Provider Panel: Navigating Current Therapies

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Understanding Current Therapies

Dr. Salley Pels – Director of RI Hemostasis and Thrombosis Center

Current Hemophilia Prophylaxis Therapy Strategies

Effect on Hemostasis

- Factor – fluctuating hemostasis from normal to a severe hemophilia state of bleeding
- EHL – slower fluctuations from normal to mild bleeding state
- Non-Factor Therapies – maintains stable hemostasis at level of mild hemophilia

What are they?

- Factor Products - Replace what's missing
  - Human plasma derived
  - Recombinant – several generations over the years

- Extended half-life - Longer lasting in blood, less frequent dosing
  - Modified to decrease processing and degradation thus lasting longer in the blood – less fluctuation in hemostasis
  - Longer protection with less frequent dosing

- Non-Factor Therapy – emicizumab (Hemlibra)
  - Antibody that helps to bring coagulation factors together to promote clotting
  - Subcutanous admininistration (under the skin) - easier way of administering
  - Maintains stable hemostasis

Advantages/Disadvantages

- Standard Half-life Factor
  - Pros
    - Standard of care for decades
    - Well studied – we know how to use them to reasonable maintain factor levels and prevent recurrent bleeding episodes
  - Cons
    - IV admininistration – challenging for those with veinous access issues (young children or later in life) and may require need for intravenous access device or port-a-cath which may require surgery, are at risk for infection, clots
    - Not sustained, requires regular dosing
    - Inhibitor development risk – requires further intervention

- Extended Half-Life
  - Pros
    - Fewer infusions
    - Considered improvement on standard of care
  - Cons
    - Requires IV administration – same challenges as standard factor products
    - Still requires regular dosing, some people respond better than others
    - Inhibitor development still a risk

- Non-factor: Bispecific Antibody
  - Pros
    - Subcutaneous administration
    - Dosing every 1-4 weeks
    - Works despite inhibitor status
    - Keeps hemostasis in the mild hemophilia status
  - Cons
    - Available only for Hemophilia A patients
    - Interferes with lab testing – cannot measure factor levels
    - Provider unfamiliarity – ER doctors need further education on this product, how it works and how it will impact lab results
    - Potential thrombosis risk primarily for those with inhibitors using a by-passing agent (ex: FEIBA)
    - Still need factor for bleeds, injuries, surgeries

Questions to consider

- Remember that each individual patient has specific needs and must be considered on an individual basis
- Please discuss treatment options with your provider to determine what is best for you

  - Is this therapy safe?
    - Current products are documented to be safe
    - We know how they work, how to administer, and how to keep patients safe
    - An important question as emerging therapies continue to develop

  - Will this therapy be easier to take or give?
    - IV administration more challenging, while subcutaneous administration is easier
    - We still need to ask if there are other things to consider when making this choice

  - How often will I need to take this therapy?
    - Based on therapy as well as individual condition
    - Standard half-life products are given more often
    - EHL products are given potentially less often
    - Non-factor therapy given in largest intervals

- Will this therapy allow me to avoid spontaneous bleeding but also have an active lifestyle?
  - Very important as goal is to have a healthy and active life with as few bleeds as possible
  - Need to make sure protection is sufficient for activities
  - A therapy may work better for one patient and not another
  - Discuss goal of care with provider

- Does my body need factor for other reasons?
  - Role of FVIII in long term bone health – what happens long term if you are not getting FVIII
  - If you are very active or at higher risk for bleeding, you will need therapy

- Will therapy choice affect my ability to pursue other therapies in the future?
  - Inhibitor patients and daily therapy to suppress – how will non-factor affect future choices such as gene therapy
  - Think about your long term goals and be sure to discuss with provider as you are considering new therapy options

Q&A with attendees

Q - Have there been issues identified when using standard factor therapy for trauma or breakthrough and a long-acting therapy for prophylaxis – is there the potential for a thrombotic event?

A - When dosing, must consider last dose of prophy product when injury takes place before dosing with standard half -life product. As physicians, we want a sense of what factor levels might be based on what you are taking and when you last infused. It is recommended to contact HTC to confirm correct dose. It is generally recommended not to give repeated high doses without speaking to your doctor.

Q – Is the rate of patients developing an inhibitor the same for standard vs. EHL products?

A - No new large study comparing products since SIPPET, but no significant spike identified since the emergence of EHL products. Remember there are numerous factors to consider with inhibitor development and physicians are keeping an eye on this.

Q – If you have history of clot formation in past – higher risk on Hemlibra?

