

Chill Burn after Cryotherapy in a Thrombocytopenic Recipient: The Adverse Effect of Thrombocytopenia on Dermal Wounding

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Abstract

Oral cryotherapy is an evidence-proven standard care for cancer patients. The efficacy of oral cryotherapy during chemotherapy is established especially for the treatment using melphalan. However, the patients' neutrophil and platelet are usually decreased when undergoing cytotoxic chemotherapy, and the influence of which has not been fully evaluated clinically. We experienced the case complicated with chill burn like skin wound by direct damage of cryotherapy and discussed the function of neutrophils and platelets in the process of wound healing.

Keywords: Cryotherapy; Stem cell transplantation; Thrombocytopenia; Oral care; Supportive care; Chill burn; Oncology

Case Report

A 64-year-old Japanese female diagnosed with aplastic anemia underwent stem cell transplantation (SCT) from an unrelated donor with a reduced-intensity conditioning regimen. Oral cryotherapy is the evidence-based standard for cancer patients [1], and transplant recipients are routinely treated with preparations containing high-dose melphalan, in collaboration with an oral care team. She therefore received preparation chemotherapy, consisting of fludarabine (25 mg/m²/day for five consecutive days, from day -6 to day -2; total 125 mg/m²) and melphalan (90 mg/m²/day for two consecutive days, day -3 and day -2; total 180 mg/m²) prior to stem cell infusion (day 0). Oral cryotherapy was performed on both days of melphalan administration, she received oral cryotherapy, consisting of orally administered ice chips and application of a refrigerant pack cooled to -20°C. Cooling was started 30 min before melphalan administration, continued through the 15 min of melphalan administration, and stopped 30 min after melphalan administration (total 75 min). Although this protocol eliminated oral mucositis, the patient developed a frostbite-like skin eruption 3 days before transplantation (Figure 1), lasting from day -3 to day 3. This eruption was temporary and cured itself, without progressing to erosion or ulceration.

Cryotherapy has been shown to be effective supportive care for patients receiving chemotherapy, which frequently induces oral mucositis [2,3]. Oral cryotherapy has been found to alleviate mucositis in patients treated with high-dose melphalan, together with both non-myeloablative [2] and myeloablative [3] treatment regimens. Although some adverse effects have been observed in clinical practice, these have never been reported in clinical studies due to their relatively low severity.

Several reports have described the effects of thrombocytopenia on wound healing [4,5]. Wound healing usually starts as platelet activation and hemostasis, but the role of platelets is not limited to coagulation. Rather, platelets are involved in other aspects of tissue protection. For example, thrombocyte count has been associated with increased levels of complement components and coagulation factors [6], which are required for tissue remodeling. In addition, platelet-derived growth factor (PDGF) and fibroblast growth factors



Figure 1: Frostbite-like skin rash (arrows) observed in the patient on the day of transplantation (day 0).

(FGF) secreted by thrombocytes have been shown to be attenuation factors involved in healing connective tissues [4]. Stromal cell-derived factor-1α (SDF-1α) is another important mediator of wound healing, recruiting CD34⁺ stem cells to local sites [5]. Neutrophils are also involved in the wound healing process [7]. PDGF and FGF promote angiogenesis and enhance the concentrations of additional cytokines, including tumor necrosis factor-α (TNF-α), in the microenvironment, suppressing inflammation and apoptosis and supporting healing reactions [5]. Recent clinical research has shown that cytokines in platelet-rich plasma (PRP) can promote the repopulation of fibroblasts and other soft tissue cells [8].

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Received December 29, 2015; **Accepted** January 30, 2016; **Published** February 07, 2016

Citation: Imataki O, Ohbayashi Y, Ohue Y, Oku M, Matsuka H, et al. (2016) Chill Burn after Cryotherapy in a Thrombocytopenic Recipient: The Adverse Effect of Thrombocytopenia on Dermal Wounding. J Oral Hyg Health 4: 196. doi: 10.4172/2332-0702.1000196

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This case study showed that oral cryotherapy can have adverse effects, especially when combined with a patient's hematological condition, such as thrombocytopenia and neutropenia. These adverse effects, however, are subtle and of low grade when assessed by clinical toxicity criteria (CTC-AE). These findings indicate that the degree of cooling of refrigerant packs be modified in cytopenic patients to avoid skin damage.

Competing Interests

The authors declare that they have no competing interests.

Conflict of Interest

The authors declare that they have no competing interests.

Ethics, Consent and Permissions

Informed consent to participate in the study was obtained from the participant.

Consent to publish

Informed consent to publish was obtained from the participant.

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