Adaptation in hemophilia A patients during long term prophylactic

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Background

Therapy of pdFVIII concentrates is one of the most effective and commonly used treatment in hemophilia A patients. Yet there are no data if long term prophylactic treatment can cause any adaptation in patients. We monitored a group of patients with severe hemophilia A to answer this question.

Conclutions

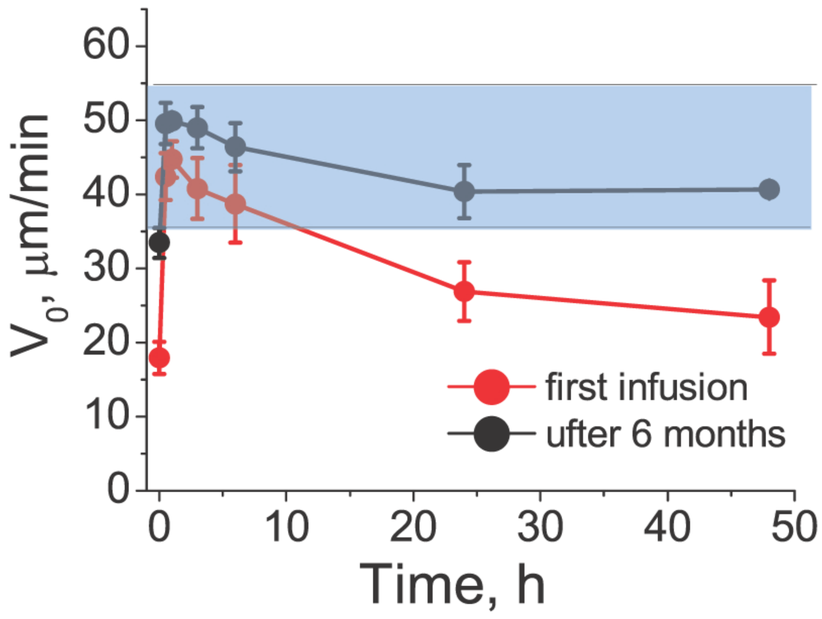
Long term prophylactic treatment using 50 IU/ kg of pdFVIII concentrate in severe hemophilia A patients did not have any negative side effects, but increased time period of hemostasis normalization. The Thrombodynamics assay monitors changes in the bleeding state of patients.

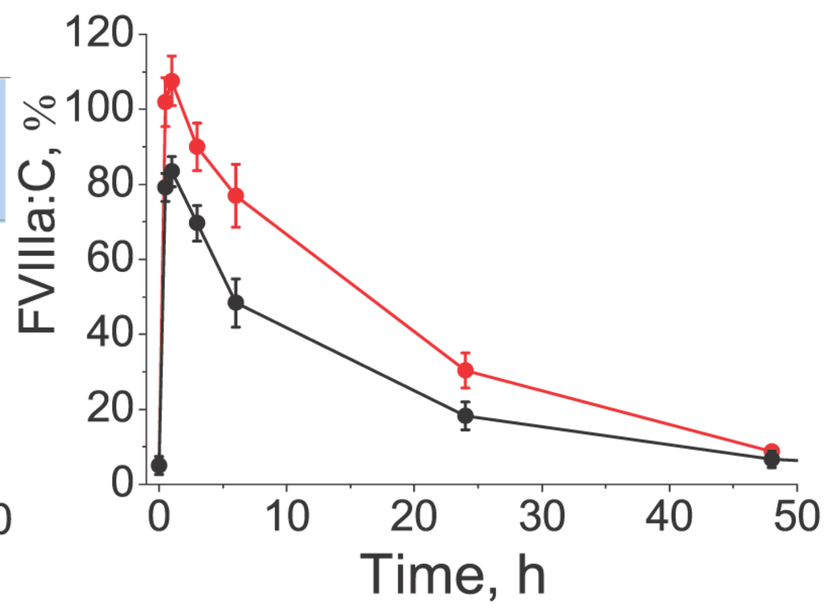
Results

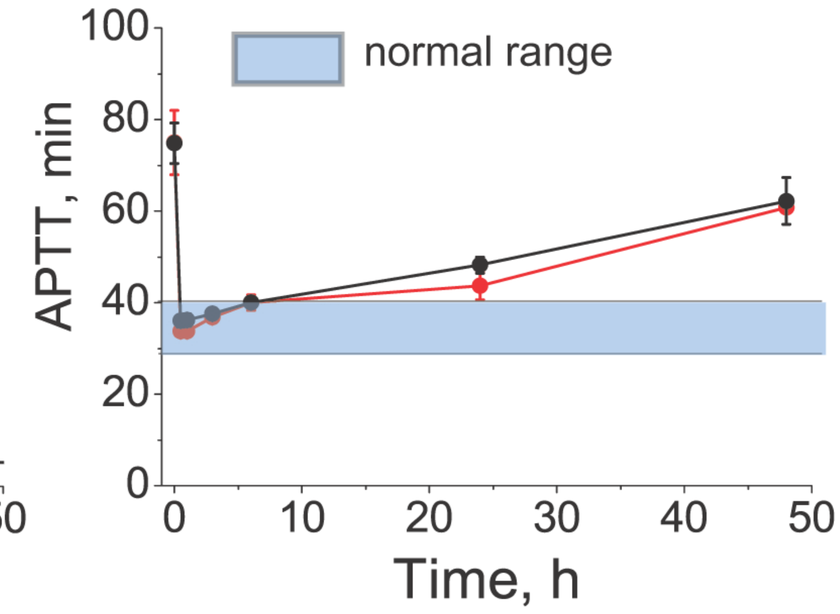
After 6 month of continuous prophylactic therapy of 50 IU/kg pdFVIII the period after pdFVIII infusion when TDx was normalized increased from 14 up to 54 hours, and amount of bleedings decreased from 1-2 down to 0 per month. Yet only the peak level of FVIII after administration decreased from 108% down to 84% and APTT pharmacodynamics did not change. Data for 5 patients (mean±SE) are shown in the Figure.

