Journal of Pharmaceutical Research International

33(59A): 745-753, 2021; Article no.JPRI.78436
ISSN: 2456-9119
(Past name: British Journal of Pharmaceutical Research, Past ISSN: 2231-2919, NLM ID: 101631759)

Intraoperative Bleeding Management: An Updating Literature Review: Review Article

Mansur Suliman Alqunai [a*], Rawan Humaidy Alshammary [b], Alanoud Saleem Almuhaysin [b], Rahaf Abdulsalam Alsubayti [b], Amani jadid Alsharari [b], Jumanah Mohammed Alanazi [b], Nujud Hayyal Alruwaili [b], Noof Falah Aldhuwayhi [b], Faridah safar AlMutairi [b] and Atheer Zaid Alfuhiqi [b]

[a] Department of Surgery, College of Medicine, Jouf University, Sakaka, Aljouf, The Kingdom of Saudi Arabia.
[b] Jouf University, The Kingdom of Saudi Arabia.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/JPRI/2021/v33i59A34324

Open Peer Review History:
This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: https://www.sdiarticle5.com/review-history/78436

Review Article

Received 01 November 2021
Accepted 15 December 2021
Published 16 December 2021

ABSTRACT

Background: Intraoperative bleeding remains a major complication during and after surgery, leading to increased morbidity and mortality. Several influences determine the complex causes of bleeding in surgical patients. About 75 to 90% of early intraoperative and postoperative bleeding is due to technical factors. In some cases, however, acquired or congenital coagulopathies can stimulate, if not directly cause, surgical bleeding.
Objectives: This paper aims to overview etiology, causes, diagnosis, and updated management of intraoperative bleeding.
Methods: The review article ran from July 1, 2021 to October 31, 2021. We searched articles on etiology, causes, and treatments published in English worldwide in the Medline, EBSCO and PubMed databases. No software was used to analyze the data. Team members reviewed the data to determine initial results.
Results: All patients scheduled for elective surgery should be screened for possible hemostatic defects using tests, and, if necessary, laboratory tests. Treatment of intraoperative bleeding

**Corresponding author: E-mail: m.alqunai@gmail.com;*

consists of identifying patients at risk and understanding the effect of surgery on hemostasis. For patients at high risk of bleeding, a pre-operative meeting with a multidisciplinary team (anesthesiologist, surgeon, hematologist, radiologist) can discuss the correct surgical procedure.
Conclusion: Technical variables account for 75-90% of initial intraoperative and postoperative bleeding. However, in other cases it is associated with acquired or congenital coagulation disorders. All patients scheduled for elective surgery should be checked for problems with hemostasis. Treatment of intraoperative bleeding involves identifying those at risk and understanding the effect of surgery on hemostasis.

Keywords: Intraoperative; bleeding; complication; surgery; management.

1. INTRODUCTION

Intraoperative bleeding, continues to be a serious problem during and after surgery, increasing morbidity and mortality. Blood loss, hemodilution, acquired platelet dysfunction, introduction of coagulation factors into the extracorporeal circuit, fibrinolysis and activation of inflammatory pathways, and hypothermia are all variables contributing to the development of complex bleeding causes in surgical patients [1]. Acquired hemostatic disorders are seen in surgical patients as a result of oral anticoagulants (warfarin, dabigatran, rivaroxaban, apixaban, edoxaban) and platelet inhibitors (P2Y12 receptor inhibitors, clopidogrel, prasugrel or ticagrelor). It happens often. Postoperative bleeding includes both pre-existing hemostatic disorders and acquired hemostatic disorders. Congenital bleeding is less common and goes away with surgery [2].

Surgical bleeding is often characterized as a single bleeding localized to the surgical site. Careful surgical technique, patience, and careful patient selection go a long way in reducing surgical bleeding in high-risk patients. Standard treatment options for patients with bleeding include the use of allogeneic blood products, the use of concomitant medications, and increased use of pure and recombinant hemostatic agents. Various hemostatic changes occur before and after surgery after trauma and major surgeries such as heart surgery and liver transplantation [3]. Concentrates of tranexamic acid, desmopressin, fibrinogen and prothrombin complex were developed for the prevention and treatment of perioperative bleeding. Patient examination at the time of treatment using platelet angiography, rotational platelet counts and platelet function tests allowed for a more complete evaluation of hemostatic-specific targeted therapy. Strategic complex management is required to improve management, limit the use of allogeneic blood products, and reduce transfusion risk [4].

2. METHODS

2.1 Study Design

Review article.

