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ESTIMATE OF THERAPEUTIC EFFECT OF DITRANOL BY APPLYING HIGH FREQUENCY ULTRASOUND IN PSORIASIS PATIENTS

SUMMARY

High frequency 20-MHz ultrasonography is accessory, noninvasive diagnostic method that visualises acoustic tomograms of pathological changes of the soft tissue. With the technique available today, ultrasound can not be considered an alternative for pathohistological finding that still remains a "gold standard" when diagnostics is in question. However, ultrasound has certain advantages which are primarily related to the examination being noninvasive, the results being obtained directly, and to the possibility of observing a large area of the skin, with a good presentation of microanatomical structures.

In the controlled, clinical, prospective study, the modification of ultrasonographic skin parameters during the treatment with a topical antipsoriatic, ditranol, was noted. The examination included 30 patients with clinically verified psoriasis vulgaris diagnosis, to whom 1% ditranol was applied on the psoriatic changes, in the duration of 21 days. The changes were measured before and every 7 days since the beginning of the therapy. By the combined application of A- and B- mode echosonography, the width of the enter echo, the width of hypo-echogenic strip shadow under the enter echo and the thickness of the dermis, were measured. The obtained results were parameters for the estimate of the therapeutic efficacy of ditranol. The evaluation of the ultrasonographic characteristics revealed a significant reduction of values in the course of the therapy. The ultrasound examination of the skin offers enough qualitative and quantitative data that can be numerically expressed and used for a more objective estimate of the applied treatment procedure efficacy.

Key words: psoriasis, 20-MHz ultrasound, ditranol

INTRODUCTION

Psoriasis is chronic dermatosis with the prevalence of 1-2% in the general population (1,2). Although it can not be completely cured, there are numerous therapeutic procedures that can lead the patient into remission and allow for it to last a longer period. The basic aim of the treatment is to decrease the activity of the illness and to reduce the spreading of changes to the level that does not significantly influence the work capability, nor does it in any other

way hinder the social life of the patient (3-5). The treatment protocols subsume local application of medicines, phototherapy, systemic therapy and the combination of these methods (6).

For almost an entire century, ditranol (antralin, cignolin) has had an important place in topical psoriasis treatment (7). Applied in the prescribed dose and concentration, it is highly efficient and practically a nontoxic medicine. Antiproliferative effect is expressed through the inhibition of replication and reparation of DNA

keratinocytes, inhibition of respiratory cell function on the level of mitochondrias, blocking of polyamines synthesis and the activity of gluco-6-phosphate-dehydrogenase which decreases the ATP synthesis in the epidermis cells (8). The therapeutic performance of ditranol is clinically demonstrated by the decrease of erythemas, inflirtration and desquamation. The estimate of its efficacy can also be objectivized with ultrasonographic examination of psoriatic lesions (9).

The continuous study of longitudinal cross-sections of psoriatic plaques in a chronical stable plaque psoriasis offers quantitative information on the dynamics of pathological processes and their regression during treatment. A-scan (amplitude mode) shows the changes of the reflected echo signals amplitude depending on time. Their position is in accordance with the depth of the reflecting structures (10). B-scan (brightness mode) combines pieces of information that stem from separate A-scans and displays them as dots whose place is determined by the position of the observed tissue structure, and the size and brightness are determined by the strength of the echo. B-scan allows for the creation of a two-dimensional image that in detail corresponds to the presentation of the anatomical cross-section of the scanned tissue. B-mode scanners that use high frequency ultrasound systems today are a basis for numerous ultrasonographic procedures in dermatology (11,12).

The research was conducted with the aim to examine the possibility of the application of 20-MHz ultrasound in the assessment and verification of the therapeutic effect of ditranol based on the modification of ultrasonographic parameters during the treatment.

