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Technical issues of starting prohylaxis in children with hemophilia – an international survey on when, why and how we start (pilot study)

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Background: While the benefits of prophylaxis for patients with hemophilia (PWH) are undisputable, there is a discussion about when to start prophlyaxis. Further, there are technical issues raised by prophylaxis such as venous access, the use of central venous access devices (CVAD) and possible complications (e.g. infections, inhibitor development triggered by CVAD-implantation).

Aim: To collect data on the start of prophylaxis in PWH, including the use of CVAD and the protocols to use such devices. As a pilot study, this survey focused especially to identify areas, in which more detailed data must be collected in future studies.

Methods: Survey among the members of the Global Emerging Hemophilia Expert Panel (GEHEP). GEHEP is a discussion forum for hemophilia doctors funded by Bayer Healthcare. Eight of the participating centres treat pediatric patients, representing smaller and bigger centres around the world.
Data were collected by using a web-based survey (www. surveymonkey.com).

Results: GEHEP members care for 425 pediatric PWH, among whom 245 have severe hemophilia A (Figure 1). Diagnosis was established within the first year of life in 80% (Figure 2). Reason for diagnosis was in 43% a positive family history (Figure 3). Whether or not genetic analysis was carried out was highly dependent on the country, with most patients in Europe undergoing genetic testing but less patients in the US.

Prophylaxis was started in 4 centres before and in 4 after the first joint bleed with a dose between 20 U/kg BW once per week to 50 U/kg BW 3 times per week. 6/8 centres use a dose escalation scheme, however, doses and frequency differed between the centres. Also, the person who does the injections at the start of prophylaxis differed between nurses and physicians.
It was the aim of all centres to train the parents to allow home treatment.

Peripheral venous access is preferred by all centres, but while some centres use CVAD only for immune tolerance induction, some centres use CVAD in up to 50% for regular prophylaxis (Table 1). This was also dependent on the catchment area of the centres, ranging between rather compact cities to large rural areas. Most centres use port-a-caths, only 2 Broviac catheters. Arteriovenous fistulae are used in 2 European centres.

When CVAD are placed, the measures applied to avoid complications such as infections differ (e.g. different antiseptics used). However, not all centres do follow a standardized protocol. An example of the Munich SOP is given in table 2. An analysis of the complications encountered is currently ongoing.

In general, the decision when and how to start prophylaxis is made on individual considerations, which makes comparison of studies difficult.

Conclusion: When and how to start prophylaxis depends on individual decisions for each patient but also on local preferences. This makes the conduction of controlled studies difficult. The use of registries and cohort studies could help to identify treatment related risk-factors. To allow comparison, the exact circumstances on why, how and when prophylaxis was started should be documented. This does also apply to the use of CVAD, since every centre uses its own protocols due to the lack of widely accepted guidelines. The development and evaluation of such guidelines is desirable.