2.2 Study Duration

Data was collected from 1 July– 31 October, 2021.

2.3 Data Collection

We searched articles on etiology, causes, and treatment published in English worldwide in the Medline, EBSCO and PubMed databases. The keyword search title included "Intraoperative, Bleeding, Complication, Surgery, Management" and a combination of these was used. A literature listing for each included study will find additional confirmatory data.

2.3.1 Data extraction

In the first step, authors review headlines, critically evaluate eligible articles, and select articles that meet inclusion criteria for data extraction.

2.3.2 Inclusion criteria

Papers were selected based on the importance of the topic. Exclusion Criteria: All other publications or replicates and summary studies that did not use these topics as their primary purpose were omitted.

2.3.3 Statistical analysis

No software was used to analyze the data. Team members reviewed the data to determine initial results. Each member's results were double-corrected to ensure validity and minimize errors.

2.4 Etiology

The mortality from surgery is about 0.1%, the mortality from elective vascular surgery is 5-8%, and the mortality from severe bleeding is 20%. Excessive blood loss is associated with high mortality, morbidity, and ICU stays for major procedures for liver disease and cardiac surgery [5]. Descriptive variables ranged from 75% to 90% of initial intraoperative and postoperative bleeding. However, in rare cases, acquired or congenital coagulation disorders, although not directly the cause, can exacerbate surgical bleeding. The consequences of uncontrolled bleeding combined with hemodilution, hypothermia, reduced clotting factors and acidosis, in turn, make blood clotting procedures less effective and exacerbate the vicious cycle [6].

3. THE MOST COMMON CONGENITAL AND/OR ACQUIRED CAUSES OF PERIOPERATIVE BLEEDING

3.1 Chronic Liver Disease and Orthotropic Liver Transplantation

The hemostatic changes found in end-stage liver disease are complex and are caused by qualitative plasmin-associated platelet dysfunction, glycoprotein abnormalities, and depot depletion due to inadequate production of lower amounts of the procoagulant and anticoagulant protein, thromboxane A2. Platelet Ib Isolation and Ib Platelet Isolation [7]. On the other hand, the deficiency of platelet function is alleviated by high amounts of von Willebrand factor (vWF), which is caused by a deficiency of ADAMTS 13 protease produced by the liver. Deficiency of plasminogen activator inhibitors (PAI1 and 2) reduces TPA clearance from tissue plasminogen activators and improves fibrinolytic potential. This scenario is exacerbated by decreased levels of thrombin-activated fibrinolysis inhibitors (TAFIs) and alpha-2 antiplasmin [8]. Because tPA is significantly released into the bloodstream, hyperfibrinolysis may occur after the donor liver reperfusion procedure. As a result, these people may benefit from antifibrinolytic drugs while avoiding the possibility of overcoagulation. The balance of bleeding and coagulation fluctuates, with the potential for hepatic artery or portal vein thrombosis during reperfusion and significant coagulopathy bleeding during the postoperative period, particularly during the incisional stage after liver transplantation [9].

Cirrhosis inhibits the synthesis of all procoagulant factors (except factor VIII, which is produced in the endothelium) and is often combined with vitamin K deficiency, which is indicated by increased prothrombin time (PT), which is extremely sensitive to factor VII. density. PT and activated partial thromboplastin time (APTT) are frequently used as observers in cirrhosis patients, but do not usually indicate a state of pro- and anticoagulant insufficiency or excessive fibrinolysis [10]. Recent efforts to find important biomarkers have focused on pro-inflammatory cytokines such as monocyte chemoattractant proteins. In patients with cirrhosis, PT or APTT is not correlated with surgical bleeding, liver biopsy, or other potential bleeding disorders that may be better controlled with more comprehensive tests such as viscoelastic or endogenous thrombin potential (ETP). Reducing the concentrations of protein C, antithrombin, and factor II leads to a 25% reduction in thrombin production in cirrhosis, indicating a stable state of almost "simultaneous" deficiency of anticoagulants and procoagulants [11]. This unstable balance is lost after a severe stress response B infection or blood loss, and blood thinning leads to severe disability and severe bleeding disorders. Under these conditions, viscoelasticity tests often show a normal coagulation profile [12]. People with cirrhosis experience venous thromboembolism twice as often as the general population. Certain mutations in thrombotic coagulation factors may cause portal vein thrombosis in cirrhosis [13]. In a retrospective observational study of laparoscopic splenectomy, portal vein thrombosis occurred in 4% of cirrhotic patients treated with antithrombin III (ATIII) compared to 36% of those who did not. ATIII supplementation is being studied after liver transplantation to reduce allogeneic thrombosis, but qualitative evidence is lacking.

