Blood management strategies in lower limb arthroplasty

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Abstract

Rates of post-operative allogenic blood transfusion in primary hip and knee arthroplasty can be as high as 50%. Risks of allogenic blood transfusion include increased risk of orthopaedic and non-orthopaedic infection in addition to the general risks of transfusion. Measures have been developed to minimise the requirements for post-operative allogenic blood transfusion in lower limb arthroplasty. These include pre-operative screening of patients, risk stratification, raising pre-operative haemoglobin pharmacologically, pre-operative autologous donation, minimising intra- and post-operative blood loss and suitable post-operative transfusion practices. Pharmacological, haematological and surgical methods of blood management in lower limb arthroplasty are discussed.

Keywords arthroplasty; blood; hip; knee; management

Introduction

The UK blood transfusion service collects about 1,900,000 blood donations per year. According to the United Kingdom National Joint Registry (UK NJR) there were 82,267 primary total knee replacements and 76,274 primary total hip replacements in 2013. Rates of allogenic blood transfusion (ABT) have been reported to be as high as 50% in elective primary total knee replacement[1] and 56% in primary total hip replacement.[2] Transfusion rates in revision hip and knee arthroplasty surgery are higher still. Direct comparison of transfusion rates between different studies can be difficult, as different institutes often have different transfusion triggers/protocols, and the details may not be specified in the paper. High transfusion rates put a considerable strain of the availability of donated blood.

Allogenic blood transfusion has been shown to be associated with an increased risk of orthopaedic and non-orthopaedic infections in elective hip and knee arthroplasty.[3]

With an aging population, it is expected that the number of arthroplasties performed per year will continue to increase. There is a limited availability of allogenic blood, and transfusion of allogenic blood carries risks to the recipient. In view of these issues there is a strong emphasis on setting up routine departmental practices for identifying and addressing all possible variables to optimise a patient's pre-operative haemoglobin, minimising peri- and post-operative bleeding and having clear guidelines for transfusion so that patients are not transfused unnecessarily by overzealous staff.

The various methods of blood management in lower limb arthroplasty are discussed below.

Pre-operative autologous donation

Pre-operative autologous blood donation (PABD) aims to provide a supply of safe blood for patients undergoing surgery who might need a blood transfusion. It increases the patient's total red blood cell (RBC) mass due to the PABD induced stimulation of erythropoiesis before elective surgery.[4] It avoids the risk of an immunogenic reaction, and possible transmission of blood borne viruses associated with an allogenic blood transfusion. It may also be more acceptable to patients who are reluctant to receive an allogenic transfusion for religious or personal reasons.

Blood is collected pre-operatively. The sudden drop in haemoglobin that is caused stimulates erythropoiesis as the body tries to raise the blood haemoglobin concentration back to a normal level. It is expected that the patient's haemoglobin will have normalized by the day of surgery, and therefore any blood lost at the time of surgery can be replaced with the blood that was pre-donated.

Pre-operative autologous blood donation typically reduces pre-operative haemoglobin levels by 1.23 g/dl, and has been shown to decrease the rate of allogenic transfusion by 43%.[5] The timing of donation varies slightly between practices; however, it has been shown that it takes an average of 36 days for haemoglobin levels to recover to pre-donation levels,[6] suggesting that the time interval from donation to surgery should be no shorter than this.

Withdrawing two units at a single sitting, rather than one unit at two separate sittings, results in a larger increase in RBC mass.[7] This single large donation seems to stimulate erythropoiesis more aggressively and should be the preferable practice, provided the patient can cope with it physiologically.

Pre-operative autologous donation of blood being made available for post-operative transfusion is very safe. However, it has high non-usage rates (45%),[8] indicating that its routine use is unnecessary and that is should be reserved for selected cases. Therefore, it is rarely used in the arthroplasty setting nowadays.

Erythropoietin

Erythropoietin (EPO) is an erythropoiesis-stimulating glycoprotein that is 90% made by the kidneys. EPO allows erythroid precursor cells in the bone marrow to mature and eventually become erythrocytes. This process takes over 1 week, and erythrocytes have a normal survival time of 120 days. Pharmaceutical EPO is human erythropoietin produced in cell culture using recombinant DNA technology. It is administered prior to surgery and often for a few days after surgery to patients deemed at high risk of post-operative transfusion (haemoglobin <13 g/dl) in order to boost pre-operative haemoglobin. It can be administered intravenously or subcutaneously.

There is evidence that pre-operative administration of EPO to patients deemed to be at high risk of transfusion results in higher

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immediate post-operative haemoglobin levels and lower rates of allogenic transfusion compared with controls. However, in view of the large cost associated with this drug, it was deemed not to be cost effective when compared to allogenic blood transfusion administrated as and when necessary.[9]

Potential side effects of EPO use include:

- headache
- joint or muscle aches, pain, or soreness
- nausea/vomiting/indigestion
- weight loss
- sores in the mouth

Iron supplement pre- and post-operatively

Iron is a transition metal that forms the core of the haemoglobin molecule to which the alpha and beta proteins are attached. Daily requirements of iron for erythropoiesis are approximately 20–30 mg, and it is absorbed in the duodenum.

