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Case Study

Topical Heparin Preparation in the Treatment of Varicose Veins with Superficial Thrombophlebitis

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Abstract

The varicose syndrome of the lower extremities is characterized by symptoms and signs that are the result of inflammatory processes, the cause of which is venous hypertension and related damage to the structure and function of the veins. Early symptoms include soreness, heaviness and swelling of the legs, cramps, itching, tingling and restlessness in the legs. The proportion of patients with any of the mentioned venous symptoms increases significantly with the CEAP clinical classification, and it is associated with a reduced quality of life, especially with regards to pain, physical function and mobility. Early detection and treatment of varicose syndrome stops the progression of the disease [1].

Heparin was discovered in 1916 and has been in clinical use for almost half a century [2,3]. The goal of topical heparin therapy is to achieve an optimal concentration of heparin locally and a very low in the systemic circulation, in order to achieve the best possible systemic tolerability. It is used alone or in combination with systemic therapy.

The multifaceted effects mediated by heparin are: anti-inflammatory effect, to support neoangiogenesis and epithelization and to act as an anti-exudative by reducing permeability of the vascular walls. It prevents the formation of oedema, acts as an anticoagulant and to has mitigating effect [2-5].

Keywords: Hypertension; Chronic Venous Disease (CVD); Varicose Syndrome

Introduction

It is important to differentiate between chronic venous disease (CVD) and chronic venous insufficiency (CVI) because it can help ensure accurate diagnosis. According to CEAP clinical classification and VEIN- TERM Consensus, chronic venous disease (C0-C6) is (any) morphological and functional abnormalities of the venous system of long duration manifested either by symptoms and/or signs indicating the need for investigation and/or care. Chronic venous insufficiency (C3-C6) is a term reserved for advanced CVD, which is applied to functional abnormalities of the venous system with advanced signs such as oedema, skin changes, or venous ulcers. Appropriate early treatment in CVD can lead to prevention of CVI [6]. Treatment of choice in patients with varicose veins, especially in cases where the proximal part of saphenofemoral junction is affected, is low molecular heparin and use of compression bandages.

Complications

Unsuccessfully treated or untreated varicose veins can lead to superficial vein thrombophlebitis. This is an inflammatory thrombotic process that can develop due to patients' history of local trauma, previous similar episodes, use of hormonal

preparations, smoking, prolonged immobilization or occurrence of coagulopathy in the family. Hypercoagulabilities are connected with many malignant diseases, for example Trousseau syndrome, a thrombotic event that appears before malignant disease usually visceral carcinomas that produce mucin [6].

The main risk factors for thrombophlebitis which can be clinically confirmed are history of superficial phlebitis, deep vein thrombosis and pulmonary embolism. Patients who had deep vein thrombosis have increased risk of new postsurgical vein thrombosis from 26% 68% and patients who had deep vein thrombosis together with pulmonary embolism have almost 100% risk of new thrombosis [7].

Risk of developing thrombophlebitis also increases in pregnancy and lasts until 6 weeks after giving birth. Taking oral contraceptives with high estrogen component can increase the risk of thrombosis in women from 3 to 12 times even though the risk still remains low. New oral contraceptives with low estrogen component are connected with much lower risk of thrombophlebitis, however, absolute risk is still not completely determined [8,9].

Diagnostic procedures

Laboratory results are rarely helpful when it comes to diagnosing thrombophlebitis except in case of patients with high risk of hypercoagulability disorders. D- dimer is a unique product of plasmin- mediated proteolytic degradation that is often measurable when assessing DVT and PE. Every patient that suffers from superficial thrombophlebitis above the knee should have doppler ultrasound as a first diagnostic method to exclude DVT. Magnetic resonance venography is a non- invasive test more sensitive and specific than ultrasound in the area of DVT diagnostics, however, it is still not accepted for use. Because of their invasiveness, radiation and iv contrast application, invasive venography is not a method of the first choice. Moreover, it can lead to scarring of affected veins or thrombophlebitis. CT venography is a better alternative for assessing pelvic vein system than doppler ultrasonography [11].

Therapy

Heparin was discovered in 1916, and has been in clinical use for almost half a century [2,3]. Non-fractioned (NH) or standard heparin is heterogenic mixture of sulphate polysaccharides. Low molecular weight heparins are made with controlled chemical or enzymatic depolarization of NH. In mammals, heparin is produced in mastocytic and basophilic granules. Heparin is anticoagulant agent which primarily potentiates the effect of antithrombin III. The main role is to prevent formation of thrombus, therefore absence of antithrombin III increases predisposition for thrombosis. Heparin binds and activates antithrombin III which decreases agglutination, with participation of other factors. Anticoagulant effect of heparin develops fast, after 4 applications and it is also adequate for preventing thrombosis and its healing. It works as a catalyser that strengthens antithrombin III effect in neutralisation of thrombin and activated factor coagulation X. Neutralization of thrombin prevents conversion of fibrinogen to fibrin which prevents formation and stabilization of fibrin clot.

All above mentioned effects of heparin contribute to its anticoagulant effect. Other heparin-mediated effects are: anti-inflammatory effect (affects inflammatory cells such as lymphocytes, neutrophils, monocytes, mastocytes and inflammatory mediators), promoting neoangiogenesis and epithelization. The goal of local topical heparin therapy is to achieve an optimal concentration of heparin locally, and a very low one is the systemic circulation, in order to achieve the best possible systemic tolerability. Applying low doses in a form of gel leads to long lasting and localized effect. Indications for therapy are: superficial vein disorders such as varicose syndrome and its complications, superficial thrombophlebitis, superficial periphlebitis, postoperative varicophlebitis after saphenectomy [12].

Conclusion

Varicose veins are subcutaneous veins over 3 mm dilatated usually on lower extremities. If not treated they can develop into severe vein disease with ulcers. Potential complications include acute thrombosis with or without inflammation of the vein wall. Conservative treatment of varicose veins include compressive treatment, lifestyle changes and in some cases topical drugs. Heparin is known as main treatment in acute thrombosis whether used topically or orally. Topical heparin is used in most of the European countries for treatment of local symptoms and prevention of acute thrombosis and thrombophlebitis. When used as local therapy main systemic side effects can be avoided which that leads to a better tolerance.

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