

Bromocriptine Improves Central Aortic Stiffness in Adolescents with Type 1 Diabetes: Arterial Health Results from the BCQR-T1D Study

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Background: The presence of vascular dysfunction is a well-recognized feature in youth with type 1 diabetes (T1D), accentuating their lifetime risk of cardiovascular events. Therapeutic strategies to mitigate vascular dysfunction are a high clinical priority. In the bromocriptine quick release T1D study (BCQR-T1D), we tested the hypothesis that BCQR would improve vascular health in youth with T1D.

Methods: BCQR-T1D was a placebo-controlled, random-order, double-blinded, cross-over study investigating the cardiovascular and metabolic impact of BCQR in T1D. Adolescents in the BCQR-T1D study were randomized 1:1 to phase-1: 4-weeks of BCQR or placebo after which blood pressure (BP), peripheral vascular stiffness by brachial artery distensibility (BrachD), endothelial function by reactive hyperemic index (RHI), and central aortic stiffness measured by pulse wave velocity (PWV), relative area change (RAC) and distensibility from phase-contrast MRI, were performed. Following a 4-week washout period, phase 2 was performed in identical fashion with the alternate treatment.

Results: Thirty-four adolescents (mean age 15.9 ± 2.6 years, HbA1c $8.6 \pm 1.1\%$, BMI %ile 71.4 ± 26.1 , median T1D duration 5.8 years) with T1D were enrolled and had MRI data available. Compared to placebo, BCQR therapy decreased systolic [$\Delta = -5$ mmHg, (95%CI: -3, -7), $p < 0.001$] and diastolic BP ($\Delta = -2$ mmHg, (95%CI: -4, 0), $p = 0.039$). BCQR reduced ascending aortic PWV ($\Delta = -0.4$ m/s, $p = 0.018$), and increased RAC ($\Delta = -2.6\%$, $p = 0.083$) and distensibility ($\Delta = 0.08$ %/mmHg, $p = 0.017$). In the thoraco-abdominal aorta, BCQR decreased PWV ($\Delta = -0.2$ m/s, $p = 0.007$) and increased distensibility ($\Delta = 0.05$ %/mmHg, $p = 0.013$). BCQR also decreased BrachD in normal-weight participants ($\Delta = 0.56$ %/mmHg, $p = 0.023$).

Conclusions: BCQR improved BP and central and peripheral aortic stiffness and pressure hemodynamics in adolescents with T1D over 4 weeks vs. placebo. However, BCQR decreased peripheral RHI. BCQR may improve aortic stiffness in youth with T1D, supporting future longer-term studies.