Fasting Serum Blood Measures of Bone and Lipid Metabolism in Children with Myelomeningocele for Early Detection of Cardiovascular and Bone Fragility Risk Factors

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- Does not intend to discuss commercial products or services.
- Does not intend to discuss non-FDA approved uses of products/providers of services.
- Support provided by NIH-NICHD Grant # 5R01HD059826.
- Authors have no disclosures.
Background

• Obesity in the general pediatric population:
  – Increased over the past 2 decades.
  – At least 80% of overweight youth are overweight/obese as adults.

• Obesity is a chief risk factor for:
  – Metabolic syndrome, type II diabetes, cardiovascular disease, cancer, sleep apnea
• Higher incidence of obesity in children and adolescents with myelomeningocele (MM).
• Youth with MM often experience prolonged periods of inactivity due to:
  – Surgeries, pressure sores, UTIs, braces/assistive devices
• Youth with MM have an increased risk of abnormal lipid profiles, metabolic profiles, bone metabolism markers and vitamin D levels.
• Early detection for prompt intervention, greater possibility of prevention and better treatment outcomes is crucial.
Purpose

• Assess all serum levels within a single population.
• Investigate differences among varying degrees of disease severity.
Methods

• Population
  – Aged 6-13 years
  – No medication affecting growth/development
  – No chronic conditions (other than MM/hydrocephalus for patient group)
    • 28 children with MM
      – 8 sacral, 5 low lumbar, 15 mid lumbar and above (IMSG)
    • 58 without MM

• Clinical measures
  – Height, weight, manual muscle testing completed by a PT
  – Blood pressure (within 6 months of study visit) accessed from medical record retrospectively for patient group
  – Percent body fat and trunk fat from DXA
Methods

• Serum levels
  – Fasting (>8 hours) blood sample
  – Lipid panel: cholesterol, triglycerides (TG), high-density lipoproteins (HDL), low-density lipoproteins (LDL)
  – Insulin resistance calculated from insulin and glucose levels using the homeostatic model assessment of insulin resistance (HOMA-IR)
  – Others: leptin, aspartate aminotransferase (AST), Alanine transaminase (ALT), alkaline phosphatase, albumin, creatinine, calcium, adjusted calcium, phosphate, intact parathyroid hormone (PTH), total 25-hydroxyvitamin D (25 OHD)
• **Metabolic syndrome if 3 or more were present:**
  - High blood pressure: systolic or diastolic ≥90th percentile for age, height, sex
  - Excessive trunk adiposity: ≥30% for males, ≥35% for females
  - Insulin resistance/glucose intolerance: glucose ≥100mg/dL
  - High levels of TG: ≥100mg/dL
  - Low levels of HDL: <45mg/dL for males, <50mg/dL for females
Methods

• Vitamin D status
  – Sufficient: ≥30ng/ml
  – Insufficient: 20-29ng/ml
  – Deficient: <20ng/ml

• Obesity categorized based on BMI percentile
  – ≥95\textsuperscript{th} percentile
• **Statistical analyses:**
  
  – Participant characteristics and serum levels - MM group vs. controls
    
    • Student’s t-tests (normally distributed)
    
    • Mann-Whitney rank sum (not normally distributed)
  
  – Generalized linear model including trunk fat as a covariate
  
  – Differences among neurosegmental levels and controls
    
    • ANOVA, post-hoc tests (normally distributed)
    
    • Kruskal-Wallis, post-hoc tests (not normally distributed)
    
    • Bonferroni adjustment to p-values for multiple comparisons.
**Results - Participant Characteristics**

- Control and MM groups not different (p≤0.46) in:
  - Sex distribution
  - Ethnic distribution
  - Age
  - Tanner stage
  - Body mass
  - BMI
  - % classified as obese
  - % trunk fat

- MM group had shorter stature, higher total % body fat, watched more TV (p≥0.06).
Results - Serum Levels, MM vs. Controls

• Lipid panel
  – MM had:
    • Lower HDL (p=0.03); similar cholesterol, TG, LDL (p=0.26)

• Metabolic panel
  – MM had:
    • Higher insulin (p=0.10), HOMA-IR (p=0.12), and leptin (p=0.12)

• Bone metabolism
  – MM had:
    • Lower calcium, PTH, vitamin D
    • Trend toward higher phosphate

