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Does Early ART Preserve Pulse-Wave Velocity in Children? Evidence from the CHER trial cohort

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Background

- Cross-sectional evidence strongly suggests increased prevalence of vascular disease in HIV+ children on antiretroviral therapy (ART) after adjusting for traditional atherosclerosis risk factors [1-7]

  Vascular abnormalities are typically associated with advanced HIV disease and with ART, particularly lopinavir/ritonavir (LPVr) [3, 4, 7]

- Thus far, pediatric studies have focused on children initiating ART much later than 3 months of age
- Whether very early ART will prevent HIV-related vascular disease is unknown
- Aorto-femoral pulse wave velocity (PWV) measures arterial elasticity & predicts incident cardiovascular events in asymptomatic adults [8]

Aim

To measure PWV in school children who initiated LPVr-based ART before 3 months of age in a well-resourced trial setting

Methods

- Cross-sectional design
- PWV and fasted lipid measurements on primary-school-age children who initiated LPVr-based ART in the CHER trial [9, 10] by 3 months of age, with an HIV-uninfected control group from the same communities and socio-economic background
- Multivariate linear regression to determine the association between PWV and HIV infection

Results

- Unadjusted PWV and growth parameters were similar in both groups
- After adjustment for age, gender and body-mass-index-for-age Z-score, HIV+ children had:
  - adjusted mean **total cholesterol 0.7 mmol/L higher** than controls (p<0.0001)
  - adjusted mean **LDL cholesterol 0.5 mmol/L higher** (p=0.001)
  - adjusted mean **triglycerides 0.4 mmol/L higher** (p<0.0001)
  - adjusted mean **triglyceride to HDL cholesterol ratio 0.3 higher** (p<0.0001)
- After adjustment for age, gender, and systolic blood pressure, HIV was not associated with PWV differences (p=0.40) despite 90% power to detect difference >0.31 m/sec

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Table 1: Demographics and clinical characteristics Variables are presented as median (interquartile range)	HIV-infected n = 59	Uninfected controls n = 43	Unadjusted p-value (2-tailed)
Age at study visit (years)	7.7 (7.6 – 7.8)	8.5 (7.8 – 8.7)	<0.0001
Gender (male/female)	46% / 54%	77% / 23%	<0.0001
Age at ART initiation (*weeks*)	8 (7 – 10)	---	---
Cumulative time on ART (years)	7.1 (6.6 – 7.5)	---	---
Dominant ART regimen (ZDV / 3TC / LPVr)	84% / 93% / 93%	---	---
Cumulative time with undetectable HIV RNA PCR viral load (<400 copies/ml) (months)	28 (19 – 44)	---	---
Proportion with undetectable HIV RNA PCR viral load (<400 copies/ml) at study visit	91%	---	---
Cumulative time with low CD4 or CD4% § (months)	4 (0 – 14)	---	---
Current CD4 (cells/mm^3)	1072 (826 – 1427)	---	---
Maximum WHO clinical stage ever reached (1 or 2 / 3 / 4)	10% / 44% / 46%	---	---
Weight-for-age Z-score	-0.4 (-1.0 – 0.3)	-0.2 (-1.0 – 0.8)	0.42
Height-for-age Z-score	-0.8 (-1.3 – 0.1)	-0.4 (-1.4 – 0.3)	0.24
Body mass index-for-age Z-score	0.0 (-0.5 – 0.7)	0.0 (-0.6 – 1.1)	0.77
Waist circumference to height ratio	0.5 (0.4 – 0.5)	0.4 (0.4 – 0.5)	0.17
Systolic blood pressure (mmHg)	96 (88 – 100)	96 (92 – 103)	0.05
Total cholesterol (mmol/L)	4.3 (3.7 – 4.9)	3.5 (3.1 – 4.0)	**<0.0001**
LDL cholesterol (mmol/L)	2.6 (2.0 – 3.2)	1.9 (1.4 – 2.4)	**<0.0001**
Triglycerides (mmol/L)	0.8 (0.7 – 1.2)	0.6 (0.4 – 0.7)	**<0.0001**
HDL cholesterol (mmol/L)	1.2 (1.1 – 1.4)	1.3 (1.1 – 1.5)	0.57
Triglyceride to HDL cholesterol ratio	0.7 (0.5 – 1.0)	0.4 (0.3 – 0.6)	**<0.0001**
Glycosylated hemoglobin (%)	5.4% (5.2 – 5.7%)	5.8% (5.6 – 6.0%)	0.16
Pulse-wave velocity (meters/sec)	4.8 (4.4 – 4.9)	4.9 (4.4 – 5.2)	0.20

§ Low CD4 or CD4% was defined as CD4<1000 or CD4%<25% for <12 months of age; CD4<750 or CD4%<20% for 12-35 months of age; and CD4<500 or CD4%<20% for >36months of age

ZDV = zidovudine; 3TC = lamivudine; LPVr = lopinavir/ritonavir

Conclusions

- Despite significantly elevated lipids and prolonged LPVr-based ART exposure, arterial elasticity was preserved in HIV+ school-age children on ART from <3 months of age
- Very early ART may prevent HIV-related inflammatory vascular damage in HIV+ school-age children