Ethanol Consumption Impairs Osseointegration in a Murine Tibial Implant Model

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INTRODUCTION: Chronic alcohol consumption affects bone metabolism by impairing osteoblast proliferation and by increasing osteoclastic activity.¹ Despite chronic alcohol consumption affecting over 29 million people in the United States alone, the effects of alcohol on implant osseointegration have not been well established.² The purpose of this study was to evaluate the bone formation that occurs around titanium implants in a mouse tibial implant osseointegration model in the setting of alcohol consumption.

METHODS: All experiments were approved by the local IACUC. Eighteen-week-old, male C57BL/6 mice (n=48) were given 10% ethanol in the drinking water (n=24), or standard water (n=24) for 4 weeks before receiving bilateral implantation of a 3D-printed porous titanium tibial implant (Yang et al., 2015). The implant stem with 1.0 mm diameter was press-fit into a 0.9-mm-diameter (press-fit) or loosely inserted into a 1.4-mm-diameter (over-drill, N=48 tibiae per treatment group) hole drilled through the tibial plateau to the proximal tibial medullary canal. Ethanol consumption was continued until mouse euthanasia at 4 weeks after surgery. Mouse weight was measured weekly to detect the systemic effect of the ethanol consumption. Peri-implant bone architecture was determined by microCT. Bone and fibrotic tissue percentage was measured histologically. Bone-implant interface strength was assessed by pull-out mechanical testing. Statistical analysis: Data are reported as mean ± standard deviation. Two-tailed student’s T-test was used to compare groups. p<0.05 was considered as statistical significance.

RESULTS: Chronic ethanol consumption exerted systemic effects, as exposed mice failed to regain weight after surgery and weighed less in comparison to mice with standard water intake (28.9±1.8g vs. 30.7±2.0g, p=0.003) four weeks after surgery. One mouse of the ethanol group died one day after surgery. Ethanol consumption reduced the quantity and quality of intact bone without trauma, as shown by the decreased bone volume fraction (15.7±4.6% vs. 24.0±3.1%, p=0.004, Figure 1) and bone mineral density (203.9±68.9 vs. 311.2±39.0, p=0.004, Figure 1) of proximal femoral metaphyses measured by microCT.

In tibiae receiving press-fit tibial implantations, ethanol consumption also decreased peri-implant bone formation, with a lower bone volume fraction (25.8±2.6% vs. 30.8±4.6%, p=0.049, Figure 2). Furthermore, it also caused a significant lower percentage of bone (7.5±3.1% versus 13.1±3.4%, p=0.025, Figure 3) and a trend to higher percentage of fibrotic tissue (10.4±9.1% vs. 5.0±7.2%, p=0.056) measured histologically (Hematoxylin and eosin staining). A 24% decrease in pull-out strength did not reach significance (15.8±10.1N vs. 19.6±9N, p=0.32). In tibiae receiving over-drill implantation, no differences between treatment groups were found in peri-implant BV/TV (37.4±7.9% vs. 35.5±9.3%, p=0.71), bone mineral density (908.4±142.2 vs. 839.1±175.6, p=0.47), or pull-out strength (4.1±6.4N vs. 2.3±2.9N, p=0.3).

DISCUSSION: Adverse effects of ethanol on general bone health, mouse body weight, and osseointegration were demonstrated in this study. The mouse death and failure to regain body weight after surgery in the ethanol treated mice indicate ethanol consumption may lead to less tolerance to trauma or surgery. The loose implantation resulted in deleterious biomechanical strength relative to the press-fit implantation, and the insignificant effect of ethanol consumption in an over-drilled implant interface indicates that implant instability is a more critical factor for osseointegration. Based on this study’s translational findings, ethanol consumption should be avoided to enhance osseointegration. All efforts should be taken to ensure pressfit implantation especially in patients at risk. Further studies are required to evaluate the effect of preoperative and postoperative abstinence of ethanol.

SIGNIFICANCE/CLINICAL RELEVANCE: With the availability of numerous genetically engineered mouse lines, the establishment of an alcoholic murine osseointegration model provides a viable platform to further identify molecular and cellular mechanisms of the effect of chronic ethanol consumption on the formation of a bone-to-implant interface. As a potentially modifiable risk factor, further studies on this topic may eventually guide the treatment of patients that chronically consume alcohol in orthopedic settings.

²SAMHSA, Center for Behavioral Health Statistics and Quality. 2021 National Survey on Drug Use and Health.