Pre-operative oral iron supplementation is cheap and aims to maximize iron stores and subsequently haemoglobin prior to surgery. It is usually administered for 3–4 weeks pre-operatively. It can increase pre-operative haemoglobin and decrease the post-operative drop. This beneficial effect is most pronounced in patients with pre-operative anaemia due to iron deficiency, whilst those with normal haemoglobin levels generally do not benefit from pre-operative iron supplements.[10] Gastric side effects such as dyspepsia, nausea, diarrhoea and black stool may limit patient compliance with drug therapy.

Post-operatively, routine administration of oral iron supplements to anaemic patients does not significantly increase iron levels, although there is some evidence that administration of intravenous iron in the first 1–3 days post-operatively can result in a significantly higher haemoglobin levels at 72 h post-op, resulting in lower rates of post-op allogenic blood transfusion.[11,12]

Tourniquets

A tourniquet is a device used to limit bleeding or blood flow. In the lower limb setting it is typically elevated to 100–150 mmHg above systolic blood pressure. The limb is usually drained of venous blood by elevation or exsanguination before inflation. Although not practical for a hip replacement, tourniquets are frequently used in knee replacement surgery. Their primary purpose is to limit intra-operative blood loss and improve visibility at the time of surgery. However, they are associated with a slight increase in post-operative blood loss compared with no tourniquet use, and there is no convincing evidence that they limit blood loss overall. This is because once the tourniquet is deflated, the vessels that were incised intra-operatively will start to bleed, resulting in hidden blood loss and bruising; conversely, when a tourniquet is not used these bleeding vessels are likely to be identified and cauterised intra-operatively.

Clinical thromboembolic events have been shown to be higher amongst patients who had a tourniquet applied compared to those who did not. This is probably influenced by the stasis that occurs due to the temporary cessation of venous return in the limb. Tourniquet use has also been shown to result in a higher incidence of skin problems, including blistering, haematoma and oozing.[13] Application of a tourniquet may also tether the quadriceps muscle intra-operatively, affecting patellar tracking.

Tranexamic acid

In the final common pathway of the coagulation cascade, thrombin acts upon fibrinogen, converting it to fibrin, leading to fibrin deposition and the activation of platelets to form blood clots.

Plasmin is a proteolytic enzyme derived from plasminogen that hydrolyses fibrin into soluble products. Tranexamic acid is an antifibrinolytic that competitively inhibits the activation of plasminogen to plasmin. At high concentrations it is a non-competitive inhibitor of plasmin. It works by blocking the lysine-binding sites of the plasminogen molecule, which prevents it from binding to fibrin, as outlined in Figure 1. Its half life is approximately 2 h and it is excreted by the kidneys.[14]

A large multicentre review of hip and knee replacements has shown that intravenous tranexamic acid significantly decreases rates of allogenic of autologous blood transfusion and early post-operative complications, including thromboembolism and renal failure. It is suggested that a dose of 2000 mg has the best effectiveness and safety profile.[15]

Tranexamic acid has traditionally been given via the intravenous route; however, proponents for topical administration state that topical (intra-articular) administration will provide a maximum concentration of tranexamic acid at the bleeding site whilst being associated with 70% lower systemic absorption, theoretically reducing any side effects. Topical tranexamic acid has been shown to be effective (1 g/50 ml saline) in decreasing the absolute risk of transfusion by almost 20%, as well as pre-to-post haemoglobin drop by 0.84 g/dL in total hip replacements.[16] Topical tranexamic acid reduced the absolute risk of blood transfusion by 15.4% and reduced blood loss by 168 ml in total knee replacements.[17] In both of these studies the control drug was normal saline.

Tranexamic acid is also available for oral administration. This is infrequently used in the orthopaedic surgery setting, although there is some evidence for its use. It has been shown to result in a lower rate of transfusion, with a similar complication rate to intravenous tranexamic acid. The oral dose used was slightly higher than the intravenous dose, but it is slightly cheaper, which is pertinent in view of the constraints on healthcare budgets.[18]

The safest and most effective route of administration and dose of tranexamic acid is yet to be ascertained. Although it has been shown to decrease blood loss and transfusion requirements in general, it is unclear how beneficial it is to patients who are at a low risk of transfusion, and whether it should be prescribed to all patients or just high risk patients.

Controlled anaesthetic hypotension

Deliberate controlled lowering of mean arterial blood pressure by the anaesthetist intra-operatively has been shown to significantly decrease intra-operative bleeding.[19] Lower blood pressure decreases the risk of dislodging a recently formed clot at the operative site. This can be performed safely with general, spinal and epidural anaesthetics in appropriately trained hands. Spinal anaesthetic has been shown to be more effective than general anaesthetic in decreasing transfusion rates in hip and knee