Dyslipidemia in HIV-infected children and adolescents treated with cART between 1997 and 2009: a longitudinal analysis.

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Background

Several studies in HIV-uninfected adults demonstrated an association between high cholesterol levels during adolescence and the development of atherosclerotic plaques in young adults and the potential risk for cardiovascular disease (CVD) at adult age. PI containing regimens are associated with an increased risk of dyslipidemia and risk of MI.

Objective

We examined the effect of PIs on cholesterol and triglycerides levels in HIV-infected children and adolescents.

Methods

Study population:

HIV-1 infected children followed in the pedriatric HIV treatment centres in the Netherland's were included :

- who were treated with cART between calendar year 1997 and 2009
- with at least two cholesterol and triglycerides measurements during cART, in predominantly non-fasting blood.

Patients were divided in two groups:

- children (aged ≤12 years at time of cART initiation)
- adolescents (aged 13-18 years at time of cART initiation).

Methods continued

Definitions:

Hypercholesterolemia (HC): at least one cholesterol level>200 mg/dl (>5.17 mmol/l)

Hypertriglyceridemia (HT): at least one triglycerides level >150 mg/dl (>1.69 mmol/l).

Statistical analysis:

Logistic regression, with a generalised estimating equation method to adjust for correlations between lipid measurements within the same individual was used to estimate Odds ratios for the occurrence of HC and HT during cART amongst children and adolescents receiving a PI containing regimen compared to a NNRTI containing regimen. Analyses were adjusted for age at time of HIV diagnosis, gender, region of origin.

All measurements during the first 18 months of cART were included.

Results

- 151 children and 102 adolescents were included.
- 183 were vertically infected with HIV
- 178 were boy

Table 1 shows the clinical characteristics

Table 2 shows the risk of HC and HT.

- Children on a PI-based regimen were at least 2 times more likely to have a hypertriglyceridemia (triglycerides, > 1.69 mmol/l) compared with children on an NNRTI-based regimen. Children who were using a regimen that contained both a PI and an NNRTI were 6 times more likely to have a hypertriglyceridemia.

- The prevalence of cardiovascular disease is 3% for HIV-infected children treated with cART and 4% for HIV-infected adolescents who are receiving cART. A cardiovascular event developed in four children during follow up.

- Amongst the patients who were diagnosed with HIV as adolescents, four were diagnosed with cardiovascular disease between the ages of 25 and 34 years.

- None of the deaths of children or adolescents were related to cardiovascular disease

Table 1 Clinical characteristics of HIV-1-infected children (age 0-12 years at time of HIV diagnosis) and adolescents (age 13-17 years at time of HIV diagnosis) ever in follow-up up until 1 June 2010 in the SHM database.

	Children	Adolescents
Baseline characteristics at cART initiation		
cART use	151	102
NNRTI	40 (26%)	46 (45%)
PI	96 (64%)	44 (43%)
PI+NNRTI	4 (3%)	3 (3%)
Unknown/missing	11 (7%)	9 (9%)
Baseline CD4 cell counts ((x10^6 cells/l) (median, IQR) according to age at baseline		
<12 months	1080 (381-1585)	
1-3 years	667 (225-1310)	
4-5 years	630 (420-1280)	
6-12 years	261 (72-390)	
>12 years		256 (155-395)
Median time in months (median, IQR) between diagnosis and cART according to age		
<12 months	0.5 (0.2-1.1)	
1-3 years	3.7 (1.8-11.5)	
4-5 years	9.6 (3.7-21.6)	
6-12 years	16 (2.0-77.5)	
>12 years		8.4 (2.2-45.1)
Baseline Total Cholesterol (mmol/l) (median, IQR)	3.30 (2.87-3.70)	4.09 (3.30-4.51)
Baseline triglycerides (mmol/l) (median, IQR)	1.21 (0.94-1.96)	1.04 (0.70-1.33)
Clinical characteristics at 24 weeks		
Total cholesterol (mmol/l) (median, IQR)	4.52 (3.68-5.26)	4.10 (3.40-4.90)
Triglycerides (mmol/l) (median, IQR)	1.04 (0.78-1.72)	0.94 (0.64-1.28)
Hypercholesterolemia At least 1 total cholesterol measurement >5.17 mmol/l	33 (22%)	19 (19%)
Hypertriglyceridemia At least 1 triglycerides measurement> 1.69 mmol/l	36 (24%)	22 (22%)

Legend: cART=combination antiretroviral therapy; NNRTI=non-nucleoside reverse transcriptase inhibitor; PI=protease inhibitor; IQR=interquartile range; MTCT=mother to child transmission; baseline is date of cART initiation

Table 2 Odds of hypercholesterolemia (hc) and hypertriglyceridemia (ht) amongst children and adolescents treated with a PI-based regimen compared to an NNRTI-based regimen.

	Children		Adolescents	
	OR*	95% CI	OR*	95% CI
Hypercholesterolemia				
NNRTI	1		1	
PI	1.53	0.70-3.38	2.94	0.88-9.97
PI+NNRTI	1.04	0.34-3.18	**5.05**	**1.39-17.99**
Hypertriglyceridemia				
NNRTI	1		1	
PI	**2.36**	**1.15-4.85**	0.96	0.50-1.84
PI+NNRTI	**5.93**	**1.75-19.98**	1.84	0.71-4.80

*Adjusted for age at time of HIV diagnosis, gender, region of origin
Legend: NNRTI=nonnucleoside reverse transcriptase inhibitor; PI=protease inhibitor

Conclusions

Children on a PI regimen may be at higher risk of HT compared to children on a NNRTI regimen. Controlling for lipid levels at regular intervals, together with interventions such as lipid lowering diet or drugs and stimulating exercise may be of benefit in preventing cART-related dyslipidemia in HIV-infected children.

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