Venous thromboprophylaxis: reducing needlestick injury


Summary
This article discusses needlestick injuries in relation to the prevention of venous thromboembolism (VTE) in the healthcare setting. The article explores the use of oral anticoagulants for the prevention of VTE. The introduction of oral prophylaxis for VTE following orthopaedic surgery may help to optimise post-operative patient outcomes, as well as reduce the number of sharps-related accidents.

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The estimated number of needlestick injuries per year in the European Union (EU) is one million (European Parliament 2006) and there are approximately 800,000 in the United States (US) (Bandolier Extra 2003). Approximately 50% of all needlestick injuries are experienced by nursing staff (Health Protection Agency 2008). In a survey of nearly 5,000 nurses from the Royal College of Nursing, 90% of respondents reported that they had drawn blood at their last needlestick injury (Ball and Pike 2008).

Needlestick injuries have the potential to result in the dissemination of blood-borne pathogens, such as hepatitis B and C and even human immunodeficiency virus (HIV). The cost of treating individuals with needlestick injuries can be substantial and may increase with the long-term treatment of associated serious infections (Lee et al 2005).

The incidence of needlestick injury is under-reported (Wilburn and Eijkemans 2004). Approximately 75% of these injuries are thought to be preventable by informing and educating healthcare professionals on the appropriate procedures to minimise the risks associated with handling and disposing of sharp objects (Bandolier Extra 2003). One study reported that only 55% of nurses had received training on safe needle use, and 28% had not received information on the risks of contracting a blood-borne disease following a needlestick injury (Ball and Pike 2008).

The use of needles is associated with several other problems. Fear of needles can cause anxiety and emotional distress, not only for the patient, but also for the healthcare professional administering the injection. The emotional effect on the person injured may be significant, regardless of the potential transmission of infection, and may evoke or intensify feelings of fear linked with future needle use (Lee et al 2005). The injection itself may be associated with discomfort, a burning sensation and painful subcutaneous haematomas at the injection site, which may worsen with duration of treatment. If a haematoma occurs at the injection site, an alternative site is required for subsequent injection.

There is also evidence from patients and staff that ready-to-use syringes require concentrated effort to remove the rubber protection caps (Mengiardi et al 2009). This handling problem may result in non-adherence by the self-administering patient and increase the risk of needlestick injury for both patients and healthcare staff.
From an environmental perspective, needle disposal is associated with increased biohazardous medical waste. It is estimated that 367 million hypodermic needles and syringes are disposed of by hospitals in the US every year (Bandolier Extra 2003).

Patient adherence to self-injection of anticoagulants may be highest where adequate training and education are provided (Colwell et al 2005). Therefore, solutions to the problems of needle use should consider the needs of both healthcare workers and patients, to improve patient outcomes by encouraging individuals to adhere to prophylaxis regimens.

**Solutions to needlestick injury**

There are several potential solutions to the problem of needlestick injuries. In the first instance, patients should receive adequate supervision and training when self-injecting (not all patients receiving this type of treatment will be inpatients). Healthcare professionals should also receive appropriate training on best practice. They need to develop a greater awareness of needlestick injuries and infection control, as evidence indicates that many nurses underestimate the associated infection risk from needlestick injury (Leliopoulou et al 1999, Trim et al 2003, Ball and Pike 2008).

Investing money in staff training on the use of safer techniques is crucial, as is emphasising the importance of adhering to evidence-based guidelines and protocols. Alternative approaches include using syringes with needle-blunting features, hinged needle guards or retractable protective sheaths, or the use of gloves treated with virus-inhibiting agents. Although these methods may reduce infection rates, they can be costly (Bandolier Extra 2003). The ideal method of preventing needlestick injuries would be to eliminate the use of needles completely, where alternative administration methods and technology exists.

Hospitals within the EU are now legally obliged to take action to prevent staff acquiring needlestick injuries (Mooney 2009). This legislation agreement was made between the European Federation of Public Service Unions (EPSU) and the European Hospital and Healthcare Employers’ Association (HOSPEEM). It became law on March 9 2010, following the European Council’s adoption of the directive on preventing sharp injuries in hospital and healthcare settings (Perera and Fischbach-Pyttel 2010). European member states now have three years to implement the changes set out in the directive (EPSU 2010).

The remainder of this article considers the reduction of needlestick injury in the orthopaedic setting, an area where such injuries are common.

