

Skin Toxicity

Clinical summary of the ONS Guidelines™ for cancer treatment–related skin toxicity

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Cancer treatment–related skin toxicities are a frequent and distressing side effect of antineoplastic therapies, especially chemotherapy and targeted therapies. Skin toxicities associated with these therapies can include rashes, hand-foot skin reaction, hand-foot syndrome, and hair loss. These symptoms cause not only physical pain and discomfort but also psychological distress, and they can become a stigma of the patient's cancer diagnosis. Skin toxicities can cause treatment delays and even discontinuation, which affects clinical outcome. The prevention of toxicities and effective, early management can reduce the risk for distress and treatment delays.

THIS DOCUMENT ACTS AS THE CLINICAL SUMMARY component of the ONS Guidelines™ for the management of cancer treatment–related skin toxicity (Williams et al., 2020), developed by a panel of oncology healthcare professionals after rigorous systematic review of high-quality randomized clinical trials. The guideline is designed to establish the evidence-based efficacy of interventions to prevent and manage cancer treatment–related skin toxicities. Sources of evidence have been divided into pharmacologic and nonpharmacologic interventions. The GRADE (Grading of Recommendations, Assessment, Development, and Evaluation) approach was used to assess the certainty of the evidence and make the recommendations presented in this clinical summary.

Guideline Questions and Target Audience

What is the efficacy of pharmacologic and nonpharmacologic interventions that prevent or minimize skin, hair, and nail reactions associated with cancer treatments? The target audience for this guideline are clinicians who care for individuals treated for cancer, policymakers, and patients and their caregivers.

How the Guideline Was Developed

This guideline was developed by an interprofessional panel of healthcare professionals, a methods expert, and a patient representative. The panel prioritized clinical questions related to the management of cancer treatment–related skin toxicities and outcomes identified as critical for decision making. A systematic review and network meta-analysis of the literature was conducted to inform the clinical questions. The GRADE approach was used to assess the certainty of the evidence and provide a foundation for recommendations (Guyatt et al., 2011).

Why the Guideline Matters

Skin toxicities and changes associated with treatment are some of the most distressing adverse events for patients with cancer. They are a physical sign of the disease and can cause emotional turmoil (Salzmann et al., 2019). Skin changes not only are associated with psychologic distress, but they also induce pain and pruritus, and can contribute to infection that warrants treatment delays and discontinuation. However, prevention of toxicities and appropriate management can improve the treatment experience for patients with cancer. The guideline provides recommendations for clinicians to prevent or minimize skin toxicities in patients undergoing cancer treatment.

KEYWORDS

dermatologic adverse events; rash;
alopecia; hand-foot skin reaction; taxanes

DIGITAL OBJECT IDENTIFIER

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These recommendations intend to balance patient preference and potential harm associated with prevention and management strategies.

Skin toxicities addressed in this guideline include epidermal growth factor receptor inhibitor (EGFRI) rash, hand-foot skin reaction, hand-foot syndrome (or palmar-plantar erythroderma), and chemotherapy-induced alopecia (see Table 1). Skin toxicities are associated with various antineoplastic agents, including targeted agents, novel immunotherapies, and cytotoxic chemotherapy agents. Given the wide range of treatments associated with skin toxicities, these effects are reported in as many as 90% of patients undergoing cancer treatment (Salzmann et al., 2019).

Clinical Practice Recommendations

Assessment of Cancer Treatment–Related Skin Toxicities

Cancer treatment–related skin toxicities can be challenging to assess. They are associated with conventional therapy as well as novel treatment options. Comprehensive assessment should include identifying and grading physical symptoms. Depending on the type of toxicity being experienced, physical assessment may include size of lesions and extent of rash, extent of body surface area affected, presence of inflammation, and signs of infection. Subjective assessment should include impact on quality of life and severity, including intensity, timing, duration, characteristics and associated symptoms, distress, and aggravating and relieving factors (De Tursi et al., 2017).

Acneform rash is common among patients receiving EGFRI and typically presents during the initial one to six weeks of therapy, appearing primarily on the head and upper body (Lacouture et al., 2011). Hand-foot skin reaction, commonly associated with multikinase inhibitor therapy, presents in the initial two to six weeks of therapy. Typical presentation includes blistering of the skin, followed by changes in pigmentation (De Wit et al., 2014). Hand-foot syndrome is most commonly associated with standard cytotoxic agents, such as capecitabine; taxanes; and targeted therapies. Appearing within a day to several weeks after treatment starts, hand-foot syndrome presents with dysesthesia, paresthesia, and erythema of the palms and soles. These untoward symptoms can significantly affect quality of life and the ability to complete treatment as scheduled (Nikolaou et al., 2016). Despite advances in novel treatments, chemotherapy-induced alopecia remains one of the most distressing and stigmatizing effects of cancer treatment. Incidence varies, with hair loss occurring in 10%–100% of chemotherapy regimens (Rossi et al., 2017). Assessment includes discussion with the patient about risk based on the type of chemotherapy regimen prescribed.