3.2 Hereditary Bleeding Disorders

Hereditary bleeding disorders result from the loss or deficiency of certain clotting proteins that act as procoagulants through precise interactions in the clotting cascade. Hemophilia A (factor VIII deficiency), hemophilia B (factor IX deficiency), and von Willebrand's disease are the three most common (vWD, variable autosomal dominant disorders). Hemophilia A, the most common congenital coagulopathy, is an X-linked recessive genetic disorder that affects 1 in 5,000 people [14]. Hemophilia B is an inherited X-linked coagulopathy that affects about 1 in 30,000 newborn boys. Hemophilia B is commonly

referred to as the Christmas disease. Because hemophilia is hereditary, the frequency increases in groups that are closer together.

Women may be asymptomatic carriers of the hemophilia gene or may have a partial disorder of certain factors. vWD is an autosomal dominant trait with no gender preference. On the other hand, women are more likely to develop symptoms due to increased bleeding during menstruation. According to the CDC, vWD affects about 1% of the population [15].

3.3 Antiplatelet Agents: Aspirin and Thienopyridine Derivatives

Aspirin is commonly used for secondary prevention of atherosclerotic diseases such as occlusive and cerebrovascular thromboembolism as well as coronary artery disease and peripheral arterial disease. Aspirin may increase blood loss during major surgery, but it is unlikely to increase the need for blood transfusions and should always be weighed against the risk to benefit [16]. Therefore, aspirin should not be discontinued prior to surgery except in neurosurgery. Clopidogrel (Plavix), prasugrel (Effient, Effient), ticagrelor (Brilinta) and cangrelor (Kengreal) are thienopyridine derivatives that inhibit platelet function by inhibiting the P2Y12 adenosine diphosphate (ADP) receptor. The current standard of care after percutaneous coronary intervention (PCI) is double platelet aggregation inhibitor drugs in combination with aspirin and clopidogrel, but this combination is associated with an increased risk of bleeding [17].

The choice to discontinue or even antagonize dual platelet-suppressing antithrombotic therapy requires careful consideration of the risk of thrombotic versus hemostatic effects, especially in patients who have recently received drug-eluting stents rather than non-metallic stents. Hemostasis deficiency may be corrected by administering platelet concentrate (2 units) after 12-24 hours of platelet aggregation inhibitor suspension (free drugs may inhibit transfused platelets). Aspirin should be resumed 6 hours after surgery, and P2Y12 receptor blockade should be started 12-48 hours after surgery. If permanent P2Y12 receptor blockade is required, Cangrelor injection can serve as a bridge to surgery. Platelet dysfunction testing has been considered inaccurate in patients with active bleeding because most tests require a sufficiently normal platelet count and most platelet function tests may not function properly after dilution changes and activation after CPB [18]. However, a recent prospective observational study found that ADP-induced preoperative platelet aggregation predicted the risk of severe bleeding in cardiac surgery patients who received ticagrelor prior to surgery [19].

4. DIAGNOSIS AND PREOPERATIVE EVALUATION

All patients scheduled for elective surgery should be screened for possible hemostatic defects using a medical history, examination, and, if necessary, laboratory tests. Amnesia is the most important part of a hemostasis test. Treatment includes a family history of bleeding. Positive for a maternal grandparent, maternal uncle, or sibling indicates hemophilia (A or B). In either a parent or a brother or sister, this indicates a history of vWD (variable autosomal dominant inheritance), a tendency to bleeding (such as multiple spots or minor bruising) [20]. age of onset of bleeding; Long history and childhood outbreaks indicate genetic diseases [21,22].

Secondary hemostatic disorders (coagulation/fibrinolysis) with deep bleeding such as vasculopathy, muscle contusion, retroperitoneal or visceral contusion or mild contusion. The onset of surgery or injury is delayed, and local pressure is often ineffective. Mucosal bleeding is rare. Excessive fibrinolytic or thrombolytic agents cause extensive bleeding such as wounds, drainage, or intravenous infusions [23].

If a bleeding tendency is found, perform the next preoperative patient examination. Assess skin and mucous membranes for signs of liver disease, such as jaundice and arachnoid nevus, and for bleeding, petechiae, or musculoskeletal contusions system. vasculopathy (coagulopathy), hepatomegaly, and splenomegaly are all symptoms of coagulopathy. Thrombocytopenia may be caused by the latter. Hemostasis testing is recommended for patients with a personal or family history of irregular bleeding, those with a medical condition, or those taking medications that could potentially interfere with hemostasis. Hemostasis tests include platelet count (normal = 150,000-400,000/μL), bone marrow aspiration and biopsy, bleeding time, platelet function tests, PT, PTT, and thrombin time (TT) [24].

