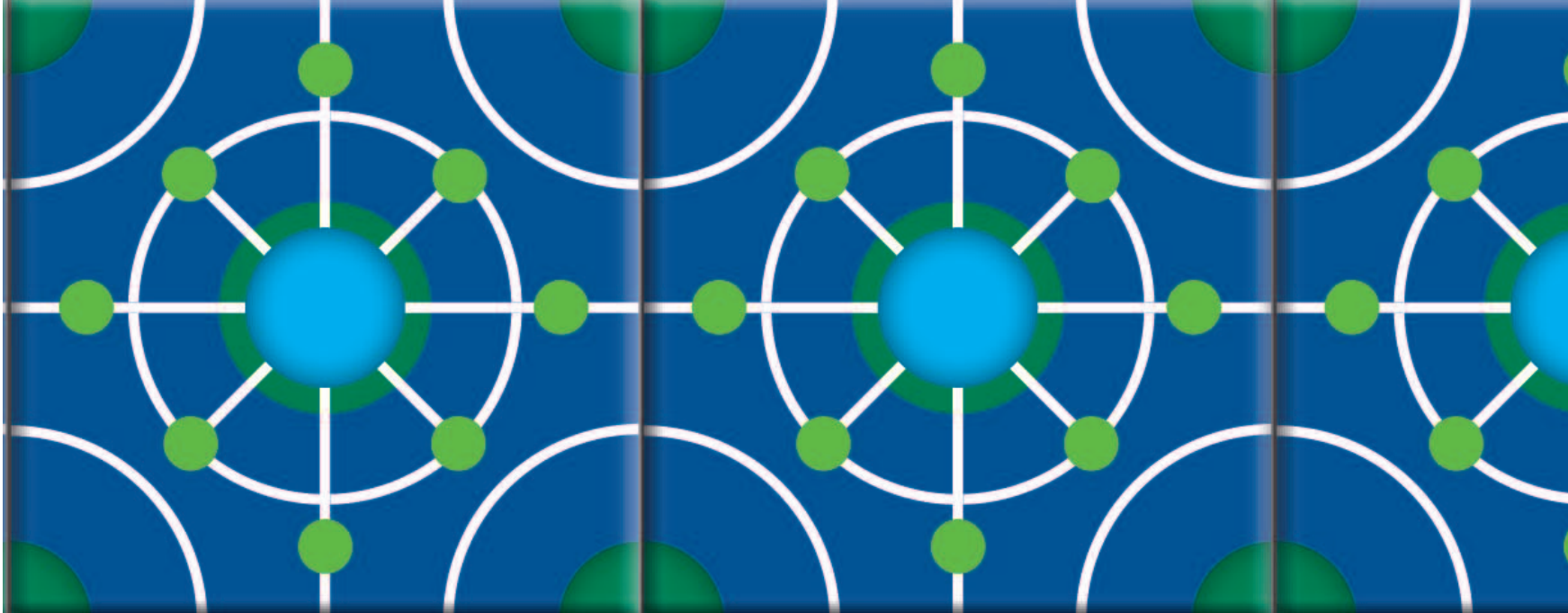
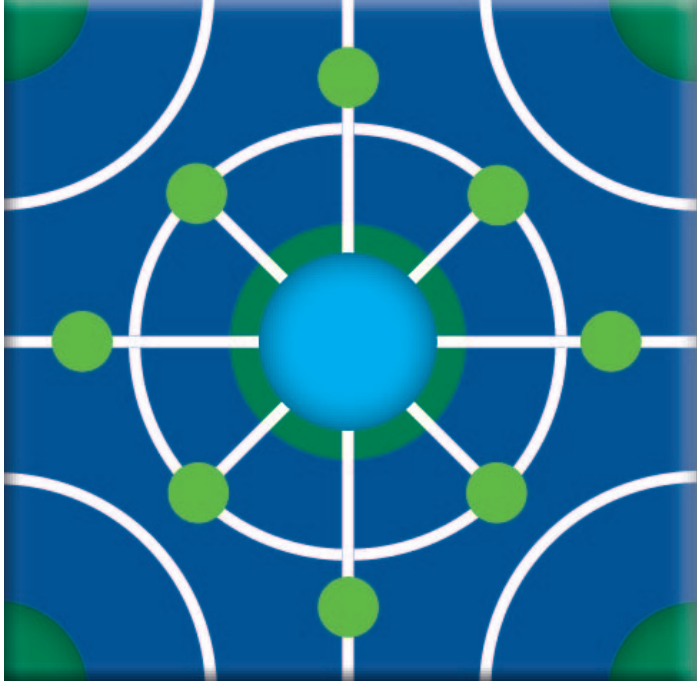