**Venous thromboembolism**

Venous thromboembolism (VTE), which manifests as deep vein thrombosis (DVT) or pulmonary embolism (PE), poses a serious threat to surgical patients both intra and post-operatively. It is the most common preventable reason for hospital-related deaths (Geerts et al 2008). VTE is responsible for more than 500,000 deaths in Europe, equating to approximately 10% of all hospital deaths (Cohen et al 2007), and more than 273,000 deaths in the US each year (Heit 2005). Studies have shown that PE is responsible for more than twice as many deaths as acquired immunodeficiency syndrome (AIDS), breast cancer and road traffic accidents combined (Cohen et al 2007). The number of fatalities associated with PE is believed to be underestimated (House of Commons Health Committee 2005).

The burden of VTE on the healthcare system in the UK is significant, with costs of £640 million each year associated with the management of the condition (Cohen et al 2007), and $1.5 billion annually in the US (Spyropoulos et al 2002). It is believed that implementing protective measures, such as anticoagulant prophylaxis, could reduce costs by 60-80% (House of Commons Health Committee 2005).

In the orthopaedic setting, the risk of VTE can be high, depending on the type of surgery performed. Major orthopaedic surgery, such as hip or knee arthroplasty, or major surgery for cancer will put patients at a higher risk of developing VTE. Additional risk factors for VTE include increasing age, obesity, cancer and a previous history of VTE (Geerts et al 2008).

In terms of assessing patients at risk of VTE, a study carried out by the All-Party Parliamentary Thrombosis Group in 2009 reported that 85% of acute NHS trusts were performing mandatory risk assessments for all hospital inpatients. The equivalent figures were 70% in 2008 and 32% in 2007 (All-Party Parliamentary Thrombosis Group 2007, 2008). This represents a positive step forward in identifying patients at risk of VTE. However, the implementation of good clinical practice still needs to be encouraged. A global study of VTE risk and prophylaxis practices reported that, in 32 countries, VTE was a risk for 64% of surgical patients in the acute hospital setting, and the recommended prophylaxis for VTE, as set out in American College of Chest Physicians (ACCP) guidelines (Geerts et al 2008), was prescribed to only 59% of at-risk patients (Cohen et al 2008).
Venous thromboembolism prevention

A preventive approach to VTE is crucial, as patients are often asymptomatic, making the diagnosis of VTE difficult. The ACCP recommends anticoagulant therapy for at least ten days after major orthopaedic surgery (Geerts et al 2008). Patients undergoing hip or knee arthroplasty or hip fracture surgery should receive thromboprophylaxis for a minimum of ten days; for hip arthroplasty and hip fracture surgery the ACCP recommends continuing thromboprophylaxis for up to 35 days (Grade 1A recommendation). The use of anticoagulants for up to 35 days after total knee arthroplasty is also suggested, but this is a Grade 2B recommendation (implying that the values of the individual patient may determine choices) (Geerts et al 2008).

Studies have shown that the risk of symptomatic VTE in patients undergoing major orthopaedic surgery continues to be higher than expected for at least two months after surgery (Geerts et al 2008). However, ensuring a satisfactory duration of prophylaxis can be a challenge for healthcare professionals and patients, especially after hospital discharge. Self-injection has been the traditional method of administration and may cause distress to some patients, particularly older people who may require assistance from community or practice nurses. As a consequence, pharmacological thromboprophylaxis is discontinued in many patients at the time of hospital discharge, preventing such patients from having thromboprophylaxis for the required period.

Anticoagulant therapy

Heparins and vitamin K antagonists (for example, warfarin) were, for many years, the anticoagulants of choice in thrombosis prevention. Enoxaparin, an injectable low-molecular-weight heparin (LMWH), is now regarded as the standard treatment for the prevention of VTE (Blann and Lip 2006, Geerts et al 2008). Enoxaparin inhibits factors Xa and IIa in the coagulation cascade, through the co-factor antithrombin, and ultimately prevents the formation of clots (Figure 1).

When an antagonist uses antithrombin as a mediator for inhibition, this is known as indirect inhibition. Direct inhibition occurs when an inhibitor binds directly to a factor without relying on antithrombin.

The administration of enoxaparin for the prevention of VTE in patients undergoing major orthopaedic surgery involves subcutaneous injections once or twice daily. One alternative, fondaparinux, is a synthetic pentasaccharide that acts as an indirect factor Xa inhibitor, and is also administered by subcutaneous injection. Fondaparinux demonstrates a benefit over enoxaparin in reducing the risk of VTE, although major bleeding occurs more frequently with fondaparinux (Turpie et al 2002).

