The painful necessity of chemotherapy and radiation treatments for cancer in children is often accompanied by further traumatizing adverse effects. One of these is oral mucositis (OM), characterized by mouth ulcers, erythema, edema, burning, and intolerance to spicy or hot foods. As OM significantly impacts quality of life, impedes nutrition, and can escalate into clinical infections, efficacious treatments for OM are a medical priority. Pycnogenol® (Horphag Research; Geneva, Switzerland) is a standardized French maritime pine (Pinus pinaster) bark extract that has been shown to have anti-inflammatory, antioxidant, and wound-healing activity. In addition to vitamin E's established antioxidant and wound-healing properties, it has been used in OM treatment and has a well-documented role in the repair and maintenance of cellular membranes. In spite of the urgent need, few pediatric trials for OM treatment have been conducted due to ethical and medical concerns. Thus, this randomized, single-blind, placebo-controlled trial assessing Pycnogenol and vitamin E in the treatment of OM in children with cancer is an important contribution to evidence-based treatment.

The trial was conducted at the Department of Pediatrics, CSM Medical University in Lucknow, India. The inclusion criteria were children aged 6-15 years on chemotherapeutic regimens who demonstrated clinical signs of chemotherapy-induced OM and were not scheduled for further chemotherapy during the 7-day evaluation period. Excluded were children who received head or neck radiotherapy, antiplatelet or anticoagulant therapy, or those who had pre-existing oral trauma, ulceration, or disease prior to chemotherapy.

As OM occurs with most types of chemotherapy, the primary outcome was any attenuation of mucositis regardless of the specific drug regimen. The availability of...
patients during the study period was a limiting factor. Initially, 85 children with chemotherapy-related OM were enrolled in the study, but 13 could not finish the protocol for various reasons; hence, the data for 72 children were reported. Included patients with acute lymphoblastic leukemia or acute myeloid leukemia were in either the induction or intensification phases of treatment, and patients with non-Hodgkin's lymphoma were on the MCP-842 protocol.

Enrolled patients were randomly assigned to receive either placebo (1:1, water:glycerine), 200 mg/day of vitamin E (Evion® Paediatric Drops; Merck Limited; Aurangabad, India), or 1 mg/kg per day of Pycnogenol. They were instructed to hold the solution in their mouths for 30 seconds and then swallow. To mask the astringent taste of Pycnogenol, both the Pycnogenol and vitamin E treatments were prepared as 1% (w/v) in the placebo solution. As it was unethical to withhold treatment, all patients were also given a uniform oral hygiene program (ultra-soft toothbrush for mechanical plaque removal and a 0.12% chlorhexidine-gluconate mouth rinse).

The treatments were topically administered 3 times daily for 1 week. OM severity was assessed using 3 validated scales. The functional World Health Organization (WHO) system rates the ability to eat (solids, liquids, or nothing) and total healing. The objective Oral Mucositis Assessment Scale (OMAS) scores OM according to the degree of ulcers and erythema at 8 oral sites, and the subjective Children's International Mucositis Evaluation Scale (ChIMES) is a qualitative scoring system for mouth pain and function.

On the WHO scale, 4.2% of patients in the placebo group were completely healed; while 75% and 58.3% were healed in the vitamin E and Pycnogenol groups, respectively. The 2 treatment groups had significantly more patients that completely healed than did the placebo group (P<0.001). Significant improvements in OMAS scores were also observed in the treatment groups as compared to the placebo group after 1 week of treatment (P<0.001). Based on the ChIMES scores, significant improvement in pain associated with eating, swallowing, and drinking was observed beginning at day 5 for the vitamin E group as compared with the placebo group (P=0.019), and beginning at day 4 for the Pycnogenol group as compared with the placebo group (P=0.004). On days 6 and 7, both treatment groups were significantly improved compared to the placebo group (P<0.001).

On all 3 scales (WHO, OMAS, and ChIMES), both vitamin E and Pycnogenol significantly improved OM in children as compared to placebo. Comparing the efficacy of vitamin E and Pycnogenol, there were no significant differences in the OMAS and ChIMES scores. On the WHO scale, the 2 treatments were equally effective in treating OM with severity grades of 1, 2, and 3. The only significant difference between the 2 treatments was in the grade 4 (greatest severity) OM scores: Pycnogenol was no better than placebo, while vitamin E "continued to show significant response."

As the progression of OM is largely associated with reactive oxygen species followed by an inflammatory response, it is suggested that the efficacy of vitamin E and Pycnogenol may be attributed to their antioxidant activity, although vitamin E also has documented wound-healing properties and Pycnogenol has been shown to modulate inflammatory signaling pathways. It is noted that while the sample size was relatively small, the use of multiple scoring instruments adds rigor to this study.
The authors conclude that vitamin E and Pycnogenol are safe, efficacious, and cost-effective treatments of OM in children, with the exception of grade 4 (greatest severity) OM where Pycnogenol was not effective. They point out that since the patients swallowed the mouthwash after rinsing, it is uncertain whether there may have also been additional benefits due to systemic absorption. They suggest further studies should be carried out to assess the combined benefit of vitamin E and Pycnogenol.

—Amy C. Keller, PhD

Reference


The American Botanical Council has chosen not to reprint the original article.