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Passive HIV-hyperimmunoglobulin therapy in paediatric AIDS

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Sir: Until now there is no experience with passive HIV hyperimmunoglobulin therapy in paediatric AIDS. Referring to the data of Levy et al. [3] we would like to present our experience with a special HIV hyperimmunoglobulin (HIVIG). Plasma for this hyperimmunoglobulin was pooled from different asymptomatic donors to provide a heterogeneous variety of HIV-neutralizing antibodies. This preparation was virus inactivated with β-propiolactone and UV, showed a 100% inhibition in a HIV 1 neutralization test of 1:10–1:100 dilution and in HIV 1 western blot analysis was specific for p 16, 24, 32, 39, 51, 55, 66, gp 41 and gp 120. Three paediatric AIDS patients (two vertically infected, aged 6 and 7 years; one haemophiliac infected by clotting factor concentrates, aged 16 years) with CD 4 cell counts under 50 cells/μl had been treated with polyvalent immunoglobulins and maximum tolerated doses of Zidovudine for 3–4 years according to our graduated therapy concept [1]. They were considered as Zidovudine resistant and "burnt out". All of them were highly HIV p24 antigen positive, displayed a progressive disappearance of western blot bands and subfebrile temperatures. HIVIG was given at a dosage of 250 mg/kg body weight twice a week for a duration of 9–18 months. HIV P24 antigen, western blot analysis and virus culture tests were done prior to and after HIVIG administration. The use of human subjects was in accordance with the ethical standards of the human subject protection committee of our institution.

As a result, p24 antigenaemia disappeared, subfebrile temperatures normalized and physical powers were regained despite no significant change in CD 4 cell counts [4]. We observed a reappearance of a broad range of antibodies in the western blot profile of each patient and a transient delayed propagation of HIV1 in lymphocyte culture for 9–13 days (Table 1–2). This delayed propagation was not seen with a dosage of 250 mg/kg body weight once a week (Table 3). In the haemophiliac, lymphocyte stimulation due to SAC and CD3 mitogens improved under HIV immunoglobulins about two to four fold respectively. The efficacy in delaying propagation in virus culture was temporary for 50–100 days (Table 1, 2), p24 antigen negativity persisted.

Patient 1 died because of cardiac failure, the haemophiliac and patient 3 died due to intestinal cryptosporidiosis and CMV myelitis respectively [2]. They survived as "burnt out patients" 24, 26 and 36 months, respectively, after initiation of HIVIG therapy.

In conclusion, HIV immunoglobulins had a temporary clinical benefit in paediatric full blown AIDS patients. We had also hints of a dose dependent reduction of the viral burden. More studies with HIVIG in paediatric AIDS patients and less severe immunocompromised HIV infected children are necessary.

References

1. Güngör T, Funk M, Linde R, Kynast I, Allendorf A, Lotz C, Ehrenforth S, Hofmann D, Kornhuber B, Kreuz W (1993) Combined therapy in human immunodeficiency virus-infected children – a 4-year experience. Eur J Pediatr 152:650–654
2. Güngör T, Funk M, Linde R, Jacobi G, Horn M, Kreuz W ((1993) Cytomegalovirus myelitis in perinatally acquired HIV. Arch Dis Child 68:399–401
3. Levy J, Youvan T, Lee ML, and the Passive Hyperimmune Therapy Study Group (1994) Passive hyperimmune plasma therapy in the treatment of acquired immunodeciency syndrome: results of a 12-month multicenter double-blind controlled trial. Blood 84:2130–2135
4. Linde R, Mentzer D, Beeg T, Funk M, Güngör T, Ehrenforth S, Klarmann D, Rübsamen-Waigmann H, Doerr HW, Kreuz W (1992) HIV-immunoglobulin in paediatric AIDS. VIII. Internal Conference on AIDS, Amsterdam, 19–24 Jul, Pob 3703

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Table 1 Delayed HIV propagation time in virus culture in patient 1 with vertically acquired HIV infection under HIVIG therapy (250 mg/kg body weight/twice a week). Persistent negativity of HIV p24 levels.

Culture for HIV			
Days before (–) and after onset of HIVIG	Results in cell culture	Propagation time (days)	p24 antigen
–88	Positive	15	Positive
41	Positive	27	Negative
68	Positive	28	Negative
133	Positive	15	Negative
302	Positive	10	Negative

Table 2 Delayed HIV propagation time in virus culture in patient 2 with horizontally acquired HIV infection (haemophilia A) under HIVIG therapy (250 mg/kg bw/twice a week). Persistent negativity of HIV p24 levels.

Culture for HIV			
Days before (–) and after onset of HIVIG	Results in cell culture	Propagation time (days)	p24 antigen
–253	Positive	11	Positive
–155	Positive	09	Positive
– 66	Positive	15	Positive
01	Negative	–	Negative
26	Positive	24	Negative
53	Positive	16	Negative
98	Positive	15	Negative

Table 3 HIV propagation time in virus culture was not influenced by "low dose" HIVIG (250 mg/kg bw/once a week) in patient 3 with vertically acquired HIV infection. Nevertheless, HIV p24 antigen became negative

Culture for HIV			
Days before (–) and after onset of HIVIG	Results in cell culture	Propagation time (days)	p24 antigen
–131	Positive	30	Positive
– 65	Positive	21	Positive
0	Positive	17	Positive
22	Positive	14	Negative