

Abstract

インヒビター除去のための免疫吸着：1980年から1995年までのMalmö-Lundにおける治療の最新情報

Immunoabsorption for removal of inhibitors: update on treatments in Malmö-Lund between 1980 and 1995

C. Freiburghaus, E. Berntorp, M. Ekman, M. Gunnarsson, B. M. Kjellberg and I. M. Nilsson

インヒビターが発生した血友病患者における重篤な出血の治療や手術の実施には重大な問題が伴う。一般的には、止血をコントロールするために一定期間十分な第VIII/IX因子の循環レベルを維持することができれば、最も有効な治療と考えられている。インヒビター除去のためのプロテインAを用いた免疫吸着により、初めのインヒビターの力価が非常に高く補充療法のみでは中和させることができない患者

の治療が進歩した。本論文はMalmöにおいて実施された免疫吸着および止血に関する経験をまとめたものである。10例の患者に計19回の免疫吸着が実施された。そのすべてで、インヒビターを完全に除去、または凝固因子濃縮製剤によって中和できる程度まで低下させることができた。止血レベルは1人を除く全例で5～9日間維持された。この期間は出血を止め、外科的手術での過剰出血を防ぐのに十分であった。

Table 1. Clinical material.

Patient	Treatment	Age (years)	Weight (kg)	Known duration of inhibitor (years)	Historical peak (Miu)
Haemophilia A					
1A	1	17	58	14	> 100
	2	17	58	15	> 100
	3	18	60	16	> 100
	4	21	65	19	> 100
2A	1	27	85	11	> 1000
	2	29	82	13	> 1000
3A	1	6	30	4	> 100
	2	7	38	6	> 100
4A	1	21	65	19	> 300
5A	1	13	45	12	> 100
Haemophilia B					
1B	1	37	49	22	> 10
	2	39	50	24	> 50
2B	1	10	31	5	> 200
	2	11	35	6	> 200
3B	1	13	40	10	> 50
4B	1	5	18	3	> 100
5B	1	5	17	3	> 100
	2	5	17	3	> 100
	3	6	22	4	> 100

Table 2. Immunoabsorption treatment.

Patient	Treatment	Inhibitor start (Miu)	Inhibitor end (Miu)	Processed plasma volume (L)	Length of treatment (days)	Processed vol $\text{kg}^{-1} \text{day}^{-1}$
Haemophilia A						
1A	1	4.7	1.8	5.9	1	102
	2	30	1	6.5	1	112
	3	10	0.7	14.7	2	123
	4	0.9	0.1	10	1	154
2A	1	531	9.2	42.5	5	100
	2	10	0.9	52	6	106
3A	1	11	0	11	2	183
	2	9	0.6	4.8	1	126
4A	1	17	2	19	2	146
5A	1	6	0.1	12	2	133
Haemophilia B						
1B	1	7	1.2	6	2	61
	2	4.5	0.5	4.7	1	94
2B	1	50	2.4		2	
	2	8	0.6	4.8	1	137
3B	1	15	0.1	12.6	2	158
4B	1	10	0	5	2	139
5B	1	30	2	2	1	118
	2	53	0	8	2	235
	3	5	0	5	1	227

Table 3. Haemostatic levels of FVIII/IX following immunoabsorption and the dosage (IU) of FVIII/IX given per day.

Patient	Treatment	Days of haemostasis	FVIII (IU per kg body weight day^{-1})	Range FVIII:C (IU dL^{-1})
Haemophilia A				
1A	1	6	284	2–21–86
	2	8	358	26–50–98
	3	8	249	2–36–88
	4	> 10*	273	1–116
2A	1	1†	1352	5
	2	7	663	26–80–172
3A	1	6	966	5–80–262
	2	8	328	5–80–310
4A	1	5	833	1–10–50
5A	1	6	160	35–107
Haemophilia B				
1B	1	7	169	9–145
	2	> 10*	141	90–100
2B	1	6	161	2–38–45
	2	7	310	23–190
3B	1	5	215	22–111
4B	1	> 10*	94	40–300
5B	1	6	794	100–274
	2	6	664	40–87–400
	3	7	370	40–81–210

*The patients became tolerant. †The patient had not received factor concentrates for a very long period of time, and still had persistently high and stable inhibitor levels, indicating active and highly productive plasma cells.

Table 4. Indication and outcome of treatment.

Patient	Treatment	Indication for treatment	Outcome of treatment	Adverse events
Haemophilia A				
1A	1	Bleeding in right angle + traction of left knee	Bleeding stopped	None
	2	Bleeding in elbow joint + performance of chemical synovectomy	Bleeding stopped, synovectomy without complications	None
	3	Bleeding in left elbow	Bleeding stopped	None
	4	Bleeding in left knee joint + performance of chemical synovectomy	Bleeding stopped, tolerance induced	None
2A	1	Induction of tolerance	Tolerance induction failed	None
	2	Induction of tolerance	Tolerance induction failed	None
3A	1	Bleeding in right knee + haematuria	Bleeding stopped	None
	2	Port-A-Cath insertion	Surgery without complication	None
4A	1	Acute life-threatening abdominal and intestinal bleeding with lung complications	All bleedings stopped	None
5A	1	Traction of left knee + induction of tolerance	Tolerance induction failed	1*
Haemophilia B				
1B	1	Prophylactic treatment prior to surgery of large pseudotumour in elbow	Surgery without excess bleeding, wound healed without delay	None
	2	Prophylactic treatment prior to dental surgery and removal of infected bone cysts in all four quadrants	Surgery without excess bleeding, wounds healed without delay, tolerance induced	None
2B	1	Traction of left knee joint	Traction performed without bleeding	None
	2	Severe acute head bleeding with increasing obstruction of the respiratory tract	All bleeding stopped	None
3B	1	Bleeding in ileopsoas	Bleeding stopped	2‡
4B	1	Bleeding in right ankle + induction of tolerance	Tolerance induced and bleeding in right ankle stopped	None
5B	1	Induction of tolerance	Tolerance induction failed	3‡
	2	Induction of tolerance	Tolerance induction failed	None
	3	Induction of tolerance	Tolerance induction failed	None

*Septicaemia and complications with isoagglutinins in AHF. †Thrombotic heart complications caused by infusion of FIX. ‡Complications on placing needles, leading to compartment syndrome. Surgery performed successively during period of haemostasis following immunoadsorption.