A - Depends on situation in which clot occurred – need complete picture.

NEW ENGLAND HEMOPHILIA ASSOCIATION

Serving the Bleeding Disorders Community Since 1957

Establishing a Healthy Relationship with Your Provider

Emily Bisson, *CPNP-PC* – Associate Director of CT Children's Hemostatis and Thrombsis Center

- Collaborating with your HTC Team
  - We are your partners in your journey living with a bleeding disorder
  - Strong partnerships involve two-way communication
    - We often go long periods of time without contact with our patients, but always thinking of our patients. We want to hear from you!
    - We can help you best when we know you and your goals! Individualizing a treatment plan requires your provider to understand your: lifestyle, bleeding disorder history, health concerns, other medical history, and goals
  - Please share what is working and what's not about your current therapy
  - Provide updates on lifestyle changes – new job, new sports/fitness regimen, moving, college, etc. These will all impact our treatment plan.
  - Keep HTC team in the loop
    - Consider us primary source for BD healthcare info – we are also trying to understand how the newer meds work and what might work better for you
    - Community support is an excellent resource, but we know your full history and have knowledge and understanding others may not
    - New treatment regimens require new treatment strategies
      - Management of bleeding and injuries is evolving – no longer just treat early and often
      - Collaborate with your HTC team for individualized recommendations
  - Interested in a specific new treatment option? Please ask!
    - With so many new developments, it can be challenging for providers to review them all in a single visit – let us know what you are thinking!
    - Programs like NEHA's Consumer Medical Symposium or FallFest offer an excellent overview of new and future treatment options in an unbiased way

- Connecting for Collaboration
  - CALL your HTC for urgent matters – save important #'s in your phone
    - Bleeds or injuries
    - Urgent procedures or surgery
  - Utilize online Patient Portal
    - Communicate directly with team regarding tests results, questions, and non-urgent needs
    - Secure, convenient, even allows photos
  - New options for TeleHealth offers increased convenience for many visits
  - Share questions or concerns you may want to discuss on a pre-clinic appointment screening call so that we can come to appointment more prepared to help you!

Q&A with attendees

Q – What do you do when provider is pressuring you to switch to a new product and you're not ready?

A – Acknowledge this to your provider – be honest and share why/what's going on? What questions do you have? What did you hear? Provider makes suggestion to switch to get you the best care we think you deserve but change can be hard and we want to help.

Navigating ER Situations
Dr. Jeremy Madrid – Pediatric Director Hemostatis Center at Dartmouth Hitchcock Medical Center

- Emergency Planning
  - ER planning vs clinic follow up
    Recently with different products and keeping kids at home more frequently has resulted in fewer ER visits. Sometimes there is confusion of when someone needs to be seen in ER vs clinic.
  - Emergency Planning
    - We are never bothered by questions – its our job to help you navigate these questions
    - Trauma of particular concern: head and spinal chord, oral bleeds – throat/tongue, GI bleeds, large muscle bleeds, eye, deep lacerations
    - Keep cool pack in the fridge and freezer
    - Have factor and supplies ready to go for an emergency
    - Be an advocate! BD treatment can be scary for providers who don't treat bleeding disorders on a regular basis – we can contact local ER to help guide them ahead of your arrival.
    - Keep/store important phone numbers – also store medical info in phones, medical IDs
    - Keep infusion log – can be helpful to provider when a bleed is not resolving; also important for insurance purposes
    - Bleeding/Emergency letter – important to keep this updated – another way to educate your ER providers and your hematologist can help talk through it with ER; tell provider to treat first, then image
    - Specific type of bleeding disorder – mentioning this will catch the attention of the ER provider
    - Basic treatment guidelines/prophylaxis – we can help ER physicians make these decisions
    - HTC contact information
  - COVID-19
    - Are individuals with blood disorders at a higher risk?
      Answer: Not necessarily, but individuals on immunosuppressants for inhibitors is cause for concern
    - What extra pre-cautions should be taken?
      Answer: Can be state specific, but follow the advice of your provider.

- Social Media/Online Support
  - Great way to reach out to community, especially now
  - Contact your HTC with concerns – your treatment is specific to you, so what works for one patient may not work for another

Q&A with attendees

Q - Lots of patients diagnosing others in online support groups –as a new parent, how do I navigate what my doctor vs the community advises?

A – This is difficult to navigate as we are all in search of support. While it can be useful to hear what others are going through, please communicate with your provider for further clarification. Pediatrics is very collegial – we want the best for your child, and we will ask others for opinions. Final advice – appreciate input from a community group, but if there is a disconnect between medical provider and community, be sure to reach out to doctor and ask more questions.

