Managing hereditary thrombophilia

Hereditary thrombophilia increases the risk of thrombosis. Nurses can educate patients to help them understand the condition and its associated risk factors.

In this article...
- The diagnosis, treatment and management of hereditary thrombophilia
- Risk factors for the condition
- How can nurses can help patients with this disorder to understand and manage their condition

Thrombophilia is a blood coagulation disorder that increases the likelihood of inappropriate clotting; it can be inherited (known as hereditary thrombophilia), or acquired as a result of a range of conditions including cancer, some inflammatory conditions such as irritable bowel disease, nephritic syndrome and heart failure.

Hereditary thrombophilia is caused by a change in one of the genes involved in the blood coagulation cascade. This change, or mutation, increases the chances of a thrombus (blood clot) forming (Khan and Dickerman, 2006).

The majority of venous thrombi form in the leg veins and are known as deep vein thromboses (DVTs). If a thrombus fragments, it can break off and block blood vessels, causing a thromboembolism. If it then travels up the body and blocks the blood vessels in the lungs, it can cause a pulmonary embolism (PE), which can be fatal.

Hereditary thrombophilia

Venous thrombosis affects around one in 1,000 of the general population every year in the UK, contributing significantly to morbidity and mortality. The estimated mortality range is 2.3-28% (Simpson et al, 2009). Risk increases with age, and is also associated with pregnancy, oestrogen therapy, immobility and major surgery or trauma.

Around 30–50% of people with a venous thrombosis are thought to have a known form of heritable thrombophilia (Simpson et al, 2009), caused by a change in one of the genes involved in the blood coagulation cascade.

The genes for all the proteins involved in the cascade are found on the non-sex chromosomes, which means that both sexes have an equal chance of having hereditary thrombophilia. Fig 1 illustrates the reactions involved in the cascade.

Individuals can carry more than one inherited gene that causes the condition (Khan and Dickerman, 2006), but it is possible for those at risk to have no family history of hereditary thrombophilia.

Possession of an allele associated with the condition increases the risk of thrombosis but does not mean heritable thrombophilia will definitely develop (Simpson et al, 2009). Table 1 shows the increase in risk of hereditary thrombophilia from possessing particular mutations.

Genetic testing

Although routine screening for hereditary thrombophilia is not recommended in the UK, genetic testing may be carried out after a thrombotic event to determine if a DVT or PE is linked to a genetic change (Baglin et al, 2010).

Patients may also have a genetic test if there is a family history of thrombosis that could put them at risk of hereditary thrombophilia. Identification of a high-risk allele can then be used to determine who is at risk of thrombosis, or prevent further thromboses in those already affected.

Genetic testing involves analysing a blood sample to determine which, if any, type of thrombophilia is present (Simpson et al, 2009). As treatment is the same for both hereditary and acquired thrombophilia, there is no need to test for thrombophilia when patients first present with thrombosis (Haemostasis and Thrombosis Task Force and British Committee for Standards in Haematology, 2001).

Since tests to determine potential deficiencies of antithrombin, protein S and protein C are affected by both thrombosis and its treatment with anticoagulants, it is recommended that testing is undertaken at least one month after anticoagulant treatment has finished (HTTF and BCSH, 2001).

Risk factors

Although many people diagnosed with hereditary thrombophilia never develop thrombosis, a number of factors can increase their risk.
Discussion

These include: the use of combined oral contraceptives for women – particularly those with the factor V Leiden mutation; advancing age; surgery; trauma; cancer; sustained immobility; and pregnancy, particularly during the post-partum period (HTTF and BCSH, 2001; De Stefano et al, 1996).

Contraceptive use
Combined oral contraceptives are not generally recommended for people with hereditary thrombophilia, especially those containing third-generation progestogens as these are associated with a higher risk than second-generation progestogens.

Pills containing progestogen only should be considered instead as these do not appear to increase thrombosis risk (HTTF and BCSH, 2001; Bloemenkamp et al, 1995).

Pregnancy
Venous thromboembolism is the most frequent cause of maternal mortality. The risk is exacerbated by factors such as obesity, age, parity and immobilisation.

Risk increases during the postpartum period, particularly for women who have had a Caesarean section or assisted birth (HTTF and BCSH, 2001).

Surgery/trauma
Certain types of surgery pose a greater risk of thrombosis. These include major general surgery and lower-extremity orthopaedic operations.

It has been suggested that around half of elective total hip and knee replacement patients develop venous thromboembolism if they do not receive prophylaxis (Donahue, 2004; Anderson and Spencer, 2003; Lindahl et al, 1999). This falls to approximately 1-3% when prophylaxis is used (National Institute for Health and Clinical Excellence, 2010; Anderson and Spencer, 2003).

Hip or leg fractures increase the risk of thrombosis, as do major trauma and spinal cord injuries, stroke, congestive heart or respiratory failure, and varicose veins (Anderson and Spencer, 2003).

Cancer
Patients with cancer have an increased risk of thrombosis and a high risk of recurrence (Prandoni, 2005). Chemotherapy also increases the risk (Anderson and Spencer, 2003).

Immobility
Recent guidelines on travel indicate that all journeys over three hours should be considered a risk factor for developing thrombosis. The risk remains for up to eight weeks after the journey (Watson and Baglin, 2010).

