Twelve years ago, in the year 2000, the Swiss Haemophilia Society set the base of the IT concept for the Swiss Haemophilia Registry. Since 2004 the Registry runs on the actual internet platform with double password security. In 2012, the whole Registry database moved from a local to the HIN (Health Info Net) server in order to significantly improve data security, management and controlling. Data access is secured by double password and continuous monitoring of the access to the database. The latest records from October 31st 2012 are presented here.

Patients
A total number of 967 patients (compared to 950 in 2011) were included in the Registry, corresponding to a plus of 2%. This small increase was mainly due to the inclusion of more patients with other coagulo-
pathies than haemophilia or von Willebrand disease (VWD): 88 vs. 70 in the forthcoming year. We included now all patients with a clinically significant haemorrhagic diathesis, independently from the factor level. As during the former years, incidence and prevalence of haemophilia in Switzerland remained stable.

In 2012, there were no newborns newly diagnosed with haemophilia A or B. Swiss people with haemophilia are slowly but consistently ageing, with an average age of 42.1 years, compared to 40 years in 2009 and 37 years in 2006.

39 patients (compared to 43 in 2011) could not be assigned to a specific center and were excluded for this evaluation.

**Type of haemophilia, other rare coagulation disorder**

Generally speaking, the distribution of the registered coagulopathies has not changed over the years and is shown (Fig. 1a): haemophilia A 587 (63%), haemophilia B 117 (12.5%), von Willebrand disease 136 (15%), other coagulopathies 88 (9.5%), including deficiencies concerning:

- a- or dysfibrinogenaemia (n = 18)
- factor V (n = 1)
- factor VII (n = 29)
- factor X (n = 4)
- factor XI (n = 18)
- factor XIII (n = 14)
- combined factor V/VIII (n = 4)

Changing the registration criterion from "a factor level < 10%" to "a clinically significant bleeding disorder" (i.e. needing perioperative or incidental substitution), we could add 7 patients with dysfibrinogenaemia, 1 patient with FV and 10 patients with FXI deficiency.

**Disease severity**

Disease severity was classified according to the ISTH standards (1):

- severe haemophilia A/B < 1%,
- moderate 1–5%, and
- mild 6–40%.

The corresponding results are shown (Fig. 1b):

- haemophilia A patients:
  - severe 210 (36%),
  - moderate 111 (19%),
  - mild 236 (40%);
- haemophilia B patients:
  - severe 33 (28%),
  - moderate 35 (30%),
  - mild 34 (29%).

Data were missing in 30 (5%) patients with haemophilia A and 15 (13%) with haemophilia B.

**Inhibitor status**

High responding inhibitors were present in 8 patients (7 with severe haemophilia A and 1 with severe haemophilia B) and low responding inhibitors in 8 patients, all with haemophilia A (4 severe and 4 mild). However, the numbers remained not fully representative, as data on inhibitor status were still missing in 125 patients (2010–2011: 131). Taking the low and stable usage of bypassing agents into account, we assume...
that at least the number of patients with high titer inhibitors is correct.

**Haemophilia therapy**

Data on treatment types are shown (▶Fig. 2): In Switzerland overall, “on-demand” treatment still largely exceeds “prophylaxis” for both haemophilia A and B. In haemophilia A 369 (63%) patients performed on-demand treatment vs. 119 (20%) prophylaxis; the figure in haemophilia B was even more obvious: 78 (67%) on-demand vs. 16 (14%) prophylaxis. Over time however, a progressive shift was observed towards prophylactic treatment, also in adults (data not shown).

Since 3 years now, a new treatment group (sporadic therapy) (2), representing 8% of haemophilia A and 10% of haemophilia B patients, was introduced to describe mainly mild haemophiliacs requiring such a minimal treatment that it cannot be called “on-demand”. It is highly probable that not all concerned patients have already been correctly transferred from the “on-demand” to the “sporadic” group. Treatment status of about 9% of all patients remained unknown.

**Haemophilia centers**

In line with the federalist organization of public health in Switzerland, there are 18 haemophilia reference or treatment centers (▶Fig. 3) in our country for a population of just 8 million inhabitants. The five university hospitals (Geneva, Lausanne, Bern, Basel and Zürich) as well as the cantonal hospitals in Luzern and St. Gallen are acknowledged as reference centers by the Swiss Society of Haemophilia and have both, usually separated, facilities for children/adolescents and adults. The four remaining, somewhat smaller institutions care for children and adults on the same site and are graded as treatment centers because of their smaller patients and staff numbers, as well as a not around the clock running haemostaseology lab. Numbers of persons with haemophilia at the different centers vary a lot, the largest caring for about 200 adults and almost 40 children, the smallest having less than 20 patients of all age groups.