Limitations of current anticoagulant therapy may include an unsatisfactory reduction in VTE, excessive bleeding and unpredictable pharmacokinetics. In addition, frequent handling of needles to administer anticoagulant medication exposes healthcare professionals, patients and carers to potential harm, such as needlestick injury.

Oral venous thromboembolism prophylaxis

Oral anticoagulants have the potential to be a safe and effective alternative option compared to more traditional anticoagulants administered using a needle and syringe, and may be associated with a reduction in needlestick injuries. Two newer oral anticoagulants, dabigatran etexil ate and rivaroxaban, have been developed and approved for use in the orthopaedic therapy area. They have the potential to prevent VTE after major hip or knee arthroplasty while potentially reducing needle-related accidents. These oral anticoagulants are listed in Table 1 along with more established agents.

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**FIGURE 1**

Coagulation cascade

<table>
<thead>
<tr>
<th>Initiation</th>
<th>Propagation</th>
<th>Clot formation</th>
<th>Fibrinolysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>X</td>
<td>TF</td>
<td>IXa</td>
<td>thrombin</td>
</tr>
<tr>
<td>VIIa</td>
<td>Xa</td>
<td>II</td>
<td>fibrin</td>
</tr>
<tr>
<td>IXa</td>
<td>II</td>
<td>Prothrombin</td>
<td>fibrinogen</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IIa</td>
<td>+ - Plasmin</td>
</tr>
</tbody>
</table>

Key:
- Inactive factors
- Active factors
- Catalysis
- Transformation
- Tissue factor

**TABLE 1**

<table>
<thead>
<tr>
<th>Oral anticoagulants</th>
<th>Major indications</th>
</tr>
</thead>
<tbody>
<tr>
<td>dabigatran etexilate</td>
<td>major hip/knee surgery</td>
</tr>
<tr>
<td>rivaroxaban</td>
<td>major hip/knee surgery</td>
</tr>
</tbody>
</table>

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Warfarin has been in clinical use for the treatment and prevention of thromboembolism since the 1950s. It can be administered orally. However, it interacts with several medications and foods that are high in vitamin K and requires close patient monitoring and possible dose adjustments because of variations in the dose-response relationship in different patients (Colwell and Mouret 2005). Warfarin acts as an inhibitor of the synthesis of several coagulation factors and anticoagulation proteins and its effects may not be apparent for several days because of a delayed onset of action (Lin 2005).

The intensive anticoagulant effect resulting from warfarin therapy means that bleeding is a serious concern. Agents that act more selectively to inhibit individual components of the coagulation cascade may demonstrate superior efficacy and safety in the prevention of VTE (Comp 2003), with fewer adverse effects such as bleeding.

Dabigatran etexilate which was recently launched in the UK (Boehringer Ingelheim 2010) directly inhibits factor IIa in the coagulation cascade. It is approved for the primary prevention of venous thromboembolic events in adults who have undergone elective total hip or knee arthroplasty. Three phase III trials have evaluated its effects in patients undergoing hip and knee arthroplasty. In the RE-NOVATE and RE-MODEL trials, patients receiving dabigatran etexilate did no worse in terms of reducing the incidence of venous thromboembolic events than those receiving enoxaparin 40 mg once daily (Eriksson et al 2007a, 2007b). In the RE-MOBILIZE study dabigatran etexilate and enoxaparin had similar safety profiles, with no significant difference in the incidence of major bleeding events. However, there were significantly less thromboembolic events in the enoxaparin group (RE-MOBILIZE Writing Committee et al 2009).

Rivaroxaban is an orally administered direct inhibitor of coagulation factor Xa, and is undergoing research for use in a range of conditions, including stroke prevention in atrial fibrillation and VTE. It has been approved in the EU for the prevention of VTE in adults after elective total hip or knee arthroplasty. The four RECORD studies, which consisted of a number of trials, have evaluated rivaroxaban versus enoxaparin in more than 12,500 patients undergoing total hip or knee arthroplasty (Eriksson et al 2008, Kakkar et al 2008, Lassen et al 2008, Turpie et al 2009a). In three phase III trials, patients received either oral rivaroxaban (one 10mg tablet) or enoxaparin (40mg subcutaneously) once daily (Eriksson et al 2008, Kakkar et al 2008, Lassen et al 2008). In another study, rivaroxaban 10mg once daily was compared with enoxaparin 30mg twice daily (Turpie et al 2009a). Compared with enoxaparin regimens in all four studies, rivaroxaban reduced the incidence of DVT, symptomatic VTE and all-cause mortality. Rivaroxaban showed a similar safety profile to enoxaparin, with no significant differences in rates of major bleeding incidents (Eriksson et al 2008, Kakkar et al 2008, Lassen et al 2008, Turpie et al 2009a).

