Titanium particles in the surrounding tissue of oral implants could promote a local aseptic inflammatory response resulting in marginal bone resorption of osseointegrated implants

Macrophage polarization in aseptic bone resorption around dental implants induced by Ti particles in a murine model

Wang X, Li Y, Feng Y, Cheng H, Li D

Background

Titanium particles/ions detected in peri-implant tissues - a potential etiologic factor for crestal bone loss around oral implants.

- Titanium particles could induce marginal bone resorption around dental implants independent of bacterial infection.
- Local adverse inflammation microenvironment leading to peri-implant bone resorption is promoted by macrophage recruitment and macrophage polarization toward a pro-inflammatory M1 phenotype with production of inflammatory mediators.

Methods

- Sprague Dawley rats; 4 groups; titanium screw implanted in bilateral maxillary first molar area for 4 weeks for osseointegration; 20 μg titanium particles in peri-implant tissue to induce aseptic foreign body reaction.
- Macrophages depleted by local injection of 100 μL clodronate liposome (Ti + LipClod group).
- Titanium-injected rats treated with PBS (Ti + PBS) or empty liposome (Ti + Lip) and rats injected with PBS alone included as controls.
- Animals sacrificed at 8 weeks; samples collected; half analyzed radiologically to measure bone level change
- Macrophage markers (CD68, CCR7, CD163) also characterized by immunofluorescence to evaluate number, density, and phenotype distribution (CCR7+M1/CD163+M2).
- The rest of the samples used to determine the relative mRNA expression levels of TNF-α, IL-1β, IL-6, and RANKL with real-time PCR analysis.

Results

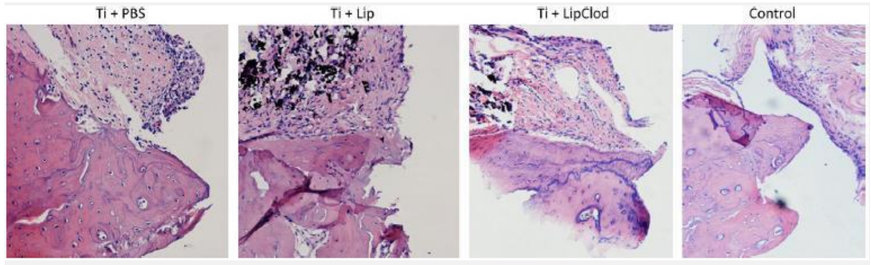

Figure. Representative images of hematoxylin and eosin stained sections 8 wk after treatment, 100× magnification. Notice the presence of a dense mixed inflammatory cell infiltrate in the Ti + PBS and Ti + Lip groups as compared to the Control and Ti + LipClod groups

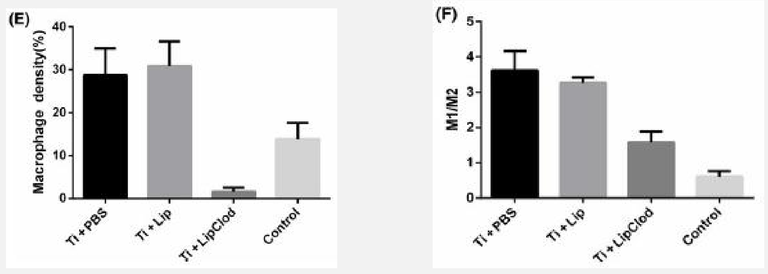

Figure. Quantification of total CD68 + macrophages in 3 randomly selected HPFs of four groups (left), quantification of the M1/M2 ratio in different groups (right)

Conclusion

Titanium particles had a negative effect on peri-implant tissue by activating macrophages which induced an M1 macrophage phenotype promoting local secretion of inflammatory cytokines. It was found that clodronate liposome treatment attenuated the severity of inflammation and bone loss by depletion of macrophages.

Table. Experimental Groups

Group	Treatment
Ti + PBS	20 mg Ti particles + 100 μL PBS
Ti + Lip	20 mg Ti particles + empty liposome (100 μL, i.v. every 3 d)
Ti + LipClod	20 mg Ti particles + clodronate liposome (initial dose at 100 μL, followed by 100 μL every 3 d, i.v.)
Control	100 μL PBS alone

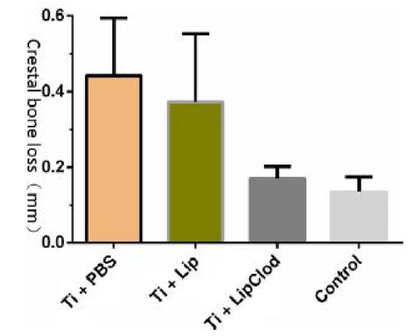

Figure. Average peri-implant crestal bone height changes as measured by the distance of the implant head to the alveolar bone crest on the mesial, distal, buccal, and palatal aspect of the fixtures

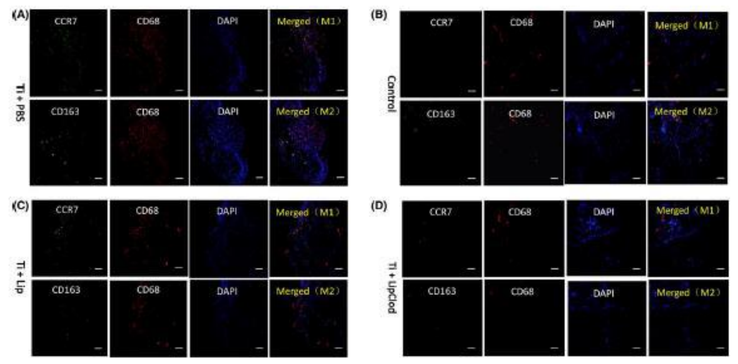

Figure. Altered M1 and M2 macrophage infiltrations around tissues bordering the bone resorption areas of implants. A and B, immunofluorescent images showed an increased infiltration of CD68 + CCR7 + M1 macrophages and a decreased infiltration of CD163 + M2 macrophages in the Ti + PBS and Ti + Lip groups. (n = 4). Scale bars, 50 μm. C, macrophages infiltrated in the Ti + LipClod group was decreased and presented as M1 phenotype. D, CD163 + M2 macrophages

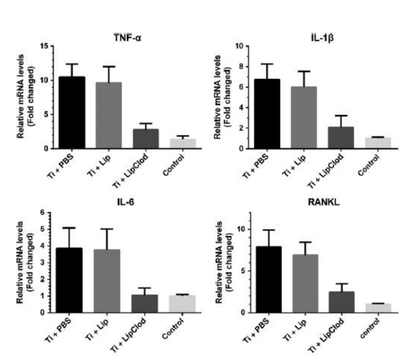

Figure. The mRNA expression levels of TNF-a, IL-1β, IL-6, and RANKL were presented as fold changes using real-time PCR

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