**Mortality statistics**

Death registration represents a small file in the Registry. In the period 1996–2012, a total number of 76 patients have been reported to be dead (▶Fig. 4).

In the 12 months between November 2011 and October 2012, three patients died: one from ischaemic cerebrovascular insult, one from a brain tumour and one from an unknown cause. The last HIV-related death was back in 2003.

**Use of factor concentrates in Swiss patients**

Switzerland had about 7.7 Mio inhabitants at the end of 2011. Table 1 shows the amounts of factor VIII and IX concentrates used in the country over the last 11 years (▶Tab. 1). The amount of factor concentrates (VIII and IX together) rose from 3.77 in 2001 to 5.52 Units per capita (for FVIII only from 3.18 to 4.84) in 2011. These numbers remain low in comparison to those from other Western and Central European countries, especially when taking their GDP’s into account (3). This finding is mainly explained by the low rate of persons with haemophilia under regular factor replacement in our country; with the exception of the age group under 20 years, where 90% of severe haemophilia A and 80% of severe haemophilia B patients are...
under prophylaxis, less than 40% of haemophilia A and about only 20% of haemophilia B patients over the age of 40 are still under this type of therapy (▶Fig. 5).

Over this 11 years observation period, there has been in Switzerland as in other affluent countries a clear-cut rise in the use of recombinant products, especially in haemophilia A. In 2011, they represented about 81% of the whole use of factor VIII in the last 24 months. Owing to the extremely expensive, also for high-income countries like ours. It is of critical importance, both for affected patients and haemophilia disease, which costs begin to be exceeded.

\[ \text{Compliance to the rules set by the Medical Committee is one of the key criteria for the accreditation and re-accreditation/validation of the corresponding Haemophilia Reference or Treatment Center.} \]

Quality control

As mentioned, there are currently 18 centers and 52 authorized users in the registry. All the users are accredited Members of the Medical Committee of the Swiss Haemophilia Society. Since the move of the database towards the HIN (Health Info Net) servers in 2011, history of individual logins as well as quality and regularity of inputs in the Registry have been controlled once a year.

Compliance to the rules set by the Medical Committee is one of the key criteria for the accreditation and re-accreditation/validation of the corresponding Haemophilia Reference or Treatment Center. In 2011–2012, both large and small centers respected the majority of the quality criteria fixed by the Medical Committee in a similar way. One important quality black box found was the fact that, again independently from the center’s size, regular (at least once a year) updates of the Registry data had been often overlooked. In fact only about 50% of all patients registered had had their data being updated during the last 12 months and only about 70% in the last 24 months.

There can be many reasons for such a bad compliance. A critical one is the lack of time of haemophilia treaters, usually overwhelmed with clinical and administrative tasks. In 2013, the Medical Committee will therefore appoint a dedicated haemophilia nurse for visiting the different centers and helping local staffs to complete missing data. First results of this strategy are expected for the end of 2014.

Conclusion

The Haemophilia Registry of the Medical Committee of the Swiss Haemophilia Society is an important tool for quality control of haemophilia care in Switzerland. It is now 12 years old and allows collecting basic clinical data on patients with an orphan disease, which costs begin to be extremely expensive, also for high-income countries like ours. It is of critical importance, both for affected patients and haemophilia specialists, that accurate data on factor consumptions are rapidly available.
For public health authorities and pharmaceutical companies, these numbers are important to correctly plan regular and emergency supplies at a national level.

From 2011, the Registry has also been used for prospective quality control of haemophilia centers and care in Switzerland, putting into light some key deficits, especially the insufficient compliance regarding regular data updates. The Medical Committee decided this year to support haemophilia treaters in this critical but time-consuming task, engaging a dedicated flying nurse who will visit the different centers and help in completing and updating their files in the Registry.

Furthermore, we will expand the spectrum of registered bleeding disorders in the near future, opening registration to severe inherited thrombopathies (a.o. Bernard-Soulier syndrome and thrombasthenia Glanzmann) as well as other rare coagulopathies. For haemophilia A and B, patients’ data are being completed, after obtaining every individual informed consent, with the results of the mutation analysis.

Patients also take direct advantage from the Registry. Their basic clinical data are available online to each haemophilia specialist, independently from its location. In emergency situations, this can be life-saving. On the other hand, they get accurate and up-to-date information on accredited haemophilia centers in their country. The Registry will clearly require continuous support from the Medical Committee and enhanced funding in the coming years to maintain highest quality requirements.

Conflict of interest

The author declares that he has no conflict of interest.

References


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