• Others
  – MM had:
    • Lower AST, alkaline phosphatase, albumin and creatinine (p≤0.03)
    • Similar ALT (p=0.91)
Results - Serum Levels, MM vs. Controls

• PTH and 25OHD were negatively correlated in both control and MM groups.
  – MM: r=-0.43, p=0.02
  – Control: r=-0.38, p=0.003
Results - Serum Levels, MM vs. Controls

• After including percent trunk fat as a covariate group differences were no longer seen in:
  – HDL (p=0.17)
  – Insulin (p=0.57)
  – HOMA-IR (p=0.72)
  – Leptin (p>0.99)
  – AST (p=0.21)

• Group differences persisted in:
  – Alkaline phosphatase (p=0.002)
  – Albumin (p=0.07)
  – Creatinine (p<0.001)
  – Calcium (p=0.004), adjusted calcium (p=0.04)
  – PTH (p=0.008)
  – 25 OHD (p=0.009)
Results - Vitamin D, MM vs. Controls

- **MM**
  - Sufficient: 12
  - Insufficient: 14
  - Deficient: 2

- **Controls**
  - Sufficient: 13
  - Insufficient: 35
  - Deficient: 10

* indicates deficiency.
Results - Participant Characteristics, Neurosegmental Levels

• No differences in:
  – Sex or ethnic distribution
  – Age
  – Hours of TV watched
  – Height, body mass, BMI, BMI percentile

• Mid lumbar group compared to controls
  – Lower height for age
  – More total body fat
  – More trunk fat
Results - Serum Levels, Neurosegmental Levels

• Lipid panel
  – HDL tended to decrease with increasing neurosegmental level while TG tended to increase
  – No differences reached significance
• Mid lumbar group compared to controls
  – Higher leptin, phosphate
  – Lower AST, alkaline phosphatase, creatinine, unadjusted calcium, PTH, and vitamin D
• Low lumbar group compared to controls
  – Lower creatinine, calcium (adjusted and unadjusted), PTH
• Sacral group not observably different than controls
• Presence of metabolic syndrome components:
  – High blood pressure: systolic or diastolic ≥90th percentile for age, height, sex
    • 29% of MM
  – Excessive trunk adiposity: ≥30% for males, ≥35% for females
    • 43% of MM
    • 31% of control
  – Insulin resistance/glucose intolerance: glucose ≥100mg/dL
    • 0% of MM
    • 4% of control
  – High levels of TG: ≥100mg/dL
    • 25% of MM
    • 19% of control
  – Low levels of HDL: <45mg/dL for males, <50mg/dL for females
    • 25% of MM
    • 17% of control
Results - Metabolic Syndrome, Neurosegmental Levels

• Presence of metabolic syndrome components:
  – MM group only
  • Those classified as having metabolic syndrome:
    – All were obese (truncal adiposity)
    – All had hypertension combined with high TG and low HDL

Number of Metabolic Syndrome Risk Factors

- 9
- 6
- 4
- 3 or more
- 2
- 1
- 0
• Children/adolescents with MM have elevated and/or adverse serum levels.
  – Some differences are related to increased adiposity.
  – Those with sacral level involvement are similar to controls.
  – Those with lumbar level involvement had abnormalities in the lipid profile, bone metabolism markers and metabolic syndrome markers.
Discussion

• 68% of the youth with MM had one or more abnormality, compared to 53% of the control group.

• Youth with MM may have an increased risk of cardiovascular disease and osteoporosis.
  – These conditions are largely preventable/treatable; early detection/intervention is likely to result in better outcomes.

• No subclinical renal dysfunction was detected.
  – Utility of routine creatinine monitoring is not supporting by study findings.

• 93% of MM participants were vitamin D insufficient or deficient, control group had a rate of 78%.

• 15% of MM group were classified as having metabolic syndrome.
Discussion

- Elevated CVD and metabolic syndrome risk factors, and possibly lower vitamin D levels, in the MM group are primarily associated with greater obesity.
- Musculoskeletal risk factors may be reflective of MM.
- Abnormalities likely exacerbated with increased disease severity.
Future Directions

• Dysregulated parathyroid function
  – Low PTH and alkaline phosphatase despite low vitamin D
• What diet and exercise interventions are most effective?
• What about older teens and adults with MM?
THANK YOU!!!

QUESTIONS?