Subcutaneous Immunoglobulin Therapy
A New Way of Permanent Treatment in Primary Immunodeficiencies

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Indications for Immunoglobulin
Primary Immunodeficiencies

- X-linked Agammaglobulinemia Bruton
- Autosomal-recessive Agammaglobulinemia
- Other Agammaglobulinemias
- Severe combined immunodeficiency (SCID)
- Common variable immunodeficiency (CVID)
- Hyper-IgM-Syndrome
- IgG-Subclass-Deficiencies
History

• 1952 First report of a boy with agammaglobulinemia (Bruton)

Treatment with subcutaneous IgG (SCIG)
AGAMMAGLOBULINEMIA

By Col. Ogden C. Bruton, M.C., U.S.A.
Washington, D.C.

RELATIVE % TOTAL PROTEIN

NORMAL

DAYS AFTER 3.2 gms. (20 cc) GAMMA GLOBULIN
History

• till 1980: intramuscular IgG Substitution (IMIG)

• since 1980: intravenous IgG Substitution (IVIG)
Disadvantages of IVIG

- Hypersensitivity reactions: mild fever, rash, anaphylactic reactions
- Difficult venous access in children
- Administration in hospital or doctor's surgery
- Costs
History

• 1978: SCIG slow (1-3ml/h)
  long infusion time

• 1990: SCIG fast (20+ml/h)
  (Gardulf et al.)
Changing to SCIG

- Patients with prior IVIG:
  start with SCIG 14 days after the last IVIG

- Patients without previous therapy:
  ➔ „filling up“ the empty IgG compartment
    - 3 - 4 times monthly IVIG before SCIG start
    - weekly SCIG-dose on 5 consecutive days
Introduction of SCIG I

- 100–150 mg/kg/week (0.6-0.9 ml/kg/week)
- Start in 1997 (Gammanorm via international pharmacy, first product licensed in Germany in 2003)
- Patient training on at least 4 appointments
- Already 61 patients trained
- Learning under interdisciplinary approach
- Regular infusions with battery-powered pumps into the subcutaneous fat tissue
Introduction of SCIG II

- Simultaneous application on 2 injection sites with 2 pumps:
  - thigh
  - abdomen
  - (upper arm)
- Injection volume: 5 – 10 – (20) ml /site
  - age-related
  - body shape-related
- Infusion rate: 10 – 20 ml / h ;1- 2 x / week
Introduction of SCIG III

• After they have successfully finished the training programme, the patients and/or parents are allowed to do their infusions at home and to take on the responsibility for the therapy.

• Clinical status and IgG levels are controlled every 3-6 months.

• Parents are requested to write down SCIG batch numbers and bring them to the appointments for documentation in the patient chart.
IgG-Biologics

• Already licensed in Germany for SCIG are:
  – Vivaglobin® (ZLB Behring)
  – Subcuvia® (Baxter)
  – Gammanorm® (Octapharma)
    – 16% / 16.5% solution

• Virus inactivation and elimination procedure
Experiences with SCIG in the first 30 patients with Primary B-Cell efficiences

• Observation period: 6.5 years
  11,751 infusions (392/patient)

• Diagnosis:
  9 x XLA
  2 x Hypogammaglobulinemia
  14 x CVID
  5 x others

• Median age: 18.5 years
  (at introduction of SCIG) (range 5 ys – 50 ys)

• Pretreatment with IVIG in 27/30 patients
  median duration 4 years
Reasons for switching to SCIG

• Systemic side effects under IVIG  22%
• Poor venous access  22%
• Request of patient / parents  56%
 Median IgG Trough Levels (mg/dl)

- **Before therapy:** 92 mg/ dl
- **IVIG:** 536 mg/ dl (256 - 871 mg/ dl)
- **SCIG:** 741 mg/ dl (496 - 1.027 mg/ dl)
Number of Hospitalisations / Patient

- Without therapy: 3.1 mean, 2.5 median
- IVIG: 1.2 mean, 1 median
- SCIG: 1.1 mean, 0 median
Need for Antibiotics

- 25 patients with fewer needs of antibiotics
- 5 patients with equal needs
- No patient with a higher need
Side effects

- IVIG: mild 72% / moderate 23% / severe 5%
  - 100% mild side effects (local reactions)
  - 4% moderate side effects (e.g. nausea, headache)
  - no systemic reactions (e.g. fever)
  - no anaphylactic reaction
Patient Preferences

27 patients with IVIG-pretreatment:

n=26 satisfied with SCIG
n=1 no preference
n=0 more satisfied with IVIG
Advantages of SCIG

• prepared solution
• excellent safety
• constant IgG trough levels
• highest possible virus safety
• reduced costs
• independance/personal responsibility
• time saving
• quality of life improved
Disadvantages of SCIG

- More frequent injections with shorter intervals
- More persistent confrontation with chronic illness
- Local reactions
- More involvement of the family
- Exigence of self-infusion