

Appendix O: Optional Treatment Modalities

The RNAO expert panel has identified biological agents, adjunctive therapies and surgery as treatment options for foot ulcers that do not heal at the expected rate. While many of the suggested treatment options are beyond of scope of nursing, the RNAO expert panel was inclusive of potential treatment options available in an interprofessional environment.

Biologic Agents and Associated Evidence

BIOLOGIC AGENTS	DESCRIPTION AND EVIDENCE
<p>Growth Factors</p>	<p>RECOMBINANT HUMAN PLATELET DERIVED GROWTH FACTOR (BB/PDGF) REGRANEX®</p> <ul style="list-style-type: none"> ■ Becaplermin gel, also known as Regranex®, is a type of growth factor. ■ The biological activity of becaplermin is similar to that of naturally-occurring PDGF, which promotes chemotaxis and the proliferation of cells involved in the wound repair process (Smiell, 1998). ■ Topical application of becaplermin gel promotes wound bed vascularization. <p>EVIDENCE:</p> <p><i>Four multicentre, randomized group studies found that one topical application of becaplermin gel daily in conjunction with appropriate ulcer care was effective and well-tolerated in clients with full-thickness, lower extremity diabetic ulcers (Smiell et al., 1999).</i></p>
<p>Bioactive Agents/ Emerging Pharmacotherapeutics (not publicly available at the time of guideline publication)</p>	<p>CHRYSALIN® (RUSALATIDE ACETATE OR TP508)</p> <ul style="list-style-type: none"> ■ Chrysalin, or TP508, is a 23-amino acid peptide similar to the sequence of amino acids in human thrombin, a clotting factor (Fife et al., 2007). ■ Unlike thrombin, Chrysalin does not have enzymatic properties and is not involved with blood coagulation (Fife et al., 2007). ■ Chrysalin may improve the rate of wound healing and closure in chronic ulcers (Fife et al., 2007). <p>EVIDENCE:</p> <p><i>In a phase I and phase II placebo-controlled trial of 60 people with diabetic foot ulcers, 10 µg of Chrysalin applied topically, twice weekly, improved tissue repair and increased wound closure (Fife et al., 2007).</i></p>

BIOLOGIC AGENTS	DESCRIPTION AND EVIDENCE
	<p>IMMUNOKINE (WF10)</p> <ul style="list-style-type: none"> ■ Immunokine, or WF10, is an aqueous solution of the chlorite drug OXO-K993 given intravenously to treat chronic inflammatory disorders (Yingsakmongkol, Maraprygsavan & Sukosit, 2011). ■ Topical application of WF10 has been shown to improve wound healing and enhance granulation tissue formation in various types of wounds (Yingsakmongkol et al., 2011). <p>EVIDENCE:</p> <p><i>Yingsakmongkol et al. (2011) conducted a randomized controlled trial to evaluate the effect of WF10 as an adjunct to the standard treatment of diabetic foot ulcers. The addition of WF10 to standard wound care significantly enhanced the formation of granulation tissue, and reduced infection, inflammation, necrotic tissue, and overall wound severity score (Yingsakmongkol et al., 2011).</i></p>

