, intravenous administration is a possibility. The recently introduced ferric carboxymaltose (Ferinject) and iron sucrose (Venofer) correct severe iron deficiency after one or two infusions. Parameters of iron disposition should be checked after four to six weeks. Failure to respond to this approach indicates the need for further investigation.

ORAL CARE IN WOMEN WITH BLEEDING DISORDERS

The World Dental Federation defines oral health as multi-faceted, and including “the ability to speak, smile, smell, taste, touch, chew, swallow, kiss and convey facial expressions with confidence and without pain, discomfort and disease.”^[4]

Periodontal disease has only recently been recognised as a modern-day epidemic. It is the most common chronic inflammatory condition, affecting an estimated 50% of adults worldwide^[5]. Oral inflammation has been linked to the development of dementia, stroke, cardiovascular disease, kidney disease, lung disorders and cancers of the mouth and pancreas. Eighty-three



Iron deficiency can result in anaemia, whereby the body does not produce enough red blood cells or haemoglobin. Anaemia is a global health problem, and due to their predisposition to bleeding, women with bleeding disorders are at risk

percent of the population present with some level of gum bleeding during their lifetime^[6]. If untreated, periodontitis can lead to accelerated toothlessness and infection, and impacts on general health. Bad breath affects personal relationships. Poor oral health therefore has a major impact on quality of life.

The dental profession has not succeeded in motivating people to look after their mouths. Oral health has long been ignored in people with a bleeding disorder because gum bleeding secondary to periodontitis is usually attributed to the underlying condition^[7]. However, it has long been recognised that healthy gums do not bleed, even in people with a bleeding disorder.

Dental health and quality of life is one element being evaluated by PROBE (Patient Reported Outcomes, Burdens and Experiences), a long-term study of haemophilia patients collecting patient-reported data to support advocacy for better care and treatment. The study has found that people with haemophilia are five times more likely than their family members to have gingivitis – even though haemophilia is not a risk factor for oral disease^[8]. In health systems funded by insurance, oral health is often not covered by policies that meet the costs of care for other aspects of a bleeding disorder. Bleeding in the mouth in people with von Willebrand disease, for example, should be managed as a part of their medical care, but there is a lack of evidence from which to develop a protocol.

There is a tendency to focus on the medical aspects of poor oral health, but there is an important psychosocial impact too. In one qualitative study (n=65) people with a bleeding disorder reported pain and discomfort; they expressed concern about finding a dentist prepared to treat them; they reported halitosis, having to cover their mouth or lower their heads in public; and they were worried about loose teeth falling out^[9]. Severe gum bleeding was also associated with an impaired sex life. It is not uncommon for people with a bleeding disorder to have difficulty finding a community dentist who is prepared to operate on them and having a long wait for specialist care. People with a bleeding disorder may believe that gum bleeding is normal, partly because some community dentists have been advising them wrongly.

Surgery for tooth extraction in a person with bleeding disorder can be carried out safely with appropriate preparation by a joint medical and dental team^[10]. Systemic and local measures should be combined as indicated by an individual's bleeding risk – this may include scaffolding and stitching of the

socket, and factor replacement and administration of desmopressin or tranexamic acid. The clot should not be disturbed by over-rinsing; food should be soft and a soft toothbrush should be used. The patient should not smoke. Healing takes about one week.

If bleeding does not stop after 20–30 minutes, the patient should be asked to bite on a damp gauze swab. If necessary, the swab can be soaked in a solution of tranexamic acid. Oral tranexamic acid 1g three times daily, beginning four hours before surgery and continuing for five days after, is a further option if bleeding does not stop. Mucosal bleeding – which is distinct from gum bleeding and is typically caused by accidental biting or trauma – may be treated with aminocaproic acid mouthwash.

