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EFFECT OF LPG–ENDERMOTHERAPY ON SKIN CHANGES RESULTING FROM LONG–TERM TREATMENT WITH GLATIRAMER ACETATE

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Multiple sclerosis (MS) is a chronic autoimmune disease affecting the central nervous system (CNS). Early initiation of treatment can slow down the whole process. The article deals with local adverse effects at the injection site when using glatiramer acetate (GA) – Copaxone®, and, in particular, with interfering with the local response by means of the LPG–endermotherapy technique. It is a unique technology that was developed based on personal experience of the founder and author, Mr. Louis Paul Guitay (LPG). Endermotherapy is mechanical stimulation of sensitive tissue with a special lift head during which activation of fibroblasts and stimulation of both the lymphatic and blood systems occur, leading to collagen and elastin neoformation.

Effect of LPG-endermotherapie on skin changes resulting from long-term treatment with glatiramer acetate

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Multiple sclerosis (MS) is a chronic autoimmune disease affecting the central nervous system (CNS). It more frequently appears in women. Early diagnosis and initiation of treatment can slow down the whole immunopathological process. Thus treatment in recent years has been initiated only when the first signs of the disease occur. In such cases, disease modifying drugs (DMD) are used. One of them is glatiramer acetate (GA) – Copaxone*. The product is delivered subcutaneously in a dose of 20 mg daily. Adverse effects of Copaxone include transient systemic reactions immediately after its administration. The reaction is characterized by chest pressure and palpitation, anxiety and/or dyspnoea. The condition mostly improves after a few minutes, which is explained by penetration of the GA into the blood, which leads to a general histamine response (Aharoni, 2013). Another adverse effect is a reaction at the injection site. Initially it is manifested by pain, itching or reddening. It concerns inflammation processes of subcutaneous fatty tissue as a response to subcutaneous injection. Gradually it results in permanent lumping of the subcutaneous tissue (lipoatrophy), which can cause significant complications when delivering subcutaneous injections.

The therapeutic possibilities of affecting the formed changes in subcutaneous tissue associated with long-term GA delivery (Lebrun et al., 2001) are mentioned in the article, which in particular focus on using the patented technology LPG-endermotherapy. (LPG – a French company, the founder and developer of the patented ROLL TECHNOLOGY being Mr. Louis Paul Guitay).

Anatomy and histopathology of skin

Subcutaneous fatty tissue (panniculus adiposus) is the deepest layer of the skin. It originates from the mesoderm and consists of fatty tissue, formed with fat cells (adipocytes), divided by the septa of the connective tissue into lobules, which are rich in supplied blood and have an active metabolism. Septa are associated with the corium fibrous tissue and create a reticulum where the lobules of subcutaneous fatty tissue are situated. The depth of the subcutaneous fatty tissue is given by age, gender, and genetic disposition, and it is also affected by endocrine and metabolic processes. Fatty tissue fluctuates in various body locations from 0.6mm (eyelids) to a few cm (abdomen, buttocks, thighs), where a fatty pillow forms.

Skin changes mostly do not spread to subcutaneous fatty tissue and conversely, fatty tissue disease is limited and relatively rarely passes to the dermis.

Inflammation processes of fatty tissue are called panniculitis. Panniculitis has various causes - infectious, physical, chemical, metabolic, immunological or ischemic. The clinical picture of all kinds of panniculitis is similar. Mostly it concerns solitary or multiple nodes or surface indurations in the acute stage, which are predominantly painful, with additional passing to the atrophic stage. Lipoatrophies are caused by loss due to dissipation of the subcutaneous fatty tissue, and can be localized (in particular when of post-traumatic origin) - as in the case of injectable drugs, or generalized (often of congenital origin), which is clinically demonstrated as a groove, maps, skin depression of various sizes, with fibrous changes in the chronic phase (Štork at al., 2013; Braun-Falco, 2011; Šťáva et Jirásek, 1977).

Panniculitis development

The acute inflammation stage is characterized by lobular panniculitis, which is initially characterized by a large amount of neutrophils (acute neutrophilic paniculitis), lymphocytes and histiocytes are presented as well. Later on, lipophagic granuloma develops with numerous histiocytes, which bind fats to themselves and then change into foam cells (granulomatous stage).

