# TITLE

# Low dose Factor VIII prophylaxis in children with severe hemophilia

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## Objectives:

•To assess the efficacy of low dose factor prophylaxis in children with severe hemophilia A.

•To compare the amount of factor used and safety issues in Prophylaxis and On demand groups

## Methods:

•Twenty one children with severe hemophilia A in age range of 1-10 years without measurable inhibitors were selected in study.

•They were randomly assigned to Prophylaxis group and Episodic group.

•Prophylaxis group children received factor VIII concentrate 10 units/kg body weight on two fixed days a week on OPD basis through peripheral veins.

•Episodic group received factor concentrate after having bleed in doses of 25units/kg body weight till bleeding subsided and symptoms improved.

•Both the groups were evaluated on monthly basis for number of bleeds and other records. Total median study duration was 11.5 months (though originally planned for 12 months).

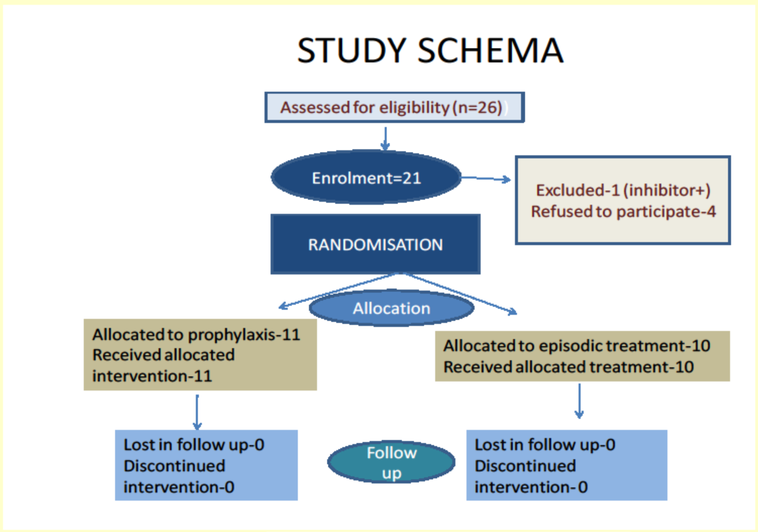


**Figure-1.** Flow diagram of the study schema

## Results:

| Variables | Prophylaxis group (n=11) Mean ± SD | Episodic treatment group (n=10) Mean ± SD | P value |
|---|---|---|---|
| Age at diagnosis (months) | 11.6± 4.7 | 11.2± 3.19 | not significant |
| Age at study entry (years) | 4.32±2.55 | 7.9±1.97 | <0.05 |
| Baseline weight (kg) | 13.45±3.42 | 18.40±4.0 | <0.05 |
| Weight at 6 months (kg) | 16.64±4.4 | 20.8±4.1 | <0.05 |
| Number of months in study | 11.45 | 11.60 | not significant |

**Table-1.** Baseline characteristics of the hemophilia children in both the groups

| Variables | Prophylaxis Group (n=11) | Episodic treatment group (n=10) | Statistical significance P value |
|---|---|---|---|
| Overall bleeds/patient/month Mean ± SD | 0.185 ± 0.183 | 0.787 ± 0.457 | <0.05 |
| Joint bleeds/patient/month Mean ± SD | 0.08 ± 0.13 | 0.48 ± 0.34 | <0.05 |
| Pettersson Score (Baseline) Median (range) | 0 (0-2) | 0.5 (0-2) | not significant |
| Pettersson Score (End of study) Median (range) | 0 (0-2) | 1.0 (0-2) | not significant |

**Table-2.** Primary outcome data in patients on prophylaxis and episodic treatment

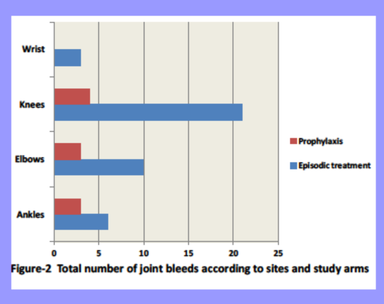


**Figure-2** Total number of joint bleeds according to sites and study arms

| Variables | Prophylaxis group (n=11) | Episodic treatment group (n=10) | Statistical significance p value |
|---|---|---|---|
| Number of emergency visits to hospital Median (min-max) | 1 (0-7) | 9 (1-15) | <0.05 |
| School absenteeism (days) Median (min-max) | 3 (0-30) | 25 (2-70) | <0.05 |
| Total factor usage Mean ± SD | 14992.7± 4057.3 | 11750 ± 7583.6 | ns |
| Factor VIII usage/kg/month | 87.51±12.86 | 56.32± 49.74 | ns |

**Table-3.** Showing major secondary outcomes in both the groups

•Eleven children were assigned to prophylaxis and 10 to episodic group.
•Children on prophylaxis had 24 overall bleeds (11 joint bleeds) in comparison to 92 bleeds (57 joint bleeds) in episodic group. Mean number of overall events per patient per month and mean number of hemarthrosis per patient per month was 0.185±0.183 and 0.08±0.13 respectively in prophylaxis group in comparison to 0.787±0.457 and 0.48±0.34 respectively in episodic group($p<0.05$).
•Overall reduction of joint bleed in the prophylaxis group was by 88.1%.
•There was no significant difference in Pettersson scores between prophylaxis group and episodic treatment group over a study period of 11.5 months.
•Total factor VIII consumption was 87.51±12.86 units/kg/month and 56.32±49.74 units/kg/month in prophylaxis and episodic group respectively (p value not significant).
• Median factor VIII trough levels in prophylaxis group just before the infusion of factor VIII (at 6 months) and at the end of the study were <1% even though there was significant reduction of bleed. Only 3 children (27%) were having factor VIII trough levels of >1% at both time points.
•Average hospital emergency visits were 1(0-7) per month in prophylaxis group and 9 (1-15) in episodic group ($p=<0.05$).
•Median days of absenteeism from school were 25 in episodic group and 3 in prophylaxis group.
•Overall, emergency visit and school absenteeism in the prophylaxis group were reduced by 88.9% and 88% respectively.
•Only one patient in prophylaxis group had discontinued prophylaxis for one week due to poor veins.
•No dropout occurred during the study period and compliance was 98%.

## Conclusions:

Low dose Factor VIII prophylaxis is efficacious, cost-effective and safe method of preventing joint bleed (and consequent joint damage) in children with severe hemophilia despite slightly higher consumption of factor VIII.

Further, patients who can not achieve factor levels of 1% do not necessarily bleed more in comparison to those with levels >1%.

## References:

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