Bromocriptine Improves Central Aortic Health in Adolescents with Type 1 Diabetes Mellitus

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Background

- The incidence rate of youth-onset type 1 diabetes mellitus (T1D) is rising annually worldwide and is projected to increase over the next 40 years.
- The presence of peripheral vascular dysfunction accelerated by large arterial stiffness, and impaired cardiac function has been clearly demonstrated in youth with T1D, predisposing young people to increase risk of cardiovascular events.
- This predisposes young patients to the life-long exposure to elevated ventricular afterload and increased incidence of cardiovascular events.
- Therapeutic strategies to mitigate vascular dysfunction are urgently needed.

Hypothesis

We hypothesized that bromocriptine quick release (BCQR) therapy would improve vascular health in youth with T1D.

Methods

- This was a placebo-controlled, random-order, double-blinded, cross-over study investigating BCQR as adjunct therapy on central aortic stiffness as measured by **phase-contrast MRI**.
- Participants also underwent flow mediated dilatio test and brachial distensibility evaluation using tonometry.
- Adolescents with T1D were randomized 1:1 to phase-1 of 4-week BCQR (minimum dose 1.6 mg daily) or placebo therapy after which all vascular measurements were performed.
- Following a 4-week washout period, phase 2 was performed in identical fashion with the alternate treatment.

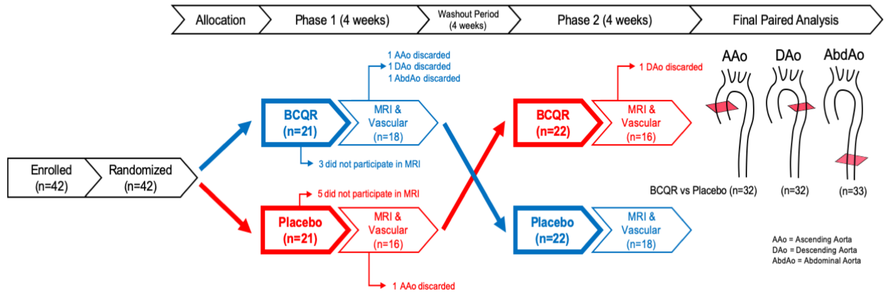

Figure 1. CONSORT (Consolidated Standards of Reporting Trials) diagram of cross-over clinical trial in adolescents with type 1 diabetes mellitus.

Results

Table 1. Baseline characteristics of T1DM Participants

	T1DM (n = 34)
Age (years)	15.9 ± 2.6
Sex (male)	13 (38.2%)
Diabetes duration (years)	5.8 (3.5 - 9.5)
HbA1c (%)	8.6 ± 1.1
BMI (kg/m²)	24.6 ± 5.8
BMI Percentile	71.4 ± 26.1
Lean body mass (kg)	43.8 ± 9.4
Fat free mass (kg)	45.8 ± 9.8
Body fat percentage	32.7 ± 8.1
Lean fat percentage	0.64 ± 0.08

Data reported as mean ± SD or median with corresponding IQR.

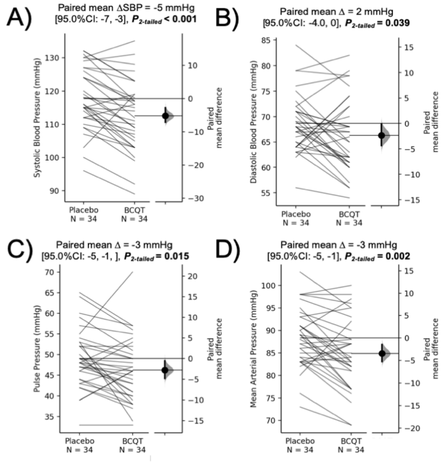

Figure 2. Bromocriptine quick release (BCQR) improves overall pressure hemodynamics. BCQR reduced systolic A) and diastolic B) blood pressure as well as pulse pressure C) and mean arterial pressure D).