Parameter	First infusion of 50 IU/kg FVIII, mean±SD	After 6 months of FVIII infusion, mean±SD	Difference, P
FVIII $T_{1/2}$*, h	18±10	10±4	0.3
TDx T_h**, h	14±11	54±22	0.036
APPT T_h**, h	6±4	6±5	1
Bleeding, case per mounth	1-2	0	0.007

*$T_{1/2}$ – half-life time
**T_h – time after administration, when normal coagulation cannot be supported any longer and hypocoagulation starts.







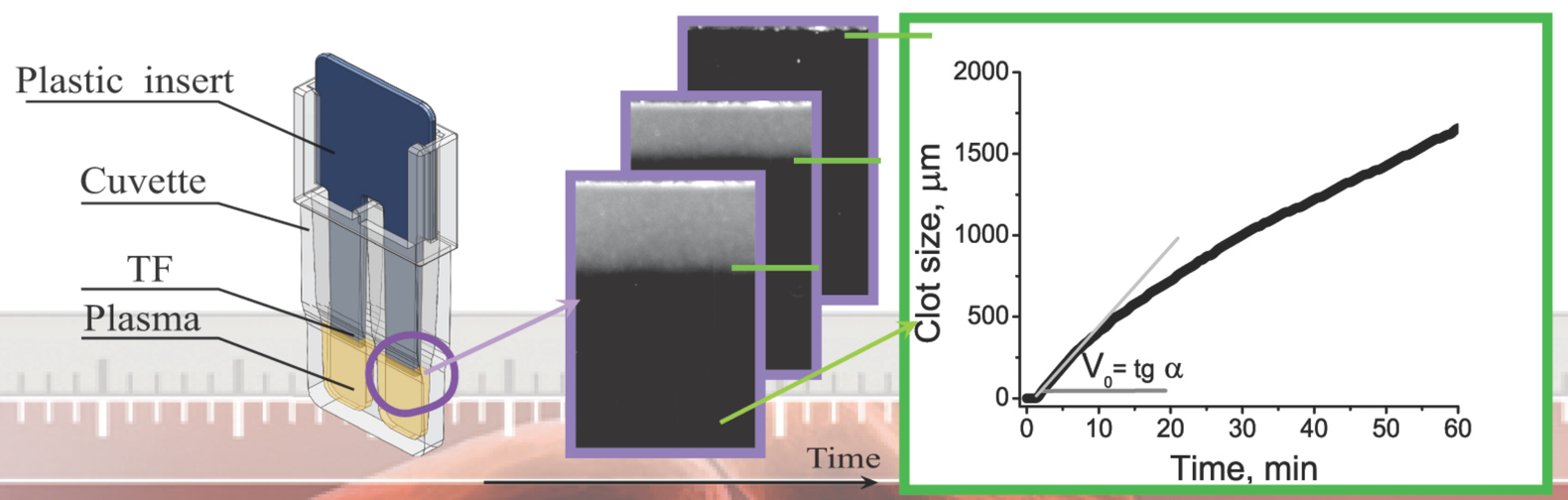
Methods

We used activated partial thromboplastin time (APTT), FVIII:C and the Thrombodynamics (TDx) assay to evaluate the efficacy of the new treatment. Standard test of pharmacokinetics included 3 days washing period and blood sampling before and during 72 h after the pdFVIII infusion. We analyzed pharmacodynamics parameters after administration of 50 IU/kg pdFVIII concentrate right after the first infusion and after 6 months of continuous prophylactic therapy. Also we analyzed amount of bleedings per month.

Five patients with FVIII:C<1% were switched from 25 IU/kg of FVIII to 50 IU/kg every 3 days therapy due to low clinical response.

Blood was drawn into 3.8% sodium citrate buffer (pH 5.5) at a 9:1 blood:anticoagulant (v/v ratio). The blood was processed by centrifugation at 1,500xg for 15 min. For the TDx plasma was processed by additional centrifugation at

The TDx is based on fibrin clot formation in a thin layer of nonstirred platelet poor plasma where clotting is initiated by a surface with immobilized tissue factor (TF) and monitored using videomicroscopy. Here we measured the initial rate of fibrin clot propagation (V_0).



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