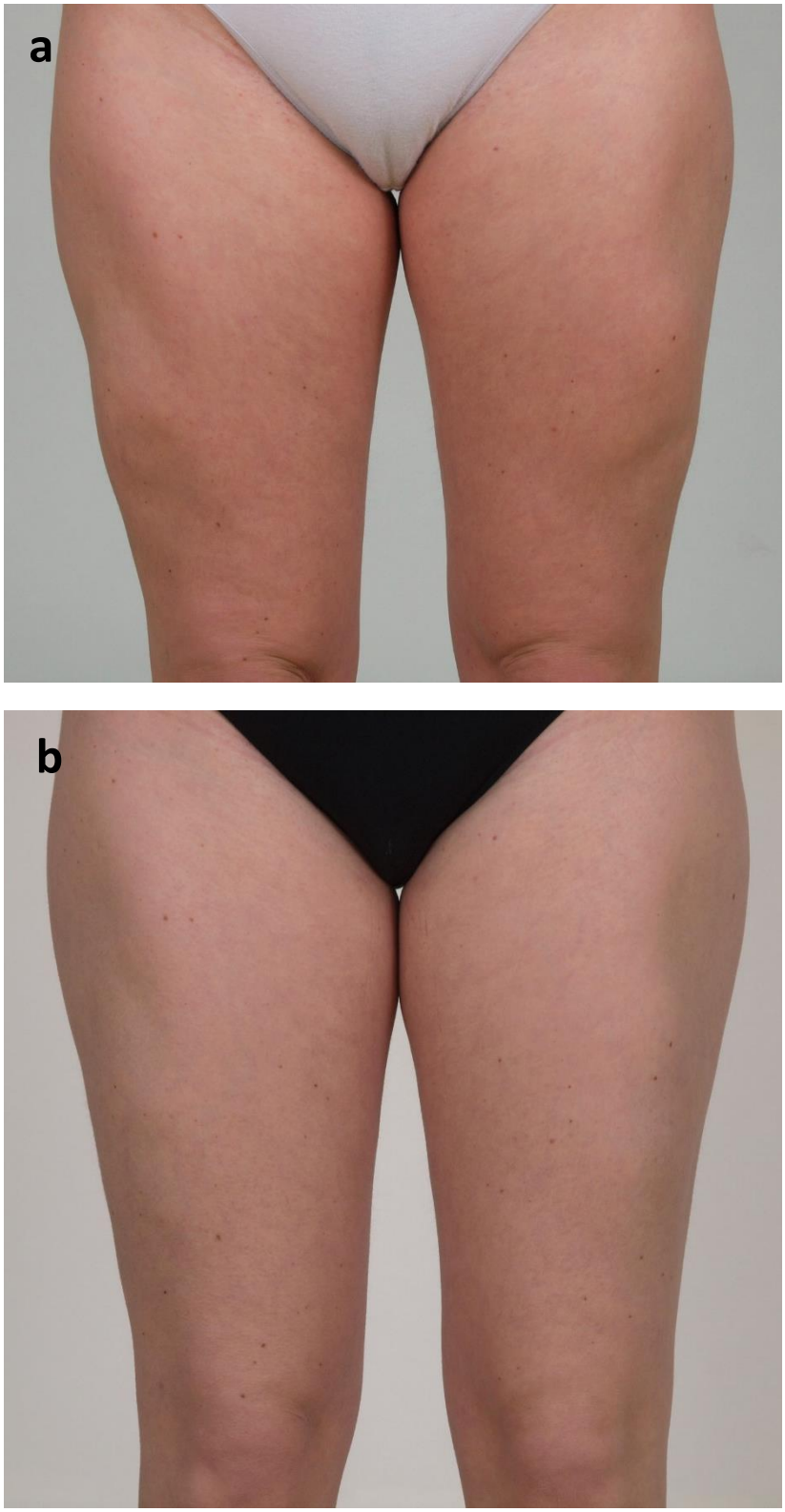

Figure 1 a) Before initiation of LPG-endermotherapy; b) After 16 treatments of LPG-endermotherapy

Lipophagic granuloma after liquefaction is directly or rarely replaced by fibrotic scarring tissue (fibrotic stage). None of the stages is specific for the disease (Štorke et al., 2013).

Copaxone® treatment management

In Copaxone therapy we take care of the general application recommendations. The drug needs to reach room temperature before delivery – remove it from the refrigerator at least 20 minutes before use. In addition, it is appropriate not to use alcoholic or other irritating disinfectants, not to inject it in damaged sites, consistently utilize all suitable body areas for application, and inspect the injection depth. The drug should be administered with the entire needle perpendicular to the skin, application should be slow, at least 10 seconds, with subsequent retention of the needle in the tissue for an additional 10 seconds. The injection site should not be massaged for 24 hours.

During acute stage development (panniculitis) showing reddening, pain and swelling, patients are instructed to perform short-term cooling of the injection site (at least 5 minutes), lubricating it with indifferent creams (oily unscented cream such as Nivea, cream with vitamin E) and in longer lasting difficulties to apply anti-inflammatory phytopharmacons (gel with aloe vera, cannabis or comfrey ointment), or topical nonsteroidal antirheumatic agents (Ibalgin cream). Sometimes a local application of thin to medium thick corticosteroid externum (group I - hydrocortisone and II - dexametazone, fluocinolone) is recommended for its anti-inflammatory, antioedematous and vasoconstrictive effects.

In order to affect the compliance of the patient in lipoatrophy development during injection therapy, it is possible to use the LPG-endermotherapy method as well.

LPG endermologie

In 1986 the LPG company developed the science of endermology concerning dermal tissue response targeted using a mechanical stimulation with LPG's patented head (i.e., a combination of dosed vacuum and grasped skinfold stimulation with LIPO motorized rollers or LIFT motorized flaps), based on the personal experience of the founder and developer of the patented ROLL TECHNOLOGY.