### TABLE 1

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>Route of administration</th>
<th>Administered once daily</th>
<th>Mechanism of action</th>
<th>Efficacy compared with enoxaparin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin</td>
<td>Oral</td>
<td>Yes</td>
<td>Inhibits the synthesis of biologically active forms of vitamin K-dependent clotting factors</td>
<td>Inferior*</td>
</tr>
<tr>
<td>Enoxaparin</td>
<td>Subcutaneous injection</td>
<td>Dosing regimen varies</td>
<td>Inhibits factor Xa and thrombin via antithrombin</td>
<td>(Not applicable)</td>
</tr>
<tr>
<td>Fondaparinux</td>
<td>Subcutaneous injection</td>
<td>Yes</td>
<td>Indirect factor Xa inhibitor</td>
<td>Superior†</td>
</tr>
<tr>
<td>Dabigatran etexilate</td>
<td>Oral</td>
<td>Yes</td>
<td>Direct thrombin inhibitor</td>
<td>Equal†</td>
</tr>
<tr>
<td>Rivaroxaban</td>
<td>Oral</td>
<td>Yes</td>
<td>Direct factor Xa inhibitor</td>
<td>Superior†</td>
</tr>
</tbody>
</table>

(*Leclerc et al 1996, †Colwell et al 1999)
Drugs in development  Oral anticoagulants including apixaban and betrixaban are currently undergoing evaluation in clinical trials. Apixaban is a direct and selective factor Xa inhibitor currently in phase III trials for the prevention of VTE and stroke associated with atrial fibrillation. It has not demonstrated equivalence, compared with enoxaparin, for the prevention of VTE in patients undergoing total knee arthroplasty. Rates of major bleeding events were not significantly different between the groups, and apixaban had a similar adverse event profile to enoxaparin (Lassen et al 2009). Further studies in VTE are ongoing, but approval for the use of this drug in the prevention of VTE is not expected until late 2010, at the earliest.

Betrixaban is a direct factor Xa inhibitor currently being assessed in a large phase II clinical trial for the prevention of stroke in patients with atrial fibrillation. A phase II, randomised, open-label trial (EXPERT) has suggested that the efficacy and safety of betrixaban was comparable to enoxaparin (30mg twice daily) for the prevention of VTE in 215 patients undergoing major knee arthroplasty (Turpie et al 2009b). The manufacturer plans to develop betrixaban for the prevention and treatment of VTE in patients in orthopaedic settings.

Other oral direct factor Xa inhibitors currently in development as additional compounds for the prevention of VTE after total hip or knee arthroplasty include LY517717 (Agnelli et al 2007), YM150 (Eriksson et al 2007c, Turpie 2007) and DU-176b (Turpie 2007).

Prescribing oral anticoagulants  A healthcare professional’s decision to prescribe a new drug is based on multiple factors, including the clinical evidence, adverse events profile, clinical pathway or a patient’s lack of response to current therapy. Potential advantages over current therapy, cost-effectiveness and potential long-term effects should also be considered. GPs are often reliant on sales representatives or advertising by the pharmaceutical industry for information about new drugs. Patient preference for a particular treatment has a significant effect on drug selection, possibly relating to convenience and ease of administration (Prosser et al 2003).

At present, the safest and most efficacious approved oral anticoagulants for the prevention of VTE in adult patients undergoing elective hip or knee arthroplasty are dabigatran etexilate and rivaroxaban (Turpie et al 2009a). There are no published trials directly comparing these two drugs. Both have demonstrated equal or greater efficacy than low molecular weight heparin, enoxaparin, in orthopaedic patients, with no significant increase in major bleeding and no requirement for patient monitoring.