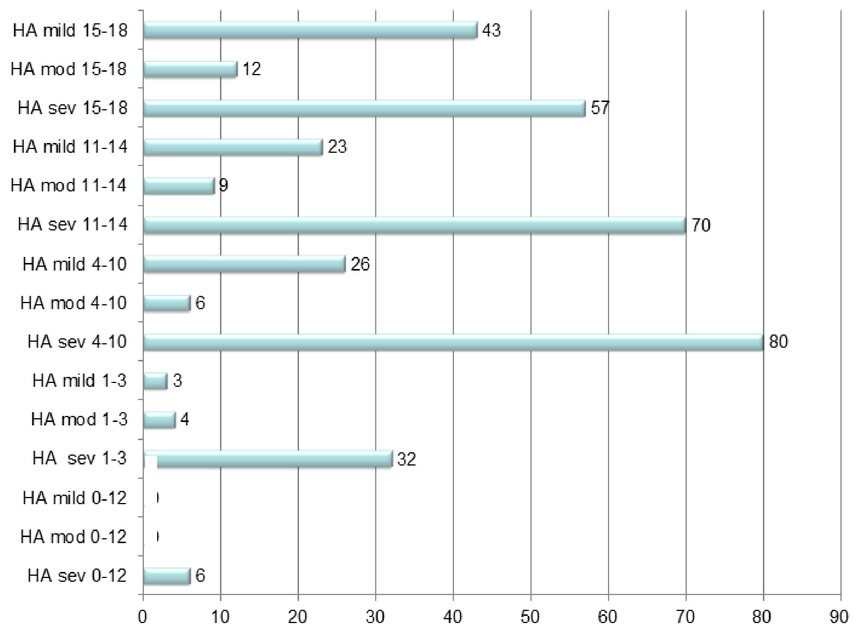

Fig 1: Age groups of children with hemophilia A at time of survey

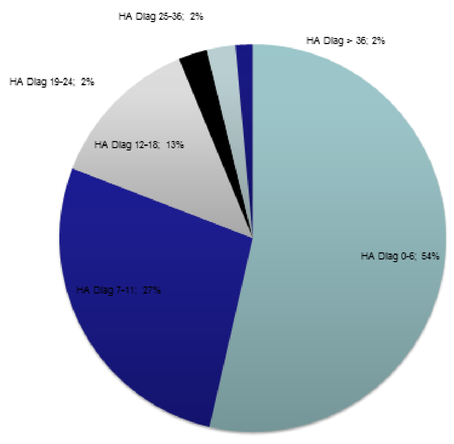

Fig 2: Age at diagnosis of hemophilia A (months)

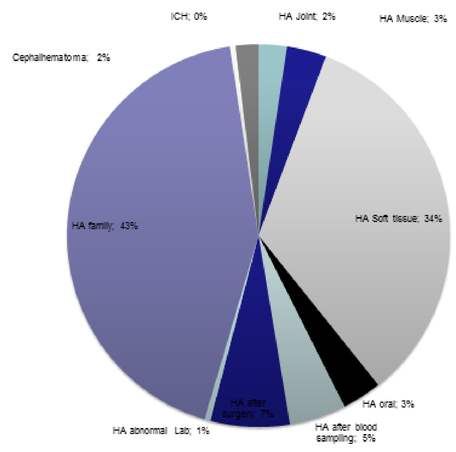

Fig 3: Reasons for diagnosis

All centres prefer peripheral venous access
8 centres use port-a-caths if necessary
2 centres also use Broviac catheters
2 centers also use AV fistulae

Necessity of CVAD in the first 2 years:
in most centres only for immune tolerance induction,
in some centres only in individual patients,
in some centres in up to 50%.

Table 1: General remarks on venous access

Factor substitution:

- Wash hands, use antiseptic
- If cough / rhinitis: use surgical mask
- Prepare everything you need on a sterile cloth (empty 2 ml syringe, NaCl 0.9% syringes à 5 ml and 20 ml, heparin syringes (200 ml / 2 ml), factor concentrate,gauze swabs, Tegaderm, sterile gloves)
- Fill Port-A-Cath Needle sterile with NaCl 0.9%. Close clipper
- Clean skin above Port-A-Cath three times with skin antiseptic (octenidine (Octenisept®) or 2-propanol (Cutasept®))
- Put on sterile gloves
- Insert needle in Port-A-Cath. Use only special Port-needles!
- Open clipper, remove old heparin-block (2ml), close clipper
- Open clipper, inject factor concentrate, close clipper
- Open clipper, inject 20 ml NaCL 0.9%; close clipper
- Open clipper, inject heparin-block (200 U / 2ml), close clipper
- Remove Port-needle, compress puncture site for 3 minutes with sterile gauze

Multiple punctures:
If the Port-A-Cath is used for the substitution of recombinant activated factor VII every 2-3 hours replace needle once a day. Otherwise do not leave the needle in place.

Urokinase:
10.000 U – 25.000 U Urokinase are applied every 10 days to the Port-A-Cath. Remove after 30 minutes.

Table 2: Example of the Munich protocol "How to use a Port-A-Cath-System"

Further reading:

Haemophilia care in children–benefits of early prophylaxis for inhibitor prevention.
Mancuso ME, et al. Haemophilia. 2009 Jan;15 Suppl 1:8-14. Review.
Overview of the use of implantable venous access devices in the management of children with inherited bleeding disorders.
Komvilaisak P, et al. Haemophilia. 2006 Dec;12 Suppl 6:87-93. Review.
How to start prophylaxis.
Petrini P. Haemophilia. 2003 May;9 Suppl 1:83-5; discussion 86-7.

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Acknowledgement: GEHEP is funded and supported by Bayer HealthCare

DOI: 10.3252/pso.eu.WFH2012.2012