Table 2. Arterial Hemodynamics of Participants with T1DM

	Placebo	Bromocriptine	P-value
Pressure Hemodynamics			
Systolic blood pressure (mmHg)	118 ± 9	113 ± 11	< 0.001
Diastolic blood pressure (mmHg)	69 ± 6	66 ± 7	0.039
Pulse pressure (mmHg)	49 ± 7	46 ± 8	0.015
Mean arterial pressure (mmHg)	88 ± 7	85 ± 8	0.002
Ascending Aorta			
Pulse Wave Velocity (m/s)	4.0 ± 0.8	3.7 ± 0.6	0.005
Relative Area Change (%)	28.1 ± 6.8	30.7 ± 5.7	0.022
Distensibility (%/mmHg)	0.59 ± 0.17	0.68 ± 0.17	0.010
Decending Aorta			
Pulse Wave Velocity (m/s)	4.2 ± 0.6	4.1 ± 0.8	0.385
Relative Area Change (%)	25.9 ± 4.5	26.2 ± 5.7	0.771
Distensibility (%/mmHg)	0.55 ± 0.12	0.59 ± 0.16	0.132
Abdominal Aorta			
Pulse Wave Velocity (m/s)	4.2 ± 0.6	3.9 ± 0.4	0.013
Relative Area Change (%)	26.1 ± 3.8	27.3 ± 3.4	0.103
Distensibility (%/mmHg)	0.56 ± 0.15	0.61 ± 0.11	0.032
Endothelial Function			
Reactive Hyperemia Index	2.30 ± 0.56	1.99 ± 0.57	0.006
LN reactive hyperemia index	0.81 ± 0.23	0.65 ± 0.28	0.003
Framingham RHI Risk Score	0.87 (0.55 - 1.04)	0.75 (0.25 - 0.99)	0.010
Peripheral Vascular Stiffness			
Brachial distensibility (%/mmHg)	0.059 ± 0.012	0.061 ± 0.013	0.156
Brachial compliance (mL/mmHg)	6.06 ± 1.16	6.25 ± 1.15	0.303
Data reported as mean ± SD or as median with corresponding IQR			

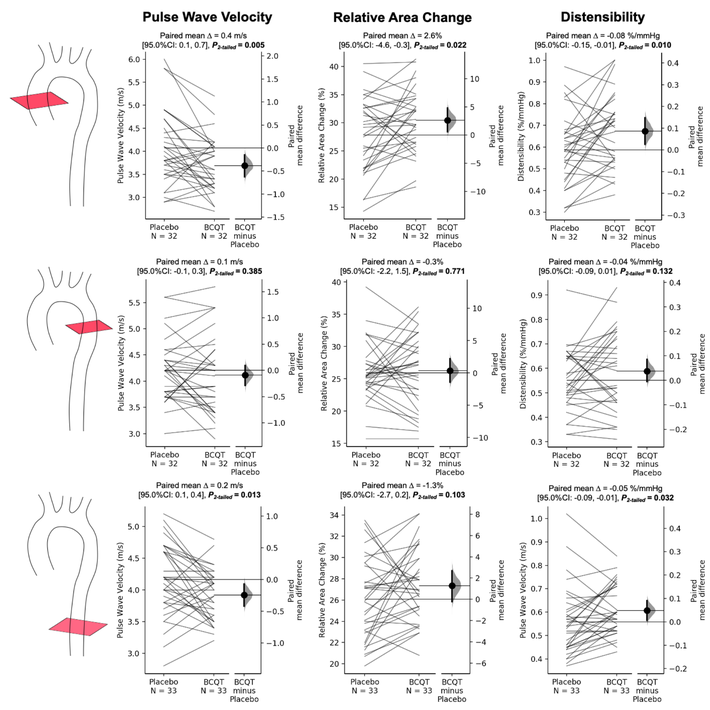

Figure 3. Bromocriptine quick release (BCQR) improves central aortic stiffness in youth with T1DM. Ascending aortic stiffness (top row) was improved by decreased pulse wave velocity (PWV), increased relative area change (RAC), and increased distensibility. There were no differences in the descending aorta (middle row). Thoraco-abdominal stiffness was improved as evidenced by decreased PWV and increased distensibility.

Conclusions

- Arterial stiffness is a predictor of all cause cardiovascular events, as such, BCQR therapy might serve as a clinical intervention to reduce cardiovascular risk in youth onset-T1DM.
- Additionally, BCQR further improves standard pressure hemodynamics, also likely to improve long-term cardiovascular outcomes.
- Further study is needed to determine the significance of BCQR's ultimate impact on cardiovascular morbidity and mortality in T1DM