Vitamin D: A Modifiable Risk Factor for Endoprosthetic Implant Infection

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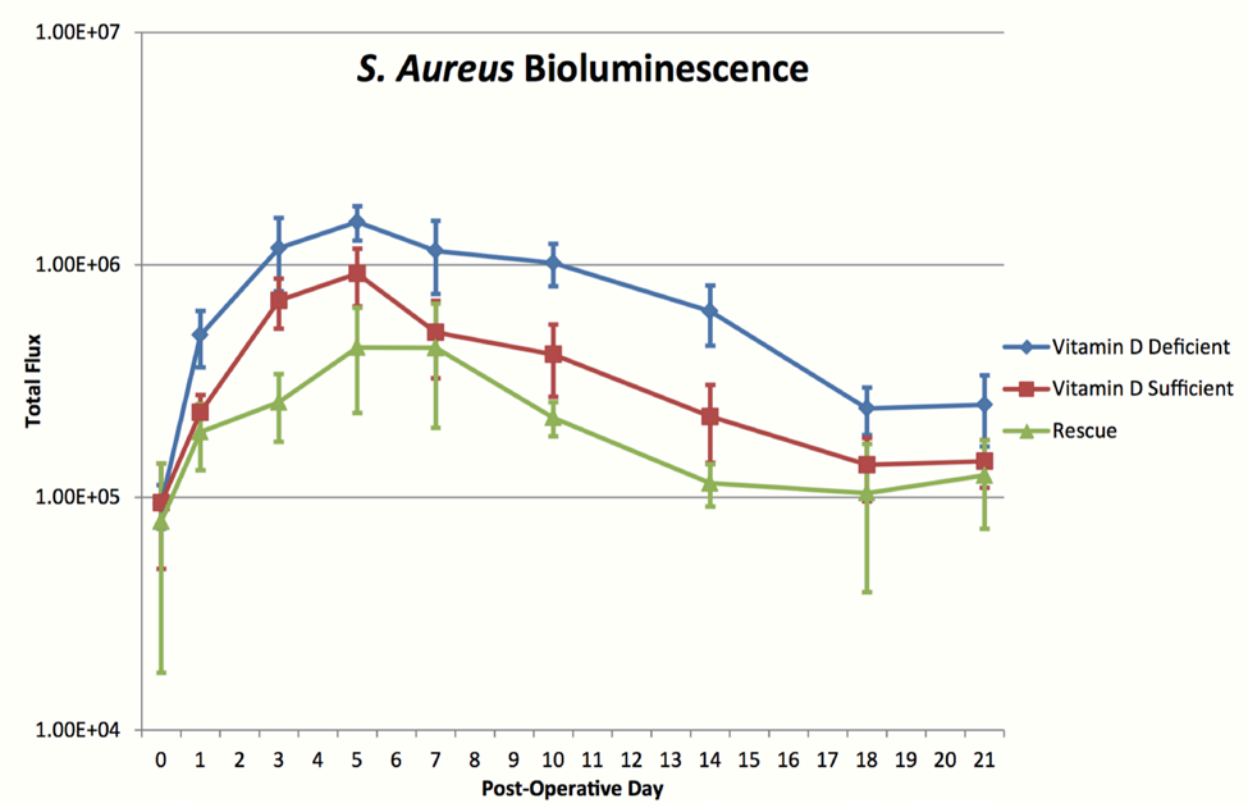
Introduction: While many of the factors rendering our endoprosthesis patient population especially vulnerable to implant infection are not modifiable – long surgeries, immunocompromised state, large metal burden – we as a community have not identified the modifiable factors at our disposal. While vitamin D is a known modulator of both innate and adaptive immunity, no studies to date have investigated the role of vitamin D as a modifiable risk factor for post-operative implant infection.

Questions/Purpose: This study uses an established *in vivo* mouse model of arthroplasty infection to **1)** evaluate the influence of vitamin D deficiency on periprosthetic infection and **2)** assess the modifiability of this factor by perioperatively "rescuing" a cohort of mice from their vitamin D-deficient state.

Methods used: Twenty-six male mice were randomized to receive a diet deficient of vitamin D (n=13) or a standard, vitamin D sufficient diet (n=13) for eight weeks preoperatively. The mice then underwent survival surgery in a well-established implant infection model in which a titanium implant was placed into the femur and inoculated with $1x10^3$ colony forming units (CFU) of a bioluminescent strain of S. aureus. Twenty-four hours post-operation, a subset of the vitamin D-deficient mice were "rescued" with an intraperitoneal injection of 3H-25D, an established method of rapidly restoring active vitamin D, then switched over to a vitamin D sufficient diet (rescue group). Infection and immune response were quantified longitudinally using bioluminescent and florescent imaging, respectively on postoperative days (POD) 0, 1, 3, 5, 7, 10, 14, 18, 21, and 28. Statistics were performed using t-test analysis to identify significant differences ($p<0.05$).

Results: Infection burden was significantly lower for mice with vitamin D sufficient diets than those with deficient diets at all time points ($p<0.05$). The immune response to the operation was also more robust in mice with a vitamin D sufficient diet ($p<0.05$) at all time points. The group rescued from vitamin D deficiency perioperatively was less susceptible to infection than the deficient group at all time points ($p<0.05$). The rescue group also showed lower infection burden on all days as compared to mice on a deficient diet.

Conclusions: Vitamin D deficiency was associated with increased infection burden and decreased immune upregulation after surgery in this established post-surgical infection model. The ability to rescue a cohort of deficient mice with an IP injection of 3H-25D underscores the causality of vitamin D deficiency in increasing post-arthroplasty infection, and perhaps more importantly, its modifiability. As vitamin D deficiency is common in patients undergoing endoprosthetic reconstructions, this is the first evidence that perhaps we should consider using the perioperative period to supplement vitamin D in order to decrease infection rates.


S. Aureus Bioluminescence
1.00E+07
1.00E+06
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Total Flux
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21
Post-Operative Day
Vitamin D Deficient
Vitamin D Sufficient
Rescue