Interventions for Skin Toxicity Prevention and Management

It is important to note that in the prevention and management of skin toxicities, interventions were compared with usual care.

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Usual care includes general skin care education to avoid topical products with fragrances or alcohol, as well as to use mild soap and water for routine bathing, a cream-based moisturizer, and a broad-spectrum sunscreen with an SPF of 30 or higher (Williams et al., 2020). Any interventions for the prevention and management of cancer treatment–related skin toxicities should include this education as well.

In addition, several skin toxicity interventions were evaluated in the prophylactic and treatment settings. Once dermatologic symptoms appear, there are interventions that can mitigate these untoward events, optimize quality of life, and maintain adherence to cancer treatment schedules. The ONS Guidelines panel reviewed the evidence surrounding skin toxicity intervention strategies and sought to weigh evidence of beneficial outcomes with potential harm, including added side effects and cost of treatment, to make recommendations for practice.

EPIDERMAL GROWTH FACTOR RECEPTOR INHIBITOR: Antibiotic therapy with tetracycline, minocycline, or doxycycline can be considered in the prophylactic setting for patients on EGFRI. These antibiotics are not without side effects or complications; therefore, based on the level of evidence, the ONS Guidelines™ panel suggests weighing the risks of antibiotic side effects with the potential benefit of preventing skin rash and improving quality of life during EGFRI therapy (Williams et al., 2020). Evidence suggests some efficacy in skin rash prophylaxis with antibiotic therapy; however, based on patient preference and clinical status, providers may choose to delay antibiotic therapy until the patient presents with a rash.

Acneform rashes commonly develop in the setting of EGFRI therapy and place the patient at risk for discomfort and treatment delays. Management of acneform rash of any severity can include oral antibiotic therapy with tetracycline, minocycline, and doxycycline accompanied by a topical steroid. There are additional side effects and costs associated with these therapies, but in the

TABLE 1.
SUMMARY OF RECOMMENDATIONS: ONS GUIDELINES™ FOR SKIN TOXICITIES IN PATIENTS WITH CANCER

RECOMMENDATION	STRENGTH OF RECOMMENDATION	CERTAINTY OF EVIDENCE
EGFRI rash		
<p>Recommendation 1 (prevention): Among individuals who are receiving EGFRIs, the ONS Guidelines™ panel suggests either prophylactic oral antibiotics or no prophylactic oral antibiotics for the prevention of skin rash.</p> <p>Remarks: Individuals who place a higher value on prevention of rash and a lower value on possible side effects of antibiotics may prefer to start oral antibiotics prophylactically. Individuals who place a higher value on avoiding unnecessary medication may prefer to not use antibiotics until symptoms present.</p>	Conditional	Very low
<p>Recommendation 2 (treatment): Among individuals who are receiving EGFRIs who have developed grade 1–3 acneform rash, the ONS Guidelines panel suggests topical corticosteroids and oral antibiotics in addition to usual skin care rather than usual skin care alone.</p>	Conditional	Very low
Hand-foot skin reaction		
<p>Recommendation 3 (prevention): Among individuals receiving MKIs at risk for hand-foot skin reaction, the ONS Guidelines panel suggests topical urea and topical steroids in addition to usual care rather than usual care alone.</p>	Conditional	Moderate/low
<p>Recommendation 3 (treatment): Among individuals receiving MKIs with hand-foot skin reaction, the ONS Guidelines panel suggests topical urea and topical steroids in addition to usual care rather than usual care alone.</p>	Conditional	Very low
Hand-foot syndrome		
<p>Recommendation 4: Among individuals receiving capecitabine, the ONS Guidelines panel suggests no treatment rather than prophylactic oral pyridoxine (vitamin B₆) for the prevention of hand-foot syndrome.</p>	Conditional	Low
<p>Recommendation 5: Among individuals receiving taxane-based chemotherapy regimens, the ONS Guidelines panel suggests cooling procedures rather than no cooling procedures for prevention of hand-foot syndrome.</p>	Conditional	Very low
Chemotherapy-induced alopecia		
<p>Recommendation 6: Among individuals with cancer receiving cytotoxic agents associated with chemotherapy-induced alopecia who are concerned about alopecia, the ONS Guidelines panel suggests scalp cooling rather than no scalp cooling for the minimization or reduction in severity of alopecia.</p> <p>Remarks: If an individual is seen at a facility without a cooling system, a cap can be used because they have similar efficacy.</p>	Conditional	Very low
<p>Recommendation 7: Among individuals with cancer on cytotoxic treatment at risk for alopecia, the ONS Guidelines panel suggests topical minoxidil rather than no treatment for the shortening or minimization of alopecia.</p> <p>Remarks: Individuals preferring to minimize or shorten hair loss may wish to use minoxidil.</p>	Conditional	Very low
<p>EGFRI—epidermal growth factor receptor inhibitor; MKI—multikinase inhibitor; ONS—Oncology Nursing Society Note. From “ONS Guidelines™ for Cancer Treatment–Related Skin Toxicity,” by L.A. Williams, P.K. Ginex, G. Ebanks, K. Gantzig, K. Ciccolini, B.Y. Kwong, . . . R.L. Morgan, 2020, <i>Oncology Nursing Forum</i>, 47(5), p. 543. Copyright 2020 by Oncology Nursing Society. Reprinted with permission.</p>		

literature reviewed by the ONS Guidelines panel, antibiotic and topical steroid treatment limited the severity of the acneform rash, with benefits outweighing the calculated harms (Williams et al., 2020).

