



Effect of Desmopressin on Bleeding After Heart Surgeries: A Narrative Review

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Abstract

Desmopressin is an analog of the antidiuretic hormone (vasopressin), which causes anticoagulant activity by increasing plasma factor 8. The use of desmopressin dates back to 1977, when this hormone was used to prevent bleeding during tooth extraction and surgery in patients with hemophilia A and von Willebrand disease. After that, this hormone was expanded to prevent bleeding in congenital defects and conditions such as chronic kidney and liver failure. Also, this hormone is used to prevent bleeding in major surgeries such as heart surgery, where the patient loses much blood and needs a blood transfusion. Considering the importance of desmopressin in bleeding control, the present study was conducted to investigate the possible effect of this hormone in heart surgery.

Keywords: Desmopressin, Bleeding, Blood Transfusion, Open-heart Surgery, Platelet Function Disorders

1. Context

Desmopressin is an analog of the antidiuretic hormone (vasopressin), which is particularly interesting due to its antidiuretic and anticoagulant role. This hormone exerts its anticoagulant activity by increasing the adhesion of platelets to vascular endothelium and vWF multimers, thereby causing the formation of platelet plaques (1,2). The role of desmopressin is well revealed in patients with VWD type 1 who have defects in platelet aggregation due to birth defects or drug side effects (3). Studies have shown that in these patients, desmopressin increases the level of VWF in the plasma and reduces the duration of bleeding, therefore improving the patient's clinical conditions. Although desmopressin does not cause any specific side effects, in some people, it can cause nausea, drowsiness, increased blood pressure, and weight gain (4,5).

The first use of desmopressin dates back to 1977 when this hormone was used to prevent bleeding during tooth extraction and surgery in a patient with hemophilia A (6). After that, extensive studies on the role of desmopressin and its side effects were conducted worldwide, and the World Health Organization introduced this drug as one of the essential anti-bleeding drugs in hemophilia patients.

In addition, this drug is used to control bleeding caused by platelet abnormalities, congenital diseases,

chronic kidney and liver disorders, and some homeostasis failures (7). Desmopressin is also a pro-receptor agent in surgeries that predict severe bleeding, and the patient may need a blood transfusion. Since this drug reduces the need to transfer blood products to the patient, it reduces the costs imposed on the healthcare system.

Therefore, considering the importance of desmopressin in controlling the patient's bleeding, the role of this drug in preventing or controlling bleeding in open heart surgery is reviewed.

2. Search Strategy

The data collection of the present study was done by searching the keywords desmopressin, heart surgery, bleeding, pediatric heart surgery, FVIII, VWF, and DDAVP in the official database of PubMed, Embase, Scopus, and Web of Science. For this purpose, all articles presented in English in this field from 1986 to 2021 were collected. In the initial search, 61 articles were obtained, and by reviewing the titles and abstracts of the articles, 43 articles were selected for the final review. The reference list is based on these related articles.

3. Desmopressin in Open Heart Surgery

3.1. Reducing Bleeding After Surgery

One of the most significant factors in increasing the cost of treatment and mortality of patients after surgeries, such as heart surgery, is severe and prolonged bleeding (8, 9). On the other hand, since the use of blood products and their transmission to the patient is associated with the possibility of transmission of various types of infectious diseases, using an alternative method can help improve the patient's health while reducing treatment costs.

Bleeding after surgery is influenced by various factors, the most important of which are homeostasis disorders. However, other factors can also be influential in postoperative bleeding. In general, bleeding management is usually done by injecting blood products such as fresh frozen plasma and platelet concentrate (10).

After open heart surgery with cardiopulmonary bypass, many patients, especially women, need to receive blood products. In some cases, the bleeding is so extensive that the surgical team has to perform the surgery again and investigate the cause of the bleeding. In some patients, the source of bleeding is the surgical site, but in some cases, using some drugs during surgery or congenital coagulation disorders and homeostatic defects can be involved in causing bleeding (11). Among the hemostatic failures that cause bleeding are low levels of plasma coagulation factors (for example, fibrinogen), hyperfibrinolysis, or dysfunction of platelets (12). The use of oxygen generators in cardiopulmonary bypass during heart surgery can cause defects in the glycoprotein membrane of platelets and disrupt the connection of platelets with coagulation proteins such as VWF and fibrinogen. Also, the use of some anesthetic drugs, the type of elective surgery, the type of oxygen generator, and hypothermia are other influential factors in hemostatic disorders (13). In the past years, controlling bleeding after such surgeries with the help of measures including the use of primary and secondary hemostasis control drugs such as antifibrinolytic drugs, returning blood in CPB tubes, collecting autologous blood before surgery and injecting it after surgery, and retransferring the spilled mediastinal blood have been done. Among the drugs used to manage bleeding in open heart surgery with extracorporeal circulation is desmopressin, which we will investigate its effectiveness in the present study.

