For best practices in health
CDBPS-H
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World Hemophilia Day, April 17th2023

Every year, on April 17, World Hemophilia Day is celebrated, with the aim of raising public awareness of the realities of a little-known disease and mobilizing as many people as possible in favor of the integration of patients.Hemophilia is an inherited hemorrhagic disease caused by the deficiency of a coagulation protein, usually present in the plasma. It is transmitted hereditarily from father to daughter and from mother to son. It is the most widespread of hereditary hemorrhagic disorders, represents a heavy social and economic burden.

The current situation in Cameroon is still a bit complex. Even at the level of hospitalizations or health facilities, it is not easy to be able to diagnose this kind of problem. Because when a patient arrives in a hospital and has a bleeding disorder, he is oriented according to his crisis, and this orientation remains fictitious. Hence the difficulties in obtaining statistical data.

This year, the theme is: "Access for all: the prevention of bleeding as a global standard of care". Building on last year's theme, this call to action for the community in 2023 aims to come together and advocate with local politicians and governments for better access to treatment and care, highlighting the focus on better control and prevention of bleeding, for everyone with a bleeding disorder. This requires the implementation of home care as well as prophylactic treatments to help these people benefit from a better quality of life.

As part of this celebration, the Center for the Development of Best Practice in Health, propose these summaries of Cochrane systematic reviews aiming to inform the patients, medical staff and others stakeholders in the prevention and the treatment of the Hemophilia.

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Journée mondiale de l'Hémophilie17 AVRIL 2023

Chaques 17 avril, se célèbre la Journée Mondiale de l'Hémophilie, avec pour objectifs de sensibiliser un large public aux réalités d'une maladie peu connue et de mobiliser le plus grand nombre en faveur de l'intégration des patients. L'hémophilie est une maladie hémorragique héréditaire due au déficit d'une protéine de coagulation, habituellement présente dans le plasma. Elle se transmet de façon héréditaire de père en fille et de mère en fils. Il s'agit de la plus repandue des affections hemorragiques hereditaires, represente une lourde charge sociale et economique.

La situation actuelle au Cameroun, reste toujours un peu complexe. Même au niveau des hospitalisations ou bien des formations sanitaires, ce n'est pas facile de pouvoir diagnostiquer ce genre de problème. Parce que lorsqu'un malade arrive dans un centre hospitalier et qu'il a un trouble de la coagulation, il est orienté en fonction de sa crise, et cette orientation reste fictive. D'où des difficultés à avoir des données statistiques.

Cette année, le thème est le suivant : « Accès pour tous : la prévention des saignements comme référence mondiale de soins ». S'appuyant sur le thème de l'an dernier, cet appel à l'action pour la communauté en 2023 vise à se rassembler et à défendre auprès des responsables politiques locaux et des gouvernements un meilleur accès aux traitements et aux soins, en mettant l'accent sur un meilleur contrôle et une meilleure prévention des saignements, pour toutes les personnes atteintes d'un trouble de la coagulation. Cela passe par la mise en œuvre de soins à domicile ainsi que de traitements prophylactiques pour aider ces personnes à bénéficier d'une meilleure qualité de vie.

Dans le cadre de cette célébration, le Centre pour le développement des Bonnes pratiques en santé, propose ces résumés de revues systématiques Cochrane visant à informer les patients, le personnel médical et les autres parties prenantes sur les moyens de prévention et la prise en charge de l'Hémophilie.

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1. Clotting factor concentrates for preventing bleeding and bleeding-related complications in previously treated individuals with haemophilia A or B

Review question

Should people, who have previously been treated for joint bleeding, be given regular preventative treatment with clotting factor concentrates to manage their condition?

Background

Hemophilia A and B are X-linked inherited bleeding disorders in which bleeding into joints is a major problem. Repeated joint bleeds can lead to affected joints (commonly referred to as 'target joints') becoming damaged and painful, with limited movement. Currently, bleeding is treated and prevented with plasma-derived or recombinant clotting factor concentrates, and more recently non-clotting factor formulations. This review looked at how useful and effective different clotting factor treatment strategies are for preventing joint bleeding and other outcomes in previously treated people with hemophilia A or B.

