

Right heart function in children and adolescents with HIV-associated chronic lung disease (BREATHE TRIAL)

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Rationale

- Chronic lung disease (CLD) complications may lead to right ventricular (RV) remodelling and subsequent right heart failure.
- Pulmonary hypertension (PH) may also develop as a complication of CLD
- The symptoms associated with CLD such as cough or breathlessness may also present in chronic cardiac disease.



Aims of the study

- To investigate
 - right-sided cardiac dysfunction and PH in children with HIV-associated CLD and stable on ART
 - whether adjuvant treatment with azithromycin results in improvement in right-sided cardiac function and PH in CLD



Specific Objectives

1. To describe baseline cardiac symptoms of HIV-associated CLD in children on ART
2. Determine baseline prevalence of right-sided cardiac dilatation, dysfunction and PH in HIV-associated CLD.
3. To investigate whether adjuvant treatment with azithromycin improves right-sided cardiac function and PH in HIV-associated CLD after 48 weeks



Methods

- a transthoracic echocardiogram was performed at baseline and 48 weeks
- focussed on assessing right-sided heart structure and function and pulmonary hypertension.
- Cardiac measures for right ventricle size, right atrial size and RV function were obtained following American Society Echocardiography recommendations
- Pulmonary arterial systolic pressures (PASP) was calculated indirectly from the pressure gradient measured across the tricuspid valve (regurgitant jet) and adding right atrial pressure an indicator of PH

Definitions for right heart abnormalities

Parameter	Importance
Tricuspid annular plane systolic excursion (TAPSE)	RV systolic function; (<i>dysfunction, <-2 z-score</i>)
RV basal diameter	RV size; (<i>dilated, >+2 z-score</i>)
RA area	right atrial size; (<i>dilated, >+2 z-score</i>)
PASP	PH on echo; (<i>likely PH, >37mmHg</i>)
LV ejection fraction	LV systolic function; (<i>dysfunction <55%</i>)

Clinical characteristics

Variable	AZM (N=82)	Placebo (N=87)
Female, N (%)	33 (40)	40 (46)
Age, y , (median IQR)	15.3 (12.9 – 17.4)	16.2 (13.0 – 18.2)
Age at ART initiation, y	7 (4 – 10)	9 (6 – 12)
CD4 <100 cell/μl, N (%)	6 (7)	6 (7)
HIV VL suppression (< 1000 copies/ml), N (%)	50 (61)	48 (55)
Weight-for-age z-score, mean (SD)	-2.29 (1.43)	-2.04 (1.57)
Underweight, n (%)	45 (55)	41 (47)
Height-for-age z-score, mean (SD)	-2.10 (1.14)	-1.92 (1.26)
Stunted, n (%)	42 (51)	35 (40)

Cardiac signs and symptoms at baseline and after 48 weeks

	Baseline			48 weeks		
	AZM (N=82)	Placebo (N=87)	P-value	AZM (N=82)	Placebo (N=87)	P-value
Tachycardia, N (%)	2 (2)	1(1)	0.478	1 (1)	3 (3)	0.333
Tachypnoea, N (%) ^a	8 (10)	7 (8)	0.696	12 (15)	9 (10)	0.397
Hypoxia, N (%)	2 (2)	5 (6)	0.247	2 (2)	-	-
Shortness of breath, N (%)	2 (2)	1 (1)	0.478	1(1)	-	-

^a n=3 had tachypnoea at baseline and 48 weeks

Right heart abnormalities

Right heart abnormalities 7(4%)	Baseline		48 weeks	
	AZM, N=82	Placebo, N=87	AZM, N=82	Placebo, N=87
PH, n (%)	1(1)	-	1(1)	1(1)
RV dilatation, n (%)	1(1)	-	-	-
RV systolic dysfunction, n (%)	3 (4)	2(2)	3 (4)	4 (5)
Pericardial effusion, n (%)	1(1)	-	1 (1)	4 (5)

n=1 had RVSD at baseline and 48 weeks



Conclusion

- Despite HCLD in these children, right heart abnormalities were relatively low
- There was no evidence of marked changes in right heart size and function following 48 weeks of treatment with AZM or placebo.