Commentary & Perspective

Vitamin-D Supplementation: A Low-Risk, High-Gain Therapy to Prevent PJI?

Commentary on an article by Vishal Hegde, MD, et al.: "Single-Dose, Preoperative Vitamin-D Supplementation Decreases Infection in a Mouse Model of Periprosthetic Joint Infection"

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Total joint arthroplasties are common and can be compromised by periprosthetic joint infections (PJIs) that are primarily bacterial in nature. Could the solution to this problem be as simple as taking a vitamin D pill? The study by Hegde and colleagues suggests that it just might help.

Vitamin D comes in many forms. The U.S. Food and Drug Administration (FDA) has approved oral 25-hydroxyvitamin D_3 ($25D_3$), which is converted inside cells to the active metabolite 1,25-dihydroxyvitamin D_3 ($1,25D_3$). In this basic science study, Hegde and colleagues investigated $25D_3$ supplementation in a mouse model of PJI. Their data reveal that intraperitoneal supplementation with $25D_3$ may have a prophylactic role in arthroplasty.

Arthroplasties alleviate pain while restoring joint function and improving quality of life[1-3]. While the number of patients undergoing total joint arthroplasty exceeds 1 million per year in the U.S.[2], a serious complication of this procedure is the occurrence of a PJI, which erodes the surrounding soft tissues and bone, leading to pain, debility, and ultimately, septic implant loosening. Even though PJIs are not common, their impact on patients, surgeons, and the entire health-care system is enormous. Moreover, PJI remains one of the most commons reasons for early and late failure of total joint arthroplasty. As such, substantial efforts by many have focused on not only treating PJIs but also preventing them. Some epidemiological studies have indicated that most patients undergoing total joint arthroplasty are vitamin-D deficient, and vitamin-D status may correlate with PJI[4,5].

The epidemiological observations may be directly linked to the well-established fact that vitamin D is necessary for normal macrophage activity and inflammatory responses[6]. This mechanistic connection was tested by the current authors using a surgical model of PJI in which mice received a stainless-steel implant in the knee joint, followed by inoculation of the joint space with *Staphylococcus aureus.* Two groups of mice were fed either a vitamin-D_3 sufficient or deficient diet. Within the deficient cohort, a group of mice were "rescued" by $25D_3$ administration prior to surgery. The results essentially showed that vitamin $25D_3$ rescue treatment reduced bacterial burden and neutrophil infiltration by increasing the macrophage activity, as hypothesized. Therefore, the authors postulated that, if vitamin $25D_3$ reduces bacterial burden, 25D deficiency may be a modifiable risk factors in the setting of PJI.

The authors justifiably arrived at the modestly stated conclusion that 25D deficiency is a modifiable risk factor on the basis of their high-quality work and the candid acknowledgment of the technical limitations of working with mice. It remains to be established whether the beneficial effects of vitamin D will be observed in larger animal models or are translatable to patients. It is also important to note that decreasing bacterial burden through a number of important precautions in the operating theater does not necessarily decrease PJIs. However, the mouse data are intriguing and conceptually provocative, as this study makes a step toward a simple potential remedy—vitamin D supplementation—to reduce PJIs. Since vitamin D is relatively harmless if not useful, this potential strategy could be distinctly "low risk and high reward."

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