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Prophylaxis in Hemophilia A Patients with Inhibitors

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Introduction

After exposure to FVIII, alloantibodies that neutralize FVIII clotting function develop in approximately 30% of patients with severe hemophilia A. Although most patients with inhibitors do not bleed more frequently than patients without inhibitors, hemorrhagic complications are severe, bleeding is more difficult to control and patients have higher morbidity and mortality.

Prophylaxis treatment is the standard of care for patients who have severe hemophilia A without inhibitors, and its benefits could be extended to inhibitor patients.

Methods

We reviewed the medical records of three adults with severe hemophilia A with inhibitors on prophylactic treatment with activated prothrombin complex concentrate (aPCC) at our center.

Our aim was to measure the efficacy of prophylactic treatment by demonstrating a significant reduction in all bleeding events during a period of prophylaxis compared to the previous on-demand period. The quality of life (QoL) of our patients was also assessed by their ability to participate in normal daily activities.

Results

32 year old patient, high responder, usually receiving on-demand treatment with either aPCC or recombinant FVIIa. Prophylaxis with aPCC (70 IU/Kg BIW) was started in 2008, after five consecutive severe muscle bleeds led to hospitalization. In the prophylactic period the bleeding events reduced by 80% without any hospitalizations or emergency room visits. The improvement in patient QoL was significant resulting in the restoration of his normal daily activities.

PATIENT 1

45 year old patient, high responder, usually receiving on-demand treatment with either aPCC or recombinant FVIIa. Prophylaxis with aPCC (50-60 IU/Kg BIW) was started after a life-threatening intra-abdominal bleed in 2006. On prophylaxis, the observed reduction in overall bleeding events was 43%. This patient also had a significant improvement in his QoL, with reduced absence from work.

PATIENT 2

50 year old patient, high responder, with a bleeding pseudotumor in the right tibia. Taking a conservative approach to this complication, prophylaxis with aPCC (55 IU/Kg BIW) was started in 2012 after failed ITI. In this setting, the patient remained asymptomatic with no further bleeds. There was no change in the frequency of all other bleeds.

PATIENT 3

Conclusion

Prophylaxis in inhibitor patients was first described in the mid 1970s. Emerging data from clinical trials suggests that all bleeding episodes, joint bleeds in particular, can be significantly reduced in many patients with inhibitors through the regular use of bypassing agents (BPA). In our center there are three patients under secondary prophylaxis with BPA. These patients began prophylaxis with aPCC after severe and recurrent bleeds, including life-threatening episodes.

The most striking findings over the last six years of experience with BPA are the absence of life-threatening bleeding episodes and reduced inpatient stays or emergency room visits, as well as significant improvement in quality of life. One patient also experienced a significant reduction in frequency of all bleeds.

Our study indicates that aPCC prophylaxis at a dose of 50-70 UI/Kg administered on 2 non-consecutive days a week decreases life-threatening bleeds and may decrease overall bleeding. No adverse effects were detected.

Regarding our actual economic constraints, one may say that the cost of BPA can be a real limitation. But the potential benefits of avoiding hospitalizations and days lost from school or work, and the prevention of long term complications, make this treatment a real option.

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