MATERIAL AND METHODS

A total of 30 psoriasis vulgaris patients were examined, with mean age 55.86 ± 16.78 years. The methodological procedure applied was a controlled clinical study. The examination was controlled, randomised, with a comparative analysis of the

investigated parameters. The markers of the observation were: the detailed disease anamnesis with the data on the initiation of disease, possible inherited and/or provocative factors, duration of changes, their localisation and diffusion, previously used therapy, along with a necessary noting down of other chronic diseases; clinical examination of the skin (palms, feet soles, capillicium, parts of the body covered with clothes), mucous and nail plaques.

The examinees used ditranol applied on the psoriatic lesion in the form of 1% cream. After 30 minutes, the medicine was removed with soap and water. The examinaton lasted for 21 days and for each patient in the experimental group there was noting down of the psoriatic changes that were ultrasonographically measured before and every 7 days from the beginning of the medicine application. For the ultrasound diagnosis, the used apparatus was Dermascan C (Cortex Tehnology ApS, Hadsund, Denmark), of ultrasound frequency 20 MHz, axial resolution 0.05mm; lateral resolution 0.3mm; scan depth 13mm.

By the combined use of A- and B-modus echosonography, the following was measured: the width of the entry echo that correlates with the thickness of the epidermis, the width of hipoechogenic strip shadow below the entry echo, and the thickness of the dermis. The obtained results were the parameters for the estimate of the therapeutic effect of ditranol. The data were processed using standard descriptive statistical methods and presented in the tables.

RESULTS

The evaluation of ultrasonographic characteristics was done between the sexes and in relation to the duration of the applied therapy. The examined group included 14 (47%) women and 16 (53%) men.

Table 1 shows the values of ultrasonographic parameters prior to the use of therapy.

Table 1. Ultrasonographic characteristics at the beginning of examination

	enter echo (mm)	hypoechoen shadow (mm)	dermis thickness (mm)
women	0.54 ± 0.35	$0.36 \pm 0.11^{**}$	3.20 ± 0.77
men	$0.85 \pm 0.7^*$	0.27 ± 0.09	2.83 ± 1.0
total	0.72 ± 0.59	0.31 ± 0.11	2.99 ± 0.92

* $p < 0.05$; ** $p < 0.01$

At the beginning of the examination, the average values of the entry echo were 0.72±0.59mm; hypoechogenic shadow 0.31±0.11mm, and dermis thickness 2.99±0.92mm. The enter echo was significantly greater in men (p<0.05), and the width of the hypoechogen shadow significantly greater in women (p<0.01). The dermis thickness did not vary significantly between the sexes (Table 1).

Table 2 shows the values of ultrasonographic parameters at first control check up, 7 days after the use of therapy.

Table 2. Ultrasonographic characteristics of the examination at first control check-up

	enter echo (mm)	hypoechogen shadow (mm)	dermis thickness (mm)
women	0.44 0.25	0.28 0.10**	2.62 0.82
men	0.55 0.34	0.21 0.07	2.50 0.88
total	0.50 0.31	0.24 0.09	2.55 0.86

** p<0.01

At first control check up, the average values of the entry echo were 0.50±0.31mm; hypoechogen shadow 0.24±0.09mm and dermis thickness 2.55±0.86mm. The entry echo was not significantly different between the sexes, while the width of the hypoechogen shadow was significantly greater in women (p<0.01). The thickness of dermis did not vary significantly between the sexes (Table 2).

Table 3 shows the values of ultrasonographic parameters at the second control check-up, two weeks after the application of ditranol.

Table 3. Ultrasonographic characteristics of the examination at the second control check-up

	enter echo (mm)	Hypoechogen shadow (mm)	dermis thickness (mm)
women	0.32 0.10	0.19 0.10	2.06 0.66
men	0.29 0.16	0.19 0.17	2.03 0.76
total	0.30 0.13	0.19 0.14	2.04 0.72

NS for all parameters

At the second control check up, the average values of the entry echo were 0.30±0.13mm; hypoechogen shadow 0.19±0.14mm, dermis thickness 2.04±0.72mm. The application of ditranol leads to the leveling of registered parameters values, so that the performed t-test did not confirm a significant difference of the measured values between the sexes. (Table 3).

Table 4 shows the values of ultrasonographic parameters at the third control check- up, after three weeks of ditranol treatment.