Dehydration
There are conflicting views about whether dehydration is a risk factor for thrombosis, but national guidance says dehydrated patients should be considered at risk (NICE, 2010).

While there is no evidence that dehydration and travel-related thrombosis are linked, Watson and Baglin (2010) say maintaining good hydration is unlikely to cause harm.

Management of hereditary thrombophilia
Initial management of thrombosis involves five days of anticoagulation treatment with unfractionated or low molecular weight heparin, followed by oral anticoagulants for six months (HTTF and BCSH, 2001).

Patients often have little understanding of hereditary thrombophilia. Nurses can educate them about risk factors and how to manage it.

Blood clot: fibrin with red blood cells

Thrombophilia: a blood coagulation disorder that increases the likelihood of inappropriate clotting
Hereditary thrombophilia: inherited form of the condition caused by a change in one of the genes involved in the blood coagulation cascade
Allele: different versions of the same gene that have different DNA sequences
Deep vein thrombosis: a blood clot or thrombus that forms in the leg veins
Pulmonary embolism: this occurs when a blood clot breaks off and blocks the blood vessels in the lungs. It can be fatal

Thrombophilia is exacerbated by factors such as obesity, advancing age and long-term immobility

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Accurate data on the risk of recurrence in patients with hereditary thrombophilia is unavailable (HTTF and BCSH, 2001); for the wider population, it is around 15–20% within two years (Prandoni et al, 1996).

There is no evidence to support the permanent use of anticoagulants in hereditary thrombophilia, as the associated risk of haemorrhage is too high (HTTF and BCSH, 2001). However, patients should be warned about the risk of thrombosis recurring and the signs and symptoms to look out for, and be advised to seek medical attention if they suspect they have a blood clot (HTTF and BCSH, 2001).

**Side-effects**

Treatment with anticoagulants can have a number of side-effects, including haemorrhaging. This can occur more frequently when patients first start taking anticoagulants, and has been linked to the fact that dosages are still being determined (Palareti et al, 1996).

Evidence suggests that side-effects may lead to patients not adhering to treatment regimens, so it is important to check that they are concordant with treatment before entering high-risk situations such as having surgery.

**Prophylaxis**

Guidance on reducing the risk of thromboembolism says patients admitted to hospital who have an increased risk of thrombosis should be offered prophylactic treatment. This includes those with thrombophilia.

The guidance also recommends encouraging patients to move as soon as possible after surgery to reduce the risk of thrombosis developing (NICE, 2010).

**Patient understanding**

Saukkko et al (2007) found that some thrombophilia patients tested for the factor V Leiden mutation were unaware they had undergone a genetic test. The researchers also found that some of those who tested positive for the mutation were only given the test result by telephone, with no further “advice and clarification”.

It is therefore important not to assume patients are aware that a genetic test to look for mutations linked to hereditary thrombophilia has been carried out. They may have only received limited information about their condition and will rely on healthcare professionals to help reduce their risk.

Patients with hereditary thrombophilia should have their increased risk of developing thrombosis explained, as well as the lifestyle factors that can increase risk, such as oral contraceptive use, being overweight and taking long flights or sitting for long periods. Guidelines recommend movement on long journeys to reduce the risk of thrombosis, and those taking journeys of more than eight hours should wear compression stockings (Watson and Baglin, 2010). Patients who have more than one risk factor for thrombosis should wear compression stockings for journeys of three hours or more (Watson and Baglin, 2010). Those with cancer should be offered anticoagulation treatment (NICE, 2010).

As the condition is inherited, patients may also need support in telling relatives about their diagnosis.

**Conclusion**

Hereditary thrombophilia is a common cause of thrombosis and is diagnosed by genetic testing.

It can be caused by one of a number of genetic mutations which can change the proteins involved in the blood coagulation cascade. This leads to an increased risk of inappropriate blood clotting and thrombophilia.

Risk factors include surgery and/or trauma, immobility, advancing age, pregnancy and the use of combined oral contraceptives.

Management of thrombosis involves the use of anticoagulants, but these are time-limited to reduce the risk of inappropriate bleeding.

Evidence suggests patients may not be aware or understand that they have undergone a genetic test for the condition, and may have received limited information about hereditary thrombophilia.

Nurses may see patients who have been admitted to hospital as a result of thrombosis, or after their diagnosis of thrombophilia when treatment becomes preventative rather than life-saving.

Nurses may assess whether patients should be offered a referral for testing based on their own or their family’s history of thrombophilia.

Patients may also need support in working out who in their family may be affected by hereditary thrombophilia. Nurses can therefore play an important role in providing advice and support to patients. **NT**

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**Table 1. Increase in risk of hereditary thrombophilia from gene mutations**

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<thead>
<tr>
<th>Protein</th>
<th>Increases risk by</th>
</tr>
</thead>
<tbody>
<tr>
<td>Factor V Leiden</td>
<td>3-8% for heterozygote</td>
</tr>
<tr>
<td>PTG2020A</td>
<td>3%</td>
</tr>
<tr>
<td>Antithrombin</td>
<td>19-50%</td>
</tr>
<tr>
<td>Protein C</td>
<td>6.5-15%</td>
</tr>
<tr>
<td>Protein S</td>
<td>5-10%</td>
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</tbody>
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**References**


