Alcohol Affects Osteoinductive Capacity

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Alcohol and Bone

• Chronic Alcohol Consumption:
  – 35% of caloric intake derived from alcohol
  – 5-6 beers or 7-8 glasses of wine/day

• This pattern of alcohol consumption can result in:
  – Increased risk for osteoporosis
  – Stunted bone growth
  – Delayed or abnormal fracture healing
Background: Osteoinduction

- Osteoblasts deposit osteoid, the organic material which is mineralized to bone
- Osteoinduction occurs during fracture healing and ectopic bone formation
Deminerlized Bone Matrix (DBM) Cylinder Method

- Ectopic bone formation occurs via osteoinduction
- Matrix contains growth factors and cytokines
- DBM cylinders implanted subcutaneously
- After 6 weeks, DBM cylinders display characteristics of mature bone
DBM Cylinder Histology

Stained section showing mineralized bone, fatty marrow and osteoid

Bone cells depositing and resorbing bone matrix
Effect of Alcohol on Osteoinduction

Hypothesis: Alcohol will reduce osteoinductive response

Frozen rat legs (m & f) ordered from Pel-Freez Biologicals

Six weeks later, rats (n=20) sacrificed and implants excised

Femurs demineralized & cut into implants (n = 80)

Bone cylinders implanted in rats fed control and alcohol diet

Other cylinders ashed for mineral content

Implants analyzed on the μCT and embedded for histology
Study Results

- Lower bone volume in implants from alcohol rats
- No significant difference in relative mineral components (ICP-AES)
- Amount of bone formed is reduced in alcohol-consuming animals
- No difference in bone quality between the two groups
Biological Memory in Bone

Hypothesis: Bone matrix deposited in the presence of alcohol will show a similar decrease in osteoinduction

Young male rats fed a control or an alcohol diet for 3 months → Femurs from these rats were demineralized and cut into cylinders → Bone cylinders implanted in rats (n=12) fed a normal chow diet → Six weeks later, rats were sacrificed and implants excised → Implants analyzed on the µCT & some embedded
Study Results

Bone formed on DBM from an animal consuming control diet

Bone formed on DBM from an animal consuming alcohol diet
Insulin-like Growth Factor 1 (IGF-1)

- Growth hormone stimulates production of IGF-1
- Alcohol decreases serum GH and therefore serum IGF-1
- Microarray data from a previous study showed IGF-1 to be downregulated in an animal model for chronic alcohol abuse
- Alcohol disrupts IGF-1 signaling in skeletal muscle
ELISA

• Enzyme-Linked Immunosorbent Assay
ELISA Results

• No significant difference in normalized IGF-1 concentration
• Need to do further analysis of experimental setup to determine sources of inter-assay variability
• Need to improve data analysis techniques
Future direction

• Continue work on IGF-1
• Test for DBM compositional differences of other osteoinductive factors
  • BMP-2
  • TGF-Beta
Take Home Message

• Impaired fracture healing in alcohol abusers could be explained in part by impaired osteoinduction
• Impaired osteoinduction may persist long after dietary conditions return to normal
• Other dietary interventions may cause similar changes in bone matrix composition
Questions?