

EVIDENCE BASED STATEMENT

DOMAIN 8, Statement 7

TOPIC: "PENTOXIFYLLINE EVIDENCE-BASED USE IN CHRONIC VENOUS DISEASE MANAGEMENT"

SEARCH TERMS & SOURCES

(pentoxifylline) AND ((vein) OR (venous))
PubMed, Embase and Cochrane Library

INCLUSION CRITERIA

Indexed Journal, English Language, lower limb
Reviews, <10 y.

SEARCH RESULT BEFORE - AFTER SELECTION

23 (before) - 12 (after selection)

PERTINENT LITERATURE NOT IDENTIFIED BY THE LITERATURE SEARCH

1. Sun S, Li Y, Gao Y, Ran X. Efficacy and Safety of Pentoxifylline for Venous Leg Ulcers: An Updated Meta- Analysis. Int J Low Extrem Wounds. 2021; 1-11.
2. Zhang M, Xu YJ, Mengi SA, Arneja AS, Dhalla NS. Therapeutic potentials of pentoxifylline for treatment of cardiovascular diseases. Exp Clin Cardiol. 2004 Summer;9(2):103-11

EVIDENCE BASED STATEMENT

Domain 8; Statement 7

IDENTIFIED REFERENCES

(from the most recent down)

1. Chaitidis N, Kokkinidis DG, Papadopoulou Z, et al. Management of Post-thrombotic Syndrome: A Comprehensive Review. *Curr Pharm Des.* 2022;28(7):550-559.
2. Pompilio G, Nicolaidis A, Kakkos SK, Integlia D. Systematic literature review and network Meta-analysis of sulodexide and other drugs in chronic venous disease. *Phlebology.* 2021 Oct;36(9):695-709.
3. Kitchens BP, Snyder RJ, Cuffy CA. A Literature Review of Pharmacological Agents to Improve Venous Leg Ulcer Healing. *Wounds.* 2020 Jul;32(7):195-207.
4. Nicolaidis AN. The Most Severe Stage of Chronic Venous Disease: An Update on the Management of Patients with Venous Leg Ulcers. *Adv Ther.* 2020 Feb;37(Suppl 1):19-24.
5. Bonkemeyer Millan S, Gan R, Townsend PE. Venous Ulcers: Diagnosis and Treatment. *Am Fam Physician.* 2019 Sep 1;100(5):298-305.
6. Ahmadi M, Khalili H. Potential benefits of pentoxifylline on wound healing. *Expert Rev Clin Pharmacol.* 2016;9(1):129-42.
7. Pascarella L, Shortell CK. Medical management of venous ulcers. *Semin Vasc Surg.* 2015 Mar;28(1):21-8.
8. Varatharajan L, Thapar A, Lane T, Munster AB, Davies AH. Pharmacological adjuncts for chronic venous ulcer healing: a systematic review. *Phlebology.* 2016 Jun;31(5):356-65.
9. Maessen-Visch MB, de Roos KP. Dutch Venous Ulcer guideline update. *Phlebology.* 2014 May;29(1 suppl):153-156.
10. Ubbink DT, Santema TB, Stoekenbroek RM. Systemic wound care: a meta-review of cochrane systematic reviews. *Surg Technol Int.* 2014 Mar;24:99-111.
11. Jull AB, Arroll B, Parag V, Waters J. Pentoxifylline for treating venous leg ulcers. *Cochrane Database Syst Rev.* 2012 Dec 12;12(12):CD001733.
12. Brölmann FE, Ubbink DT, Nelson EA, et al. Evidence-based decisions for local and systemic wound care. *Br J Surg.* 2012 Sep;99(9):1172-83.

EVIDENCE BASED STATEMENT

Domain 8; Statement 7

TEXT FOR INCLUSION IN THE DOCUMENT

(300 words, not counting the references)

DOMAIN 8, Statement 7, TOPIC: “**PENTOXIFYLLINE EVIDENCE-BASED USE IN CHRONIC VENOUS DISEASE MANAGEMENT**”

Pentoxifylline is a xanthine derivative drug prescribed for arterial claudication, venous ulceration and severe alcoholic hepatitis. Its actions include reduction of blood viscosity by erythrocyte aggregation and fibrinolysis stimulation.

It also demonstrated to improve leukocyte deformability and chemotaxis, while inhibiting neutrophil degranulation and endothelial leukocyte adhesion. Pentoxifylline can lower the production of inflammatory cytokines.

[Zhang M, Xu YJ, Mengi SA, Arneja AS, Dhalla NS. Therapeutic potentials of pentoxifylline for treatment of cardiovascular diseases. *Exp Clin Cardiol.* 2004 Summer;9(2):103-11].

A recent meta-analysis identified a total of 13 randomized clinical trials reporting how, compared with placebo, pentoxifylline significantly improved the ulcer healing rate (RR = 1.59, 95%CI 1.22 to 2.07, P < .001) and the improvement rate (RR = 2.36, 95%CI 1.31 to 4.24, P = .004). Pentoxifylline also shortened mean duration of complete wound healing (P = .007) and reduced ulcer size (P = .02).

Among the side effects, it increased the incidence of gastrointestinal disturbances (RR = 2.29, 95%CI 1.04 to 5.03, P = .04).

***[Sun S, Li Y, Gao Y, Ran X. Efficacy and Safety of Pentoxifylline for Venous Leg Ulcers: An Updated Meta- Analysis. *Int J Low Extrem Wounds.* 2021; 1-11].**

In another systematic review assessing pentoxifylline outcomes, sulodexide resulted not inferior to pentoxifylline.

[Pompilio G, Nicolaidis A, Kakkos SK, Integlia D. Systematic literature review and network Meta-analysis of sulodexide and other drugs in chronic venous disease. *Phlebology.* 2021 Oct;36(9):695-709].

More evidence is needed to high-certainty recommendations. Large-scale, well-designed randomized clinical trials are warranted.

EVIDENCE BASED STATEMENT

Domain 8; Statement 7

STATEMENT FOR PUBLIC EVIDENCE-BASED AWARENESS

DOMAIN 8, Statement 7

“Pentoxifylline can be used in venous ulcer management. International guidelines are not univocal in its indication: the drug use must follow proper evaluation of the expert physician”

4 SELECTED REFERENCES

1. Zhang M, Xu YJ, Mengi SA, Arneja AS, Dhalla NS. Therapeutic potentials of pentoxifylline for treatment of cardiovascular diseases. *Exp Clin Cardiol.* 2004 Summer;9(2):103-11
2. *Sun S, Li Y, Gao Y, Ran X. Efficacy and Safety of Pentoxifylline for Venous Leg Ulcers: An Updated Meta- Analysis. *Int J Low Extrem Wounds.* 2021; 1-11
3. Pompilio G, Nicolaidis A, Kakkos SK, Integlia D. Systematic literature review and network Meta-analysis of sulodexide and other drugs in chronic venous disease. *Phlebology.* 2021 Oct;36(9):695-709

identified LITERATURE BIAS

Not complicated ulcers are usually included in the studies.

SUGGESTED NEXT LINES OF RESEARCH

Large-scale, well-designed randomized clinical trials