Search date

Date of last search: 24 February 2021.

Study characteristics

This review includes 10 randomised controlled trials. Eight had treatment arms that compared the regular use of clotting factor concentrates to prevent joint bleeds with different dosing schemes to identify regimens that may be better; four had treatment arms that compared the regular use of factor concentrates to prevent bleeds to their 'on demand' use to treat bleeds once they occur (two trials had multiple arms and were included in both comparisons).

Key results

In people living with hemophilia A or B previously treated for joint bleeding or with existing joint damage, preventive therapy may reduce the number of joint bleeds compared to 'on-demand therapy'. This reduction in bleeds may lead to an improvement in joint function, pain, and quality of life. However, preventive therapy is linked to an increased use of factor concentrates and therefore higher treatment costs. Further studies are needed to establish the best preventive course of treatment in terms of starting time, frequency and dose level.

Certainty of the evidence

Overall, the certainty of the evidence was judged to be low because of different types of bias that could have affected the results. Future research might have an important role in changing our confidence in these results.

Citation : Olasupo OO, Lowe MS, Krishan A, Collins P, Iorio A, Matino D. Clotting factor concentrates for preventing bleeding and bleeding-related complications in previously treated individuals with haemophilia A or B. Cochrane Database of Systematic Reviews 2021, Issue 8. Art. No.: CD014201. DOI: 10.1002/14651858.CD014201. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD014201/full#CD014201-abs-0002

2. Rituximab for treating inhibitors in people with inherited severehemophilia

Review question

We reviewed the evidence available to see if rituximab is effective and safe when treating clotting factor inhibitors in people with severe hemophilia. This is an update of a previously published Cochrane Review.

Background

Hemophilia A and B are inherited conditions in which there is either reduced levels (or none at all) of factor VIII (hemophilia A) or factor IX (hemophilia B) in the blood. In severe forms there are undetectable levels of these factors (less than 0.01 international units (IU) per milliliter). People with hemophilia are at risk of bleeding events which can occur spontaneously or after trauma or invasive medical procedures. Therefore, they need to be treated with factor concentrates, either in reaction to these events or preventatively. Unfortunately, about 30% of people with severe hemophilia A and 1% to 6% of people with severe hemophilia B can develop antibodies (inhibitors) against factor VIII or factor IX, because the factors are not recognized by the immune system. The development of inhibitors is the main complication of hemophilia treatment, because their presence reduces or cancels out the beneficial effects of replacement therapy, making it very difficult to control bleeding. Moreover, when inhibitors are present, it is impossible to start preventative treatment with factor VIII or factor IX concentrates. Therefore, it is important to eliminate the inhibitors and allow treatment to proceed successfully. The 'off-label' use (currently unapproved for treating people with hemophilia) of rituximab, has shown in some studies an effect on eliminating inhibitors in people with hemophilia. Therefore, we wanted to see whether using rituximab was better than the standard treatment or other therapies without rituximab, and whether it is safe,

and could save these people from life-threatening hemorrhage and huge financial expense.

Search date

The evidence is current to: 19 March 2020.

Key results

We did not find any randomized controlled trials assessing rituximab in people with severe hemophilia. Well-designed controlled trials are needed to assess the benefits and risks of using rituximab in people with hemophilia. Until controlled trials are published, only limited and low-level evidence, based on individual cases, can guide physicians in making clinical decisions.

Citation :Jiang L, Liu Y, Zhang L, Santoro C, Rodriguez A. Rituximab for treating inhibitors in people with inherited severe hemophilia. Cochrane Database of Systematic Reviews 2020, Issue 8. Art. No.: CD010810. DOI:10.1002/14651858.CD010810.pub4.
https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD010810.pub4/full#CD010810-abs-0002

3. Antifibrinolytic therapy for preventing oral bleeding in patients with haemophilia or Von Willebrand disease undergoing minor oral surgery or dental extractions

Review question

We reviewed the evidence about whether antifibrinolytic medicine (drugs that promote blood clotting) such as tranexamic acid or epsilon aminocaproic acid, can prevent oral bleeding in people with haemophilia or Von Willebrand disease undergoing minor oral surgery or dental extractions. This is an update of a previously published Cochrane Review.