Telehealth
Sheila O'Donnell, *APRN-FNP* – Nurse Practitioner at Maine Hemostasis and Thrombosis Center

- A year ago faced with question of how would we accomplish patient care and conversations about product changes, safety, choice, maintaining patient/provider relationship, emergency visits

- Able to bring all comprehensive clinics online – all disciplines included (provider, nurses, social work, research). There is no replacement for face-to-face. Bleed triage is best done in person and very challenging online, but we are all doing our best. Patients love the option, particularly in Maine where patients may travel long distances to come to clinic. This is only hindered by tech challenges and the internet in more remote areas of the state. Going forward, we expect a hybrid system to allow for both in person and remote visits. We have much more flexibility with telehealth because clinic is always open M-F 8-4:30 so we can accommodate more people without worrying about space. There are also fewer scheduling conflicts.

- Would love feedback from the patient perspective about how telehealth visits went and if their needs were met.

- Day of appointment – patient receives morning call to make sure internet connection is working. Nurse calls 15 minutes in advance with some questions and then providers take turns from the waiting room visiting with the patient.

Q&A with attendees

Q - How is insurance doing with paying for telehealth? Will they allow it to continue?

A – Due to the COVID state of emergency, our experience in Maine has been that Medicare and private insurers (as far as we know) are reimbursing Telehealth at the same rate as an in-person visits currently (as long as there is adequate documentation). But, this will be changing in the near future where Medicare (and likely private insurers) begin reimbursing Telehealth at a lower rate.

Q – I had an awkward telehealth visit – any advice?

A – More information would be helpful, but:

- Going forward, providers should consider the process to all for more privacy and 1:1 conversation with a teenager.
- Visit is not with entire healthcare team at once to try to make it less overwhelming.
- We know it's not the same as in person and would love feedback on how we can improve your experience.

Q - Still have to go to clinic for bloodwork – how can I take more proactive approach to be sure I'm on the same page for the study being performed and when I should be infusing prior to the visit?

A - Contact the clinic and we will advise you.

Q&A Forum

Q – Regarding Stimate – What is going on with this and when will patients get it?

- Dr. Pels – Stimate (DDAVP) recalled nationwide last summer and the company cannot make it in the foreseeable future. There is an IV formulation used in the hospital setting or clinic but we don't send it home with patients. Alternatives include Amicar, or other anti-fibrinolytics tranexamic acid used in its place for mucosal bleeding.

- Dr. Madrid – Providers are aware of how important this medication is to keeping kids safe at home and we will definitely follow up with you when we have any information.

- CSL Behring Med Affairs (800) 504-5434 if you have additional questions

Q – Regarding recent new information that has come out on vWD testing, has anything changed on research and therapy side of things?

- Emily Bisson – The guidelines (testing and evaluation) are very helpful, but no significant changes to treatment recommendations were made. In terms of research questions, there are still many unanswered questions in terms of levels (genotype) versus bleeding symptoms (phenotype). American Thrombosis and Hemostasis Network (ATHN) study to collect more data to guide vWD treatment. Dr. Croteau also mentioned new treatments that may be useful for certain subtypes.

- Dr. Pels – The updated guidance supports what we are already doing and made important points about prophylaxis but does not significantly change what we are doing for our patients now. Helpful for how different subtypes can be managed.

- Dr. Madrid – vWD is so interesting to show variability in bleeding disorders, even within same diagnosis. Bleeding patterns can vary so much, changing the treatment plan from one individual to the next.

Q - Could some of the new treatments be used for the rare factor deficiencies?

- Dr. Madrid – Providers must work collaboratively to accomplish cessation of bleeding in all BD patients. We can absolutely learn something and there may be off-label uses for current products and rare disorders. We must be transparent with patients that there is no clear indication and we are weighing risks/benefits.

- Dr. Pels – Exciting time right now because of current therapeutics, but rebalancing therapies and gene therapy and the science behind them will hopefully expand treatment possibilities for all sorts of disorders.

Q – What are some good resources to learn more about subtypes of vWD?

- Dr. Pels - NHF website, Institutional websites. Be careful where you get your information! Choose reputable organizations and institutions

Q – Any evidence that Hemlibra has a negative impact on bone density?

- Dr. Pels – There is no direct evidence about Hemlibra. FVIII is believed to play a role in bone health and we are still learning about how it might be impacted if patients are not receiving factor.