5. MANAGEMENT

Identifying individuals at risk for intraoperative bleeding and understanding the effect of surgery

on hemostasis is the first step in managing intraoperative bleeding. A preoperative multidisciplinary team meeting (anesthesiologist, surgeon, hematologist, radiologist) can help discuss the best surgical strategy for patients at high risk of bleeding. This should include the feasibility of less invasive techniques (laparoscopic or radiographic procedures), the possibility of using a larger surgical team to shorten the steps of the procedure (as in spinal orthodontic surgery in two parts) or to shorten the operating time [25]. Patients with planned treatment that may require blood transfusions may consider preoperative autologous donation (PAS). Patients donate one unit of blood per week from 1 month prior to surgery, and may donate more than once a week, although the latter must be donated 72 hours prior to surgery [26]. These systems are laborious and are based on strict organization of blood collection and storage and coordination of surgical lists with guaranteed surgical dates. Patients are expected to produce additional red blood cells between donating blood and surgery. Iron supplements and erythropoiesis/erythropoietin stimulators have been thought to improve erythropoiesis in patients with PAD [27].

6. INTRAOPERATIVE STRATEGIES

6.1 Maintenance of Intravascular Volume

Typically, intravenous fluids (IVF) are administered according to protocols based on tradition, expert opinion, and in many cases insufficient evidence. Individual targeted therapy is required to maximize intravascular volume and microcirculation while ensuring adequate tissue perfusion. The purpose of fluid administration is to cover the basal metabolic rate, correct preoperative deficiencies, and compensate for losses, including those at the surgical site. Body fluids (crystals, colloids, and blood components) and their amounts are determined by modulated hemodynamic parameters [28].

6.1.1 Use of regional anesthesia

Central nerve axis blockage, such as spinal/epidural anesthesia, has been associated with reduced intraoperative bleeding (approximately 25-30%). This also applies to the postoperative period (eg treatment of pelvic, orthopedic and vascular diseases). The blood-sparing effect of neuroaxial anesthesia is caused by systemic hypotension due to sympathetic block and decreased venous tone [29].

6.1.2 Positioning

The patient's surgical posture can have a significant impact on intraoperative bleeding (obstruction of venous return can lead to venous congestion if the patient is in the wrong position). Elevating the operating bed above the level of the right atrium improves venous drainage and reduces local venous pressure. Twisting the neck should be avoided as it will stop the outflow of the jugular veins (eg during head and neck surgery) and cause blood to pool at the surgical site. In the supine position, pressure on the abdominal wall should be minimized (to reduce compression of the inferior vena cava) to reduce blood flow through the collateral venous plexus of the spine [30].

6.1.3 Ventilation

Positive pressure ventilation under general anesthesia may prevent venous return. Minimizing mean intrathoracic pressure during controlled breaths with low tidal volumes and using little positive end-tidal pressure helps to improve venous recovery and prevent blood loss [31].

6.1.4 Controlled Antihypertensives

Various drugs, including inhalants, beta blockers, alpha blockers, calcium channel blockers, direct arterial/venous vasodilators, ganglion blockers, adenosine, and prostaglandin E1 can lower mean arterial pressure to 5075 mmHg. This method, which requires continuous hemodynamic monitoring, has been used for open surgery of the hip, spine and prostate. Controlled antihypertensive procedures are contraindicated in patients with coronary artery disease, uncontrolled hypertension, cerebrovascular disease, or anemia [32].

6.1.5 Maintaining Normal Body Temperature

Hypothermia results in a temperature-dependent enzymatic reaction that results in changes in platelet activity and coagulation cascade, resulting in a patient hypocoagulant. Mild hypothermia (1°C) also increases blood loss by approximately 16% and the relative risk of transfusion by approximately 22%. Use temperature monitoring as a guide and warm equipment (hot drinks, blankets, etc.) to prevent hypothermia during surgery [33].

