Plasma Cholesterol in Adults with Phenylketonuria

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Introduction
Phenylketonuria (PKU) is an autosomal recessive disorder of phenylalanine (Phe) catabolism resulting from a deficiency of L-phenylalanine hydroxylase (PAH) [1]. An association between hyperphenylalaninaemia (HPA) and hypocholesterolaemia has been reported in children [2]. However, controversy exists as to whether this is due to the low-protein diet or to a disruption to cholesterol biosynthesis inherent to those with PKU.

Objective
We investigated the relationship between blood Phe and plasma cholesterol in healthy adults with PKU.

Methods
Forty-one apparently healthy adults with PKU (26 females, 15 males, median age 26, range 18 to 57 years) attending an outpatient PKU clinic at a tertiary adult hospital. Of these, 33 (80%) were compliant with a Phe-restricted diet and amino acid supplementation, whereas eight (20%) were not compliant. Plasma total cholesterol, triglyceride, and high density lipoprotein (HDL) cholesterol was measured on venous blood samples, after an overnight fast, using Roche reagents on a Hitachi 917 analyser. Low density lipoprotein (LDL) cholesterol concentrations were calculated by difference using the Friedewald equation. Apolipoprotein (apo) B was measured by immunonephelometry using Behring reagents on a Behring BN-II. Phe was measured by liquid chromatography tandem mass spectrometry.

Lipid concentrations were compared with local normative data from the literature [3]. LDL-cholesterol concentrations were compared with an age- (years) and gender-matched subset of a community laboratory population from Perth, Western Australia [4].

Results
The PKU subjects had a mean body mass index (BMI) of 30.3±1.8 kg/m2; 72% were obese, 14% overweight, and only 14% of normal BMI. The mean blood Phe was 1194 μmol/L (reference interval 35-85) with plasma total cholesterol, triglyceride, HDL-cholesterol, LDL-cholesterol and apoB concentrations of 4.3 mmol/L, 1.6 mmol/L, 1.2 mmol/L, 2.3 mmol/L, and 0.83 g/L, respectively. The total cholesterol was 20% lower compared to published age- and sex-matched controls from a local Australian population (5.3 mmol/L; P<0.001) [2]. The mean LDL-cholesterol was 19% lower in PKU females than that of 8944 age-matched females from a community population (2.5±0.8 mmol/L vs. 3.1±0.9 mmol/L; P<0.001; Figure 1). Similarly, the mean LDL-cholesterol was 32% lower in PKU males than 3786 age-matched males (2.1±0.7 mmol/L vs. 3.1±1.0 mmol/L; P<0.0001; Figure 1). No associations were observed between Phe and total cholesterol, LDL-cholesterol or apoB in the PKU cohort (Figure 2).

Conclusion
Adults with PKU had low-normal cholesterol concentrations, with no correlation observed between blood Phe and plasma cholesterol levels. Our findings support the concept that the HPA found in PKU, rather than an effect of a low-protein diet, leads to hypocholesterolaemia. Studies are required to determine whether this cholesterol-lowering effect confers cardioprotection.

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References