Pharmacological Inhibition of Alternative Nf-Kb Pathway Ameiliorates Periodontitis after Ovariectomy in a Murine Model

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Many studies have highlighted an association between periodontitis and osteoporosis. The defective alternative NF-κB pathway has been demonstrated to prevent bone resorption triggered by LPS, the main culprit implicated in chronic periodontitis. In the present study, we utilized a well-established NF-κB inhibitor SN-52, which specifically targets alternative NF-κB pathway. Prior ethical approval for all animal experiments was obtained. *In vitro* osteoclastogenesis and osteoblastogenesis were performed based on previously described methods. An *in vivo* study involved the administration of either 2 µl of PBS or E. coli LPS (10µg/µl) into the palatal gingiva between the right maxillary first and second molars for one month. Concurrently, intraperitoneal injections were administered twice daily as follows: sham/PBS/Veh [sham operated (Sham)], sham/LPS/Veh, OVX/PBS/Veh, OVX/LPS/Veh (OVX-Veh), and OVX/LPS/inhibitor at a dosage of 25 mg /kg/day. Statistical differences among groups were evaluated using one-way analysis of variance (ANOVA). We have observed that SN52 exhibits a dose-dependent suppression of osteoclast formation induced by MCSF and RANKL. Additionally, there is an augment impact on osteoblast generation, as evidenced by ALP staining and quantification as well as by von Kossa staining and quantification on day 7 and day 21, respectively. Compared to PBS-injected control animals, there was an increased CEJ-ABC distance in maxilla in LPS-injected animals and OVX-LPS animals. Conversely, animals administered with SN52 injections demonstrated a reduced CEJ-ABC distance, indicating that the increase in CEJ-ABC distance induced by LPS was mitigated by SN52 treatment suggesting that inhibition of NF-κB by SN52 *in vivo* is effective in reducing the ABC-CEJ distance under conditions of LPS and estrogen deficiency. The current study underscores the potential of SN52 as a promising therapeutic agent to mitigate the detrimental effects of these factors on bone health, especially in conditions characterized by exacerbated bone diseases such as osteoporosis.

Keywords: Periodontitis, Osteoporosis, LPS, Murine model, NF-κB

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