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Evaluation of Tumor Necrosis Factor Alpha In Sleep-Deprived Menopausal-Induced Rats and The Impact On Bone Health

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Osteoporosis is a metabolic bone disorder characterized by a loss of bone mass and a deterioration of the tissue that can ultimately lead to compromised bone strength and an increased risk of fractures. The disease can affect a wide range of individuals of both sexes but is most prevalent among older women, particularly Caucasians (Cosman et al., 2014). Post-menopausal women are considerably more susceptible to the disease due to their significant decreased levels of estrogen. Estrogen deficiency directly causes a notable decrease in bone due to the role estrogen plays in osteoclast apoptosis. Without the ability to regulate osteoclastic apoptosis, bone resorption goes unmediated and results in a decrease in bone strength (Kameda et al., 1997). TNF Alpha (TNF α) is a proinflammatory cytokine that is directly involved in bone turnover by inhibiting mature osteoblasts (Kotrych., 2016). Cytokines are proteins that are able to interact and carry out integral functions between cells when released. When the body is deficient in estrogen, it will produce rapid resorption of bone caused by TNF α and will result in lower bone density and strength. TNF α inhibits bone-forming cells, osteoblasts, from maturing and consequently no more bone will form (Azuma et al., 2000). TNF α has also been seen in recent findings to promote the formation of bone breaking cells through osteoclastogenesis (Osta, Benedetti, & Miosecc, 2014). When the body is in a state of inflammation and TNF α is being secreted in high amounts, the effects on the bone can be detrimental due to the upregulation of the cells to tear down the bone and the inhibition of the cells to rebuild causing an imbalance. This current study evaluates the impact of chronic sleep deprivation and Zolendronate on the of TNF α of ovariectomized Wistar rats during a five-week sleep deprivation period.

**INTRODUCTION**

Thirty-two female, ovariectomized Wistar rats were randomly placed in Control (C), Zolendronate (Z), Sleep Deprived (SD), and Sleep Deprived with Zolendronate (SDZ) groups. The SD and SDZ groups underwent a five week sleep deprivation protocol using a MMPM tank while the C and Z groups were placed in control tanks. The C group was given an injection of 0.9% saline solution and the Z and SDZ groups were administered a dose of 10% mL/g Zolendronate. The experimental group rats were randomly placed into one of three possible sleep schedules following a one week adaptation period. After the five week sleep deprivation protocol, the rats were injected with ketamine and humanely sacrificed. Blood was collected from each animal for use in the TNF α ELISA Assay.

**METHODS**

It was expected that the concentration of TNF α would be increased in the rats that experienced the sleep deprivation and lower in those that were sleep deprived but given the Zolendronate treatment. This was the outcome seen as the sleep deprivation group had a mean of 25.557 pg/mL with a standard deviation of 2.563 pg/mL and the sleep deprivation group treated with Zolendronate had a mean of 24.017 pg/mL with a standard deviation of 2.171 pg/mL. Although the difference is not great, this can be attributed to length of the sleep deprivation condition being too short. With a longer time frame, based on previous research, sleep deprived groups would have a significantly larger concentration of the TNF α. The Zolendronate groups results were the opposite of what was expected. The rats treated with the bisphosphonate drug was seen to have the greatest concentration of TNF α whereas it was expected to have the lowest concentration. TNF α levels were significantly higher in the Zol group than both the control and SD, and SDZ groups (p<0.01) In human patients, Zolendronate has been seen to cause patients to have symptoms of transient fever for twenty-one days after injection of the drug. Therefore, the cytokine levels would be in a large concentration due to immune response accounting for this unexpected result. In regards to the similar values of the SD, control, and SDZ groups, this can be attributed to a possible immune system exhaustion of the animals. Based on these findings, more research must be done in this field of study to determine if Zolendronate would positively impact on bone health with patients who exhibit chronic sleep deprivation and in a post-menopausal state.

**RESULTS**

![Figure 1: TNF α concentration values](image)

<table>
<thead>
<tr>
<th>Group</th>
<th>Mean (pg/mL)</th>
<th>Standard Deviation (pg/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Con</td>
<td>23.974</td>
<td>1.871</td>
</tr>
<tr>
<td>Zol</td>
<td>27.257</td>
<td>2.220</td>
</tr>
<tr>
<td>SD</td>
<td>25.557</td>
<td>2.563</td>
</tr>
<tr>
<td>SDZ</td>
<td>24.017</td>
<td>2.171</td>
</tr>
</tbody>
</table>

**REFERENCES**