6.1.6 Acute euvolemic hemodilution

This approach is used prior to surgical bleeding periods for major surgeries where moderate to moderate bleeding is expected (e.g. major heart surgery, orthopedic surgery, chest surgery, or liver surgery). To reach an Hkt level of 20-30%, the normal blood volume is maintained with simultaneous replacement of crystals and/or colloids. The basic idea of acute normal volume hemodilution (ANH) is to create well-tolerated intraoperative anemia [34]. Preoperative dilution of circulating blood volume minimizes the number of red blood cells and plasma components lost after surgical bleeding. Finally, after the incision has healed, new whole blood is returned to supply red blood cells, clotting factors and platelets when they are needed most. The use of ANH in non-selective procedures, the avoidance of trauma due to blood retention, and the avoidance of typographical errors are the advantages of ANH over PAD. Evidence shows that the effectiveness of ANG (reducing the risk of transfusion by 10%) has fewer hemostatic benefits than normal therapy [35].

6.2 Surgical Technique

The discovery and use of surgical procedures to control bleeding contributes to a multimodal approach to reducing blood loss. Less invasive procedures such as laparoscopy (eg, nephrectomy, splenectomy) and computerized surgery (eg, knee replacement) have been shown to reduce the incidence of bleeding. The use of surgical adhesives and tissue sealants (local hemostats), tourniquets with sufficient bleeding, and vasoconstrictors reduce the need for allogeneic transfusions [35].

6.3 Cell Salvage

During surgery, cellular structures (CS) are used in surgical procedures where bleeding can be significant. This method collects and disposes of spilled blood and reinjects autologous red blood cells lost during surgery. The end product of the procedure is red blood cells with an Hct of 50-60%. Reduced erythrocytes in terms of erythrocyte viability, pH, 2.3DPG and potassium are superior to or at least comparable to conserved allogeneic blood [36]. This approach has been proven to limit the effects of allogeneic transfusions and has been proven to include open heart surgery, vascular surgery, total arthroplasty, spinal surgery, liver transplantation, neurosurgery, and certain Jehovah's Witnesses (equipment continues to be distributed and approved agreement). The use of CS to inject unwanted substances in cancer, gynecology, and intestinal surgery (contaminated) was considered a relative contraindication. Disadvantages of CS are high equipment costs and the need for qualified personnel [37].

6.4 Clotting Factors

Certain types of isolated or mixed PCC coagulation factors (fibrinogen, factor XIII and factor VIIa) are clearly labeled to avoid excessive bleeding in individuals with congenital or acquired hemostatic disorders. There is evidence supporting the use of fibrinogen concentrate/cryoprecipitate in hypofibrinemia. Factor XIII Concentrate with Factor XIII Deficiency (30 IU/kg) (Activity 60°); Vitamin K and PCC (2030 IU/kg)/increased bleeding propensity and increased blood clotting time CT in patients taking oral anticoagulants; and recombinant factor VIIa [38] for uncontrolled bleeding and/or failure of complex coagulation therapy with conventional radiological, surgical or interventional methods.

6.5 Antifibrinolytic Agents

Antifibrinolytics are one of the key therapies to reduce the risk of blood loss and transfusion after surgical procedures (eg, cardiovascular, trauma, and orthopedic) [39]. After discontinuation of aprotinin, synthetic derivatives of lysine, tranexamic acid (TXA) and epsilonaminocaproic acid (EACA) have become the most widely used antifibrinolytic agents. TXA and EACA reversibly bind plasmin and plasminogen to inhibit thrombolysis at the site of bleeding. TXA is 610 times more potent than EACA and has a longer half-life [40].

6.6 Transfusion of Blood Components

Although an Hb range of 610 g/dL usually induces transfusions, indications for BT are specific to the specific scenario and patient [41]. It is recommended to target an Hb concentration of 79 g/dL for active bleeding, as the red blood cell restricted transfusion threshold (Hb 78 g/dL) is safer than the free transfusion threshold (Hb > 9 g/dL). Platelet transfusion, PFC, cryoprecipitate, fibrinogen, factor XIII, factor VIIa, and PCC are used to prevent and treat excessive bleeding according to abnormal monitoring parameters [42].

7. CONCLUSION

Technical variables account for 75-90% of initial intraoperative and postoperative bleeding. However, in other cases it is associated with acquired or congenital coagulation disorders. All patients scheduled for elective surgery should be screened for problems with hemostasis. Treatment of intraoperative bleeding involves identifying those at risk and understanding the effect of surgery on hemostasis. For patients at high risk of bleeding, the optimal surgical technique should be reviewed in a preoperative multidisciplinary team (anesthesiologist, surgeon, hematologist, radiology) meeting. Measures to control a patient's blood during surgery are usually aimed at reducing blood loss and/or recovering and reinjecting the patient's own blood spilled.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
https://www.sdiarticle5.com/review-history/78436