Effects of Ethanol Consumption on Biochemical Markers of Bone Turnover and Intracortical Bone Remodeling in Young Adult Male Cynomolgus Macaques

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Why study the skeletal effects of ethanol?

People drink!
Why study the skeletal effects of ethanol?

• Progress in understanding the actions of alcohol on bone metabolism are slowed by
  - Difficulty in performing intervention studies in humans
  - Limitations of commonly used animal models
  - Difficulty in accurately replicating human drinking behavior in animals

• Non-human primates are a highly relevant model for studying the effects of alcohol on the skeleton because
  - Their bones undergo intracortical bone remodeling
  - Once introduced to alcohol as part of their diet exhibit a range of voluntary alcohol consumption (moderate to excessive) observed in humans.
Experiments

Study 1
Effects of graded increases in ethanol consumption on biochemical markers of bone turnover in young adult male cynomolgus macaques (Macaca fascicularis)

Study 2
Effects of 6 months of voluntary ethanol consumption on intracortical bone remodeling in young adult male cynomolgus macaques
Study #1

Study 1

- Study population:
  - 9 young adult (6.6 ± 0.0 years) male cynomolgus macaques (*Macaca fascicularis*)
- Duration
  - 3 month ethanol induction
- Blood Collection
  - Blood Ethanol Concentrations
  - Osteocalcin
  - CTX

![Study flowchart]

- Water only (30 days)
- 0.5 g/kg/d ethanol (30 days)
- 1.0 g/kg/d ethanol (30 days)
- 1.5 g/kg/d ethanol (30 days)

Blood draw (day -4) → Blood draw (day 13) → Blood draw (day 15) → Blood draw (day 20)
Caloric Intake

Data are mean ± SE

p<0.0001
Plasma; Blood Ethanol Concentration

![Graph showing Blood Ethanol Concentrations]

Data are mean ± SE

p<0.0001
Plasma; Markers of Turnover

Data are mean ± SE

Osteocalcin

p < 0.0001

CTX

p < 0.0001

Osteocalcin:CTX Ratio

P = 0.0002
In young adult male cynomolgus macaques, ethanol consumption results in lower but unbalanced bone turnover.

- The reduction in bone turnover was dose dependent; no threshold dose was observed.

Over time, the negative remodeling balance could lead to osteopenia and reduced bone quality.
Study #2

- **Study population**
  - 11 (n = 3 control and 8 ethanol) young adult (control: 7.5 ± 0.0 years; EtOH: 7.0 ± 0.0 years at baseline) male cynomolgus macaques

- **Duration**
  - 3 month ethanol induction
  - 6 month open access

- **Tetracycline label**

- **Tibia**
  - DXA
  - µCT
  - histomorphometry
Figure 5. Daily ethanol consumption pattern in ethanol-treated monkeys.
6 months of ethanol consumption had no effect on bone size, BMC and BMD.

EtOH consumption (g/kg/d)  
1.83 ± 0.3

BEC (mg/dL)  
50.8 ± 49.8

Data are mean ± SE  (n=3 control, 8 ethanol)
6 months of ethanol consumption had no effect on cortical bone architecture.

Data are mean ± SE.
Effects of 6 months of ethanol consumption on incomplete and labeled osteons

Data are mean ± SE

Different from Control, P<0.05
Different from Control, P<0.1
6 months of chronic ethanol consumption reduced intracortical bone remodeling
Study 2: Conclusion

• Average daily ethanol intake of 1.8 ± 0.3 g/kg/d (BEC, 51 ± 50 mg/dl)
  - had no effect on tibial BMC and BMD or on cortical architecture in tibial diaphysis
  - resulted in reduced intracortical osteon density
• These findings suggest that chronic heavy alcohol consumption may negatively impact bone health, in part, by suppressing intracortical bone remodeling
  - Suppressed bone remodeling, were it to continue indefinitely, could impact bone quality and lead to reduced mechanical properties independent of bone mineral density
Questions?