To avoid confusion when advising patients, it is helpful to refer to gum bleeding due to gingivitis as 'brush bleeding' because that is often how it becomes apparent. Gingivitis is associated with inflammation caused by dental plaque, a biofilm coating the surface of teeth; its occurrence is associated with environmental, genetic and host risk factors^[11]. Affected gums bleed readily and the duration of bleeding is greater in people with a bleeding disorder. Advanced gingivitis causes periodontal disease. This is apparently associated with spontaneous gum bleeding, but the site of the bleed is actually a dental pocket around the tooth. This is a common problem and to some extent has become normalised. Again, people with a bleeding disorder are



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In people with bleeding disorders, gum bleeding is often assumed to be related to the underlying disease – however, this is not necessarily the case. Promoting good oral hygiene in people with bleeding disorders is important in maintaining oral health, but is also relevant to their psychosocial wellbeing

not at greater risk of periodontal disease than the general population, but when they bleed they do so for longer.

Plaque control by effective brushing reverses gingival inflammation, but some people feel powerless to act. In one recent study, people with von Willebrand disease described their oral health as good despite having gum bleeding after brushing^[12]. They felt they had little control over bleeding of their gums, which they attributed to poor technique or a hard brush, trauma or spontaneous bleeding. This raises the question of what constitutes "normal" bleeding from the gums. The medical criterion to qualify for a diagnosis of bleeding gums in someone with a bleeding disorder requires continuous bleeding for nine minutes; this is not a reasonable indicator of the presence of gum disease.

In a recent randomised controlled trial (part of the larger LOVIC study), gum health and bleeding score were assessed in 113 people with von Willebrand disease and gingivitis. They all received education about home dental care and were randomised to receive no other intervention or a session of professional cleaning involving plaque disclosure and a set of disclosing tablets for self-use, use of a medium hard toothbrush, and the patient's choice of floss and picks. Each received a personalised plaque and bleeding score. After six weeks, gum health had improved in all participants and the improvement correlated with levels of plaque, not baseline bleeding score. Treatment by the hygienist had no effect.

This finding emphasises the value of early dental consultations – within the first year of life – and maintaining contact throughout life, in the same way that medical contact is now accepted as the norm.

DISCUSSION

Dental implants are becoming increasingly popular, especially with the modern preference for having an appealing smile. The surgical protocol for a dental implant is the same as for tooth extraction for people with a bleeding disorder. The implant will bond provided

osseointegration occurs. The failure rate of implants is about 30% and the factors that affect bonding are the same as in the general population – in particular, smoking.

Braces may also affect oral health. Plastic braces are easier to fit (requiring little special training) and are becoming popular. They are not good for gum health because they overlie the gum and make cleaning more difficult. They are not contraindicated in people with a bleeding disorder but they are not superior to a metal brace. A brace is inadvisable for an individual who does not have good oral hygiene.

When using a tranexamic acid mouthwash, established advice is to rinse for two minutes then swallow the residue – the solution has a very unpleasant taste. However, there is no advantage to swallowing the mouthwash. Its purpose is to counteract the fibrinolytic effect of saliva and the dose of tranexamic acid it contains is too low to have a systemic effect. Overall, systemic treatment with tablets is preferable to a mouthwash.

With regard to iron therapy, the balance of risk and benefit associated with intravenous iron and oral iron was raised. Intravenous administration is indicated for severe anaemia when rapid restoration of iron levels is indicated. It may rarely be associated with an anaphylactoid reaction; this can be severe and require cover with steroid. Parenteral iron is not available in some countries. Oral iron at the traditional dose of 200–400 mg/day can cause gastrointestinal intolerance, but early experience with the low dose regimen suggests this is better tolerated. If symptoms persist, switching to a different formulation may help.

The relationship between fatigue and anaemia was explored. Severe anaemia (haemoglobin <10 g/dL) is associated with fatigue, shortness of breath, alopecia and food cravings. Chronic fatigue may be associated with low ferritin but normal haemoglobin. Low ferritin may occur in frequent blood donors, especially women, and they may require continuous supplementation to enable them to continue as

KEY LEARNING POINTS

- A low level of iron should be corrected in a woman with a bleeding disorder
- Oral iron supplementation is effective and tolerability can be improved with a low dose regimen
- Intravenous iron is an effective option when rapid restoration of iron levels is required
- Poor oral health adversely affects quality of life
- Healthy gums do not bleed, even in people with a bleeding disorder
- Bleeding gums are wrongly attributed to an underlying bleeding disorder when they are caused by plaque
- Good oral hygiene eliminates plaque and maintain gum health

donors. It is important to maintain normal iron levels in women during pregnancy and in children with bleeding disorders.

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