Adjunctive Therapies and Associated Evidence

TYPE OF ADJUNCTIVE THERAPY	DESCRIPTION AND EVIDENCE
<p>Electric Stimulation</p>	<ul style="list-style-type: none"> ■ Electrical stimulation involves applying a low level electrical current to the base of the wound or peri-wound using conductive electrodes. ■ This procedure should be performed by trained health-care professionals. <p>EVIDENCE:</p> <p><i>A meta-analysis by Foster, Smith, Taylor, Zinkie and Houghton (2004) of 17 randomized controlled trials showed that electrical stimulation was effective in treating chronic wounds. Included in this analysis were three trials with clients with diabetic foot ulcers.</i></p>
<p>Extracorporeal Shock Wave Treatment (ESWT)</p>	<ul style="list-style-type: none"> ■ ESWT is a new technology using shockwaves to treat chronic, painful conditions of the musculoskeletal system. ■ A shockwave is an intense and short energy wave traveling faster than the speed of sound. <p>EVIDENCE:</p> <p><i>Wang et al. (2009) conducted a prospective randomized controlled trial to evaluate the efficacy of ESWT in chronic diabetic foot ulcers compared to hyperbaric oxygen therapy. The ESWT group showed 31% healing versus 22% in the hyperbaric oxygen therapy group.</i></p>
<p>Hyperbaric Oxygen Therapy (HBOT)</p>	<ul style="list-style-type: none"> ■ Subatmospheric oxygen is delivered through a hyperbaric chamber and inhaled by the client. ■ HBOT increases oxygen tension in the tissues. <p>EVIDENCE:</p> <p><i>The routine management of diabetic foot ulcers with HBOT is not justified by the evidence found in the systematic review conducted by Kranke, Bennett and Roeckl-Wiedmann (2004). Although HBOT significantly reduced the risk of major amputation and may improve the probability of wound healing at 1 year, economic evaluations should be undertaken. With methodological shortcomings and poor reporting of the studies that were reviewed, Kranke et al. (2004) caution that any benefit from HBOT will need to be examined further using rigorous randomized trials.</i></p>

TYPE OF ADJUNCTIVE THERAPY	DESCRIPTION AND EVIDENCE
<p>Negative Pressure Wound Therapy (NPWT)</p>	<ul style="list-style-type: none"> ■ Subatmospheric pressure is delivered to the wound by a dressing covered with a clear membrane. ■ The dressing is attached to a pump that delivers intermittent or continuous suction within a prescribed range of settings. <p>EVIDENCE:</p> <p><i>The RNAO expert panel reached consensus to support the Health Quality Ontario: Ontario Health Technology Advisory Committee (OHTAC, 2010) in recommending NPWT as an effective treatment option in the management of diabetic foot ulcers. The OHTAC (2010) review of randomized controlled trials found evidence that:</i></p> <ul style="list-style-type: none"> ■ <i>The proportion of clients who achieved complete wound closure was significantly higher in the NPWT group than the control group.</i> ■ <i>The duration of therapy and median time to complete ulcer closure was shorter in the NPWT group than the control group.</i> ■ <i>The decrease in wound area from baseline was significantly greater in the NPWT group than the control group.</i>



Surgeries and Associated Evidence

SURGERY	DESCRIPTION AND EVIDENCE
<p>Achilles Tendon Lengthening</p>	<ul style="list-style-type: none"> ■ Achilles Tendon Lengthening is a surgical procedure that involves lengthening the tendon or attached calf muscle to reduce stress on the foot. ■ This procedure is effective at reducing ulcer recurrence in people with diabetes, peripheral neuropathy and a plantar ulcer (Mueller et al., 2004). <p>EVIDENCE:</p> <p><i>In a randomized clinical trial, Mueller et al. (2004) compared the effect of total contact casting alone to total contact casting combined with Achilles tendon lengthening in clients with diabetic foot ulcers. Outcome measures included healing rates and ulcer re-occurrence at the 7-month and 2-year follow-up. Although initial wound healing outcomes were similar, a significant reduction in ulcer re-occurrence was noted in the group with Achilles tendon lengthening at subsequent follow-up visits.</i></p>
<p>Other surgical procedures</p>	<ul style="list-style-type: none"> ■ Surgery for foot deformities in clients with diabetes can be beneficial in preventing the re-occurrence of ulcers. ■ Options include: arthroplasty, digital amputation, bunionectomy, metatarsal osteotomy, ray resection, tendon tenotomy or skin grafting. ■ Surgery may not be a viable option for select populations with impaired vascular supply. <p>EVIDENCE:</p> <p><i>To date, only anecdotal results are available.</i></p>