The orally active direct thrombin inhibitor ximelagatran was approved in some EU countries, but was subsequently withdrawn owing to safety issues relating to elevated liver enzyme levels. Because of safety concerns, ximelagatran was not approved by the US Food and Drug Administration in 2004 (Astra Zeneca 2004). No evidence of compromised liver function attributable to dabigatran etexilate or rivaroxaban has been shown thus far (Nagarakanti et al 2008, Haas 2009).

Enoxaparin has a complex mode of administration, as the dose depends on the weight of the patient. However, rivaroxaban is administered as a single 10mg tablet once daily 6–10 hours post-operatively, and the same fixed dose can be given to all patients regardless of age or body weight. Dabigatran etexilate is administered as 150mg or 220mg once daily (two 75mg or 110mg capsules), starting with a half-dose one to four hours after surgery; and a lower daily dose of 150mg is recommended in older adults (those over 75 years) and in patients with moderate renal impairment (Scottish Medicines Consortium 2008). The oral route of administration for rivaroxaban and dabigatran etexilate is more convenient compared with a subcutaneous injection. However, dosing is simpler for rivaroxaban compared with dabigatran etexilate.

From a pathophysiological perspective, the further the coagulation cascade develops the greater the quantities of each active coagulation factor formed (Figure 1). Therefore, a more effective approach for anticoagulant therapies may be to target coagulation factors earlier in the coagulation cascade. Factor Xa, for example, comes before factor IIa, suggesting that anticoagulants that inhibit factor Xa may have an advantage over anticoagulants that inhibit factor IIa (Turpie 2007).

Advantages of oral prophylaxis  Clinical trials can offer an insight into the pharmacoeconomic benefits of new products. Cost-effectiveness data for oral treatment versus subcutaneous administration has shown that rivaroxaban represents a cost saving against both the shorter (12–14 days) and longer (35 days) regimens of enoxaparin after orthopaedic surgery (Diamantopoulos et al 2008a, 2008b, 2008c). Economic analyses have suggested that dabigatran etexilate is associated with reduced healthcare costs compared with enoxaparin following hip and knee arthroplasty (National Centre for Pharmacoeconomics 2008, Scottish Medicines Consortium 2008). The National Institute for Health and Clinical Excellence (NICE) in the UK has stated that the use of
oral anticoagulants, which do not require continuous routine coagulation monitoring, may result in reduced administration costs (for example, reduced hospital resources in terms of staff and length of inpatient hospital stay) and increased adherence to prophylaxis (NICE 2008).

There are many other benefits associated with the use of oral anticoagulants in the orthopaedic setting, especially with the newer approved formulations such as dabigatran etexilate and rivaroxaban. By replacing subcutaneous injections with oral therapies, the number of needles used by healthcare professionals will be reduced, thereby decreasing the risk of needlestick injuries and the subsequent transmission of bloodborne infections.

Subcutaneous injections can be an inconvenience, especially in older people in orthopaedic settings, and needles may induce fear and anxiety in patients. The risk of subcutaneous haematoma would be eliminated if needles were not used, and the use of oral agents may reduce outpatient costs. Diamantopoulos et al (2008c) found that, compared with enoxaparin, rivaroxaban resulted in savings of £68.35 per patient after 35 days of treatment following total hip replacement. Savings of £90.99 per patient after 14 days of treatment following total knee replacement were also highlighted (Diamantopoulos et al 2008b).

References


House of Commons Health Committee (2005) The Prevention...
The current duration of anticoagulation therapy appears to be unsatisfactory, despite guidelines for the prevention of VTE. This may be because prophylaxis is discontinued for recommended intervals of time – that is, stopped at hospital discharge – because of difficulties associated with outpatient monitoring and the inconvenience of self-injection. Patients therefore may be at greater risk of preventable VTE and increased mortality. The use of oral anticoagulants may assist the continuation of anticoagulant therapy from inpatient to outpatient care and would ensure that prophylaxis is sustained for an appropriate period in patients at high risk of VTE, leading to improved post-operative results.

Conclusion

Needlestick injuries are a preventable yet common occurrence in healthcare settings. The orthopaedic setting is one example of a healthcare environment that may benefit from a reduction in needle use, to provide safer working conditions for nurses and other healthcare professionals. Oral anticoagulants, for example dabigatran etexilate and rivaroxaban, provide an effective and convenient alternative to using needles. Increasing awareness of such drugs in the clinical setting, and encouraging physicians, nurses and other healthcare professionals to alter their everyday practice, is paramount to reduce needlestick injuries and improve patient outcomes.