3.2. Desmopressin in Pediatric Cardiac Surgery

There are few studies on the use of desmopressin in pediatric heart surgery. During the past years, researchers have found that desmopressin does not significantly affect the hemostatic status of children undergoing surgery, and

this drug does not play a role in reducing bleeding after heart surgery in children (14). During the study of children under two years of age undergoing heart surgery, Reynolds et al. showed that consuming 0.3 $\mu\text{g}/\text{kg}$ of DDAVP does not affect allogeneic blood transfusion or bleeding reduction (15). Based on the results obtained from the study of the effect of DDAVP in heart operations of children with congenital heart failure, which was conducted by Oliver et al., the average bleeding of redo patients was 343 (versus placebo 357 mL/m^2). Meanwhile, the mean blood loss for primary patients was 277 versus 228 mL/m^2 (16). Therefore, using DDAVP in heart surgery of children with congenital heart failure is not useful. In another study conducted by Seear et al., (17) the effect of 0.3 $\mu\text{g}\cdot\text{kg}^{-1}$ desmopressin after the end of extracorporeal circulation was investigated in children undergoing open heart surgery. These researchers also achieved the same results and acknowledged that desmopressin does not affect reducing bleeding after surgery (18). This can be related to the maximum release of von Willebrand factor, which is increased by this drug. Therefore, in general, the use of desmopressin to control bleeding in pediatric heart surgery is not recommended.

3.3. Desmopressin in Adult Open Heart Surgery

The first experience of using desmopressin in adult heart surgery was obtained in 1986 (19). Based on the results obtained from this study, desmopressin reduced bleeding and the need for a blood transfusion by 40% in 12 hours after heart surgery (20). Subsequent studies conducted in the field showed that patients treated with desmopressin and a placebo did not significantly differ in bleeding reduction (21, 22). However, the study of the effect of desmopressin in patients undergoing valve replacement and coronary artery bypass surgery was associated with different results (2, 12, 14, 23-26). Evaluating the role of desmopressin in coronary and non-coronary surgery of adults can help to achieve more accurate results.

3.3.1. Adult Coronary Surgeries

Based on the meta-analysis conducted by Cattaneo, Erstad, and Carless et al., who reviewed 14 clinical trials (27-29), the effectiveness of DDAVP was evaluated in 818 patients undergoing CABG. Among these studies, the results obtained from 10 studies did not confirm the role of this drug in reducing the need for blood transfusions after surgery. In three clinical trial studies, aspirin use before surgery was one of the inclusion criteria (23, 30-32). The researchers also looked at CABG patients who received aspirin seven days before surgery. These studies showed that desmopressin significantly reduced bleeding during and after surgery. The study results by Dilthey et al., who evaluated CABG patients who received aspirin within five days

after the operation, showed that despite extensive bleeding after surgery, the need to receive blood products in patients using desmopressin was significantly reduced (31).

Another similar study by Mongan et al. (32) examined patients with platelet dysfunction after CPB, whose bleeding was significantly reduced by desmopressin. Considering the results obtained from these studies, it can be concluded that if aspirin is not prescribed before heart surgery or platelet dysfunction is detected in the patient, desmopressin has no role in reducing bleeding after surgery or reducing the need to transfer blood products in patients undergoing CABG.

3.3.2. Adult Non-coronary Surgeries

Based on a published meta-analysis of 17 clinical trials, 1,171 patients underwent heart surgery (27). This study showed that desmopressin could reduce bleeding after surgery by 9%. Despite the significant role of this drug in reducing bleeding within 24 hours after surgery, a quarter of the studies conducted on patients treated with a placebo were associated with extensive bleeding (27). Therefore, prophylactic desmopressin does not effectively reduce bleeding after surgery and is only slightly effective in controlling bleeding in patients with extensive bleeding. According to other studies on the role of desmopressin in coronary, valvular, and fusion surgery, the drug did not reduce the need to receive blood products (23, 33). Several clinical trials have investigated desmopressin in patients undergoing all types of heart surgery except isolated CABG (11). The researchers showed that this drug significantly reduced blood loss during and after the operation by up to 900 mL. However, it did not affect the need to transfer blood products (19). According to Rocha et al., desmopressin did not make a difference in blood loss and the need for blood products after previous surgery (20, 34). Meanwhile, none of these researchers paid attention to the role of aspirin administration and the function of platelets.

Other meta-analyses showed that desmopressin could have a negligible effect on reducing blood loss after surgery, but its effectiveness is limited and has nothing to do with reducing mortality and the need for blood transfusions and reducing complications. Another study showed that the effect of this drug on reducing bleeding after surgery and side effects is less than the effectiveness of aprotinin and lysine, and it can also increase the risk of a heart attack after surgery (10). Based on these results, desmopressin increases the risk of myocardial infarction by 4.2% compared to placebo (35). In general, it can be said that various reports on the role of desmopressin in reducing blood loss and the need for blood transfusion are inconclusive, and this drug is not recommended, especially

in people prone to severe bleeding.

4. Conclusions

Various studies show that desmopressin in adults undergoing heart surgery significantly reduces bleeding and the need for transfusion of blood products. Therefore, the routine use of this drug in adults exposed to CPB cannot be approved. Meanwhile, this drug can effectively reduce bleeding and the need to inject blood products in patients who have received aspirin before surgery and those with platelet dysfunction. Also, so far, the effectiveness of desmopressin in reducing bleeding and the need for blood replacement in children undergoing various heart surgeries has not been proven.

Footnotes

Authors' Contribution: A.J. conceived and designed the evaluation and helped to draft the manuscript. S.B.M. collected the data, interpreted them, and revised the manuscript. F.M. re-analyzed the articles and revised the manuscript. All authors read and approved the final manuscript.

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