Background

Haemophilia and Von Willebrand disease are inherited bleeding disorders. People with these disorders have an increased risk of bleeding complications during and after oral surgery or dental extractions, even if these are relatively minor and commonly performed. The number of bleeds and the severity of each depend on disease-related factors (such as the severity of the haemophilia), as well as patient-related factors (such as inflammation of the gums or blood vessel diseases) and intervention-related factors (such as the type and the number of teeth extracted or how big the surface of the wound is). Measures such as giving clotting factors directly into the blood stream, are commonly used before, during or after surgery to prevent bleeding complications. However, these measures are costly and have risks such as the formation of inhibitors and the transmission of infections. Therefore, it is important to search for alternative methods to prevent bleeding complications. In routine practice antifibrinolytic medicine is

often used before, during and after surgery. However, there is currently no clear scientific evidence for this practice.

Search date

The evidence is current to: 01 March 2019

Trial characteristics

We did not find any trials of antifibrinolytic medicine to prevent bleeding after minor oral surgery or dental extractions in people with Von Willebrand disease. The review does include two trials published in the 1970s in 59 people with haemophilia undergoing dental extraction. In one trial the people were aged between 13 and 65 years and in the second trial the people had an average age of 34 years. One trial lasted five days and used tranexamic acid; the second trial lasted 10 days and used epsilon aminocaproic acid tablets. Both trials compared the active medicine with a substance that contained no medication (a placebo) in addition to clotting factor concentrates.

Key results

Overall, the two included trials showed a reduction in the number of bleeds after dental extraction, in the amount of blood loss, and in the need for clotting factor concentrates in the people treated with tranexamic acid or epsilon aminocaproic acid tablets compared to those who received a placebo. When combining the results of both trials it appeared that antifibrinolytic medication roughly halves the bleeding rate after dental extraction and the trials reported. Side effects of the antifibrinolytic medicine rarely occurred and led to discontinuation of epsilon aminocaproic acid tablets in only one case.

Quality of the evidence

In the epsilon aminocaproic acid trial, the trial physicians assigned each person to receive a placebo or the active treatment based on a pair-matching technique for age, factor-assay and the number of extractions. The fact that the trial physicians made this decision may have introduced a selection bias. However, we do not think that this had a major impact on the trial's conclusions. Overall, the two trials were small and differed from each other in terms of how many of the people taking part had severe haemophilia, the simultaneous use of clotting factor concentrates and the different antifibrinolytic treatment schedules. We rated the overall quality of the evidence as low for using antifibrinolytic medicine to prevent bleeding in people with haemophilia after minor oral surgery or dental extractions. No evidence was found for people with Von Willebrand disease. It could however be argued that, if antifibrinolytic medicine works for people with haemophilia, it is likely that the medicine will also work for people with other bleeding disorders undergoing dental extractions or minor oral surgery.

Citation :van Galen KPM, Engelen ET, Mauser- Bunschoten EP, van Es RJJ, Schutgens REG. Antifibrinolytic therapy for preventing oral bleeding in patients with haemophilia or Von Willebrand disease undergoing minor oral surgery or dental extractions. Cochrane Database of Systematic Reviews 2019, Issue 4. Art. No.: CD011385. DOI: 10.1002/14651858.CD011385.pub3.
https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD011385.pub3/full#CD011385 abs-0005

4. Desmopressin acetate (DDAVP) for preventing and treating acute bleeds during pregnancy in women with congenital bleeding disorders

Review question

We reviewed the evidence about the effect and safety of desmopressin acetate (DDAVP) in preventing and treating acute bleeding in pregnant women with bleeding disorders. This is an update of previously published versions of this Cochrane Review.

Background

Congenital bleeding disorders cause problems with bleeding during pregnancy, labour and delivery. Bleeding complications in women with congenital bleeding disorders are an important cause of disease and death linked to childbirth. Agents to stop the flow of blood are used for women with these bleeding disorders during pregnancy. DDAVP is a drug used to effectively increase the concentration of factor VIII in the blood and to increase the clumping together of platelets to stop bleeding. It does not come from human plasma and it carries no risk of infection. It might be a precious resource in people with von Willebrand disease, haemophilia A or congenital platelet disorders to prevent and treat bleeding episodes related to pregnancy.