LPG-endermotherapy is a non-surgical and thus non-invasive, painless and entirely natural technique, which consist in the natural stimulation of dermal tissue using motorized flaps in a horizontal and vertical sequential grip supported by a dosed vacuum (patented head with rollers which stimulate the skin using 3 rotation directions depending on the required effect). Such induced tissue gymnastics results in a response at the cellular level (fibroblast activation), lymphatic and circulatory system stimulation, oxygenation improvement, and subcutaneous sediment flushing, and it leads to the formation of new fibrous structures - collagen and elastin and extracellular matrix, which improves skin tonus and elasticity. According to the frequency and selected suction intensity, various types of stimulation are formed for specific therapeutic and aesthetic purposes (it is possible to perform post-operative treatment, burns, oedemas, scars, wrinkles, fibrosis treatment, etc.). To achieve the optimal result 16 treatments once a week are recommended with subsequent maintaining care preferably once a month (Leburn et al., 2011). Contraindications for treatment with LPG-endermotherapy treatment include pregnancy, hypertension, venous insufficiency, thromboembolism, anti-coagulation and corticosteroid therapy, acute bacterial and viral diseases, decubiti and other skin defects, vaccination for a period of resorption, and oncological treatment. The treatment is painless and the duration of the whole-body treatment is maximum 35 minutes, for partial treatment maximum 15 minutes.

Group of patients, results

LPG therapy was applied in 47 patients who in 1997-2011 initiated injection treatment with GA and in whom lipoatrophy development occurred. Patients filled in an entry and exit questionnaire before and after the 16 LPG treatments, while photographic documentation was simultaneously performed with focus measurement at the beginning and after termination of the therapy. The questionnaire focused in particular on the injection application time, drug temperature at the administration time, injection site cooling before and after application, site disinfection, and injection site alteration. Attention was paid in particular to reddening, lump development, painfulness and injection application difficulties. The questionnaire's objective was to find out whether an incorrect injection technique or the administration of cooled drug would cause lipoatrophy.

In the result assessment of the entry questionnaire after sixteen LPG endermotherapy treatments, pain reduction and easier injection application was statistically significant (Figures 2a, 2b). Lumping sites disappeared or were reduced insofar as the initial lipatrophy area became usable for drug injection administration again (Figures 1). The lipatrophy range was assessed by patients' subjective feelings, objective examination and photographic documentation. Photographic documentation and objective examination results demonstrate improvements in most of the monitored patients (Jarkovský et Malúšková, 2014).

Conclusion

Lipoatrophy development during long-term GA application can worsen the adherence of patients to this safe and concurrently effective therapy, and can lead to its premature termination. Most important is the prophylaxis of the stated undesirable dermal change development - by correct injection site rotation, correct technique of subcutaneous injection application, elimination of long-term cooling, and correct skincare. In cases of the development of undesirable chronic skin reactions during GA therapy, LPG-endermotherapy provides a possible solution. Using

it can improve injection application therapy and extend the overall time of GA therapy. It is suitable to repeat the treatment according to individual difficulties to maintain the resulting positive effect of LPG-endermotherapy treatment. This treatment is not covered by health insurance.

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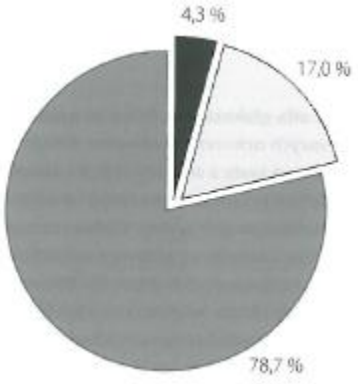


Figure 2a. Change of pain at injection site (positive change – injection site painfulness after 16 LPG® treatments is lower compared with initiation of LPG® therapy; unchanged – painfulness is the same after 16 LPG® treatments as at the beginning of LPG® therapy; negative - painfulness of injection site after 16 LPG® treatments is worse than at the beginning of LPG® therapy).

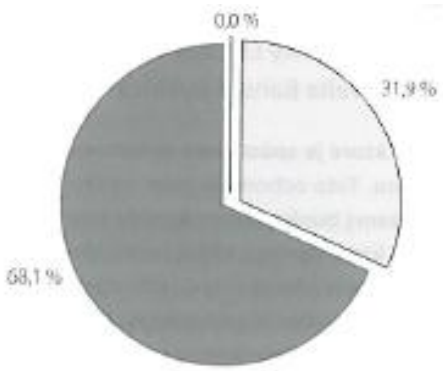
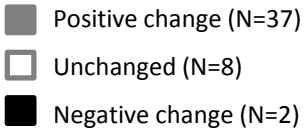
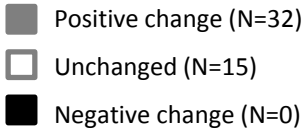


Figure 2b. Change in injection application difficulty (positive change – injection application is less difficult after 16 LPG® treatments compared with initiation of LPG® therapy; unchanged – injection application difficulty is the same after 16 LPG® treatments as at the beginning of LPG® therapy; negative - injection application after 16 LPG® treatments is more difficult than at the beginning of LPG® therapy).





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