HAND-FOOT SKIN REACTION: Hand-foot skin reaction is associated with multikinase inhibitor therapies. The ONS Guidelines panel recommends urea and corticosteroid topicals in the prevention of hand-foot skin reaction associated with these treatments for any grade of hand-foot skin reaction (Williams et al., 2020). For hand-foot skin reaction treatment rather than usual care only,

the treatment recommendation is usual care and application of a topical urea and a topical steroid. The same evidence suggests potential efficacy of topical urea and topical steroids in hand-foot skin reaction management as well as prophylaxis (Williams et al., 2020).

HAND-FOOT SYNDROME: The ONS Guidelines panel recommends cooling procedures in patients receiving taxane-based chemotherapy regimens to prevent hand-foot syndrome. In studies evaluated, the cooling procedure consisted of applying a frozen glove or sock to one of the patient’s limbs to prevent

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the development of hand-foot syndrome and nail toxicities in the limb in which the cooling sock or glove was applied. The cooling procedure should occur during the infusion of the taxane-based agent. The recommendation is based on balancing potential benefit with the risk of patient discomfort and opportunistic infection (Williams et al., 2020).

CHEMOTHERAPY-INDUCED ALOPECIA: For patients receiving cytotoxic agents associated with the development of alopecia, the ONS Guidelines panel recommends the use of scalp cooling to prevent or minimize treatment-induced hair loss. Cooling procedures are not without adverse events, including reports of headaches, discomfort, and dizziness. Few reports suggest that scalp cooling is associated with scalp metastasis and cold thermal injury, but the procedure requires additional study (Belum et al., 2016). For these reasons, the ONS guidelines panel recommends this therapy only in patients who have calculated risk and benefit and show concern for alopecia associated with treatment. It should be noted and reinforced to the patient that scalp cooling will not prevent hair loss in any other parts of the body. If a treatment facility has access to a cooling system, trained personnel should be responsible for application and removal. Cooling systems may not be available at all treatment centers, and in those instances, the ONS Guidelines panel recommends an ice cap; however, the responsibility for correct use falls on the patient and caregiver (Williams et al., 2020).

Topical minoxidil has long been prescribed to prevent hair loss associated with male pattern baldness. Although research demonstrates mixed results, there is evidence suggesting its efficacy in the minimization of chemotherapy-induced alopecia. The ONS Guidelines panel recommends topical minoxidil for the minimization of chemotherapy-induced alopecia (Williams et al., 2020). For this indication, minoxidil can be applied twice daily.

Clinical Practice

Interventions Not Recommended

Oral pyridoxine (vitamin B₆) is sometimes considered in the prophylactic setting for patients at risk for hand-foot syndrome associated with capecitabine therapy. The studies reviewed for this guideline did not appear to show benefit in the prevention of hand-foot syndrome at any grade. Given the side effects of pyridoxine (vitamin B₆), particularly at higher doses, the ONS Guidelines panel does not recommend this therapy in the prophylaxis of hand-foot syndrome. The panel limited its recommendations to patients treated with capecitabine, because the studies evaluated were limited to this cancer therapy (Williams et al., 2020).

Implications for Nursing

Skin toxicities can significantly affect quality of life, lead to treatment delays, and, most importantly, affect clinical outcomes in

IMPLICATIONS FOR PRACTICE

- Assess patients undergoing cancer treatment for skin toxicities; this assessment should include intensity and severity, body surface area affected, and potential for superinfection.
- Discuss intervention benefits balanced with potential adverse events with each patient to identify agreeable options. Pharmacologic and nonpharmacologic evidence-based interventions are available for cancer treatment-related skin toxicities.
- Effectively manage cancer treatment-related skin toxicities to reduce patient distress and treatment delays. Antibiotics, topical urea, and topical steroids, as well as minoxidil, cooling procedures, and usual skin care recommendations, demonstrate efficacy in the prevention and management of cancer treatment-related skin toxicities.

patients receiving cancer therapy. The type of skin reaction and associated management varies depending on the class of therapy prescribed to the patient. Nurses are critical to the assessment and early recognition of skin toxicities. Evidence-based measures to prevent and decrease the severity of skin toxicities can improve quality of life and treatment outcomes for patients with cancer.

Conclusion

The questions explored in this guideline addressed overarching questions aimed at determining the efficacy of pharmacologic and nonpharmacologic interventions that prevent, minimize, or treat skin and hair reactions associated with certain cancer treatments. This guideline was developed using rigorous methodology to assess the certainty and quality of the evidence for treatment-related skin toxicities. Evidence-based interventions are available, and patients who are at risk for or who are experiencing skin toxicities have options to consider.

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