Search date

The evidence is current to: 01 October 2018.

Study characteristics

We did not find any randomised controlled trials assessing desmopressin acetate in this group of women.

Key results

There were no trials included in the review. Given the ethical considerations, future randomised controlled trials are unlikely. Evidence is needed to show the risks and benefits of DDAVP when used to prevent and treat bleeding during pregnancy in women with congenital bleeding disorders. While there is evidence from observational trials that shows the drug is effective in stopping and preventing bleeding, we conclude that there is still a need to generate other high- quality controlled evidence. Given that there are unlikely to be any trials published in this area, this review will no longer be regularly updated.

Citation:Karanth L, Barua A, Kanagasabai S, Nair N S. Desmopressin acetate (DDAVP) for preventing and treating acute bleeds during pregnancy in women with congenital bleeding disorders. Cochrane Database of Systematic Reviews 2019, Issue 2. Art. No.: CD009824. DOI: 10.1002/14651858.CD009824.pub4.
https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD009824.pub4/full#CD009824-abs-0002

5. Pro-coagulant haemostatic factors for the prevention and treatment of bleeding in people without haemophilia

Review question

Do medicines that help in the prevention and treatment of bleeding reduce the risk of death, the risk of experiencing a blood clot and reduce the amount of blood lost in people who do not suffer from haemophilia (a bleeding disorder), who are bleeding, or at risk of bleeding?

Background

Coagulopathy, defined as a failure of normal blood clotting, is common in severe illness, trauma and major surgery. This can make bleeding worse and may cause death. Medicines are available that are blood clotting factors that can be given into the vein to treat coagulopathy and bleeding. However, we lack enough information about how effective and safe they are.

This review combines all the data available on these medicines to assess their effectiveness and safety.

Study characteristics

We searched the medical literature up to 18 April 2018 for randomised controlled trials (RCTs), as these provide the most reliable evidence. We identified 31 relevant RCTs that contained results from 2392 participants and compared these medicines either against placebo (inactive treatment) or another medicine or blood product. The RCTs focused on three types of factors that may improve blood clotting: fibrinogen (a clotting factor that increases clot strength), clotting factor XIII (important for holding clots together) and prothrombin complex concentrate (a combination of four precursor clotting factors).

The trials either gave these medicines before bleeding occurred (prophylactically) or to treat existing bleeding (therapeutically). Most trials focused on surgery, especially heart surgery, trauma, and bleeding after childbirth.

Seventeen of the RCTs we identified had industrial support, eight had unclear funding sources and six declared non-industrial funding.

Key results

No medicine had any effect on the risk of dying, regardless of clinical setting or how the medicine was used. However, our certainty in the results is low and this finding may change in the future when new studies are published.

No medicine increased the risk of harmful clots in the veins or arteries, but our certainty in these findings is low.

Prophylactic fibrinogen reduced bleeding after heart and orthopaedic surgery compared to placebo. Prophylactic fibrinogen, compared to placebo, almost halved the need for blood transfusion following heart surgery, and reduced the need by three-quarters in other surgery. Fibrinogen reduced the need for blood transfusion when used to treat bleeding.

Prophylactic factor XIII reduced bleeding after heart surgery.

Sample sizes in future randomised trials need to be greatly increased in order to show any differences in overall survival and death due to bleeding.

Certainty of the evidence

Our certainty in the evidence is low, but future research may change the findings of this review.

Conclusion

The low certainty of the evidence makes it difficult to draw conclusions about how well these medicines work and whether they should be used in current health care. Further research is required in larger-scale RCTs to determine the benefit and costs of these treatments and whether this outweighs their risks.

Citation:Fabes J, Brunskill SJ, Curry N, Doree C, Stanworth SJ. Pro- coagulant haemostatic factors for the prevention and treatment of bleeding in people without haemophilia. Cochrane Database of Systematic Reviews 2018, Issue 12. Art. No.: CD010649. DOI: 10.1002/14651858.CD010649.pub2.
https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD010649.pub2/full#CD010649-abs-0004

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