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The Effect of Chronic Sleep Deprivation on Tumor Necrosis Factor Alpha and Bone Health in Peri-Menopausal Rats

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The Effect of Chronic Sleep Deprivation on Tumor Necrosis Factor Alpha and Bone Health in Peri-Menopausal Rats

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Introduction

Osteoporosis is a very common progressive skeletal disease in which the microarchitecture of bone tissue is slowly deteriorated causing a decrease in bone mineral density (BMD) and an increase in bone fragility. The cessation of estrogen signaling after menopause causes an imbalance between the osteoblasts which form bone, and osteoclasts, which degrade bone. Post-menopausal osteoporosis affects one in four women in which about one third of those women will experience a fracture due to the disease in their lifetime.

Chronic sleep deprivation (receiving less than six and a half hours of sleep a night) has been found to exacerbate osteoporosis. Through the production of an inflammatory response caused by chronic sleep deprivation, pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF-α) and interleukin one (IL-1) increase production of an inflammatory response caused by chronic sleep deprivation. Pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF-α) and interleukin one (IL-1) increase the production of cytokines that may be attributable to a possible exhaustion of the measured cytokine level for the Zol group may represent residual amounts of Zolendronate present after the initial immune response to the drug.

Methods

Thirty-two female ovariectomized Wistar rats were obtained and randomly placed in Control, Zolendronate (Zol), Sleep Deprived (SD), and Sleep Deprived with Zolendronate (SDZ) groups. Prior to experimental protocol the rats were injected with either saline or Zolendronate (Table 1) and then given a one-week adaption period. Starting at 14:00 each day all rats were placed in their respected tanks (Table 1) where the SD and SDZ groups would undergo sleep deprivation and the Control and Zol groups would socialize. The SD and SDZ groups were subjected to one of three random sleep cycles (Table 2) each night for five weeks to stimulate irregular sleep cycles, experienced by many post-menopausal women. During the scheduled time the SD and SDZ groups were being sleep deprived, the Control and Zol groups were able to socialize and sleep freely in the control tank.

After undergoing the designated amount of sleep deprivation/socialization all rats were placed back into their individual cages and allowed to sleep for the allotted amount of time based off a random number generator. Food and water were available ad libitum for all groups during the entire protocol.

Two Multiple Modified Platform (MMP) tanks, housing each the sleep deprived (SD) or sleep deprived and Zolendronate (SDZ) groups, were constructed according to the dimensions found in Figure 1. A third tank, lacking platforms and surrounding water, was used to house rats in the control (Con) and Zolendronate (Zol) groups.

Results

All data were treated by Analysis of Variance (ANOVA). Significance was accepted at p<.01. A Newman-Keuls post hoc test was employed to identify the significantly different group.

Conclusions

Significant changes in overall bone strength were not found as a result of sleep deprivation or Zolendronate injection, over the course of this five-week study. The lack of significant changes may be attributed to the short time frame of the study. While five weeks has proven to be sufficient time to induce chronic sleep deprivation and to allow Zolendronate to effect bone remodeling it was not a long enough time frame for mechanical testing to show the differences in bone metabolism and architecture.

There was a significant difference in the serum concentrations of TNF-α among the experimental groups. TNF-α levels were significantly higher in the Zol group than the control and SD and SDZ groups (p<.01). The high cytokine concentration in the Zol group may be due to the fact that Zolendronate has been shown to induce a transient fever in humans for twenty-one days after injection. Therefore, it may be possible that the measured cytokine level for the Zol group may represent residual amounts of the TNF-α present after the initial immune response to the drug.

While it was expected that the SD and SDZ groups would have elevated TNF-α concentrations due to sleep deprivation, the TNF-α concentrations of the SD and SDZ were comparable to those of the control group. This may be attributable to a possible exhaustion of the animals’ immune systems. These findings warrant further research measuring the changes in cytokine concentration throughout a longer sleep deprivation protocol to determine the fluctuations of TNFo due to sleep deprivation and Zolendronate and their effect on mechanical difference in bone strength.

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Literature Cited

Please visit the link below for a full list of literature cited.
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