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Assessment of COVID-19 Vaccine Efficacy in Recipients of Allogeneic Hematopoietic Stem Cell Transplants: An Analysis of Booster Strategies

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Opinion Article

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DESCRIPTION

Allogeneic Hematopoietic Stem Cell Transplant (HCT) recipients represent a population at heightened risk of severe COVID-19, even following vaccination. However, the understanding of the immune response to SARS-CoV-2 vaccines, particularly in Recently Transplanted Patients (RTP), remains limited. In this single-center study was conducted and have investigated the cellular and humoral response to the mRNA-1273 (Spikevax®) vaccine in RTPs (n=49) compared to long-term transplanted patients (LTTP, n=19) and healthy controls at three time points: one and three months after the second dose, and one month after the third dose. Healthy controls did not receive a third dose, the findings revealed notable disparities in immune response among RTPs compared to both LTTPs and healthy controls. RTPs exhibited lower IgG anti-S1 titers than healthy controls at both T1 (mean 0.50 *vs* 0.94 arbitrary units -AU-, $p<0.0001$) and T2 (0.37 *vs* 0.79 AU, $p<0.0001$), indicating suboptimal humoral response. Moreover, RTPs had lower titers than LTTPs at T1 (0.50 *vs* 0.66, $p=0.01$), though no differences were observed at T2 (0.37 *vs* 0.40 AU, $p = 0.55$), suggesting delayed or attenuated antibody production in RTPs.

Similarly, the rate of positive T-cell responses was significantly lower in RTPs compared to controls at both T1 and T2 (61.2% vs 95%, $p=0.007$; 59.2% *vs* 100%, $p=0.001$, respectively), underscoring impaired cellular immunity following vaccination. However, no statistically significant differences in T-cell responses were observed between transplanted groups, indicating a uniform decline in cellular immunity among HCT recipients.

Interestingly, administration of a third vaccine dose (booster) elicited a positive response in approximately 50% of RTPs, effectively augmenting both humoral and cellular immunity.

However, active immunosuppressive treatment significantly hindered vaccine response, emphasizing the need for personalized vaccination strategies in this subgroup. Our study also sought to elucidate the influence of various factors, including immunosuppressive treatment, Graft-Versus-Host Disease (GVHD), and time since transplant, on vaccine response dynamics. While these variables likely impact immune function, further investigation is warranted to comprehensively understand their role in shaping vaccine efficacy in HCT recipients. Moreover, the findings underscore the importance of booster doses in enhancing vaccine-induced immunity, particularly in patients with suboptimal initial responses. Booster doses have emerged as a crucial strategy to sustain long-term protection against COVID-19, especially in immunocompromised populations such as HCT recipients. The study sheds light on the compromised immune responses to COVID-19 vaccines observed in recent Hematopoietic Stem Cell Transplant (HCT) recipients. Despite the significant strides made in vaccine development, recent transplant patients face hurdles in mounting adequate cellular and humoral immunity against SARS-CoV-2. These findings underscore the critical need for interventions to enhance vaccine efficacy in this vulnerable population. Booster doses emerge as a promising strategy to bolster immune responses and bridge the gap in vaccine-induced protection. By administering additional vaccine doses, we can potentially overcome the limitations of the initial vaccine series and provide heightened immunity against COVID-19. Furthermore, our study emphasizes the importance of personalized vaccination approaches tailored to the unique profiles of individual transplant recipients. Given the heterogeneity in immune function and treatment regimens among transplant patients, a one-size-fits-all vaccination strategy is inadequate. Instead, personalized vaccination plans that consider factors such as immunosuppressive therapy, time since transplant, and presence of Graft-Versus-Host Disease (GVHD) are essential to optimize vaccine response and efficacy.

Moreover, ongoing monitoring of immune response dynamics is crucial in guiding vaccination strategies and identifying patients who may benefit from booster doses. Regular assessment of both cellular and humoral immunity post-vaccination can provide valuable insights into vaccine effectiveness and inform clinical decision-making.

As we navigate the complexities of COVID-19 vaccination in HCT recipients, collaboration between transplant specialists, immunologists, and infectious disease experts is paramount. By leveraging multidisciplinary expertise, we can develop tailored vaccination protocols and optimize COVID-19 prevention strategies for this high-risk population.

In the era of emerging variants and evolving vaccination recommendations, continuous research and surveillance are essential to stay ahead of the curve. Longitudinal studies tracking immune responses over time, along with real-world data on vaccine breakthrough infections, will further inform vaccination strategies and ensure the ongoing protection of transplant recipients against COVID-19.

In summary, this study highlights the challenges faced by recent HCT recipients in mounting robust immune responses to COVID-19 vaccines. However, with the implementation of booster doses and personalized vaccination approaches, we have an opportunity to enhance vaccine efficacy and mitigate COVID-19 risk in this vulnerable

population. By prioritizing individualized care and ongoing monitoring, we can optimize COVID-19 prevention strategies and safeguard the health of transplant recipients in the face of this ongoing pandemic.