Table 4. Ultrasonographic characteristics of the examination at the third control check-up

	enter echo (mm)	hypoechogen shadow (mm)	dermis thickness (mm)
women	0.28 0.24	0.12 0.10	1.52 0.48
men	0.23 0.14	0.18 0.18	1.74 0.72
total	0.26 0.19	0.156 0.14	1.65 0.63

NS for all parameters

At the third control check-up, the average values of the entry echo were 0.26±0.19mm; hypoechogen shadow 0.156±0.14mm, and dermis thickness 1.65±0.63mm. The performed t-test did not confirm a significant difference of the measured values between men and women (Table 4).

DISCUSSION

Psoriasis treatment is complex and long lasting. For each patient, it is necessary to make an

individual treatment plan whose main directions are localisation and the spreading of psoriatic changes, age, and general condition of the patient. Whenever possible and clinically justifiable, the initial treatment for a stable plaque psoriasis should be topical (1). Nowadays, there is a whole spectrum of local antipsoriatics that can be sufficient for the disease control if less than 20% of the skin is affected with changes. Ditranol, applied solely or in the combination with corticosteroids, UV radiation or tar preparations, significantly reduces the duration of

psoriasis treatment, without a negative effect on the duration of remission (2,7).

Since the introduction of ultrasonographic systems into dermatological practice, many authors performed examinations of their use in the estimation of therapeutic and unwanted effects of various pharmacological substances (13,14). In the completed clinical studies, the 20MHz B-modus ultrasound was used for the estimation of the therapeutic effect of ditranol. By noting the ultrasound reflexion, the modification of a coustic

tomograms was followed, and a significant reduction of all three ultrasonographic parameters was detected. The decrease of the entry echo can be interpreted as a consequence of the hyperkeratosis decrease (15). Hypoechoic strip shadow, caused by acanthosis and inflammatory cellular infiltrate is an index of disease activity (16). During the therapy there was a decrease of the thickness of this strip, in three patients up to complete disappearance, which is a sign of a regression of a pathological process. After the clinical resolution of the plaques, the total thickness of the skin was also significantly reduced.

The ultrasonogram, obtained by 20MHz scanning, does not have the precision of the higher frequency systems, yet gives enough qualitative and quantitative data for registering changes that occur during therapy (14). The two-dimensional image of B-scan, that is synthesised from the series of A-scans developed as a result of ultrasound reflexion, can be analyzed, numerically expressed, and used as a valuable reference for objectivization of the state of pathologically changed skin before, during and after

therapy (14,15).

CONCLUSION

On the basis of the conducted controlled clinical examination, the following conclusions can be drawn:

Ultrasonol has showed a good therapeutic effect in the treatment of stable plaque psoriasis.

There is an obvious quick regression of all followed ultrasonographic parameters already after two weeks of medicine application.

At every control check up there was noted a significant reduction of measured values in relation to the prior check up (I control in relation to the initial values, II control in relation to I, and III control in relation to II).

Registering the ultrasound parameters of the epidermis and dermis, and following their modification showed statistically significant differences before, during, and at the end of the examination.

Ultrasonographic examination can be used for verification and objective estimate of the therapeutic effect of the medicine, as the followed parameters can be numerically expressed and statistically processed, which gives higher reliability of the findings and allows for qualitative evaluation

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**PROCENA TERAPIJSKOG EFEKTA DITRANOLA
PRIMENOM VISOKOFREKVENTNOG ULTRAZVUKA
KOD OBOLELIH OD PSORIJAZE**

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SAŽETAK

Visokofrekventna 20-MHz ultrasonografija je pomoćna, neinvazivna dijagnostička metoda koja vizuelizuje akustične tomograme patoloških promena mekog tkiva. Sa danas dostupnom tehnikom, ultrazvuk se ne može smatrati alternativom za patohistološki nalaz, koji i dalje ostaje "zlatni standard" kada je dijagnostika u pitanju. Međutim, ultrazvuk ima izvesne prednosti koje se prevashodno ogledaju u neinvazivnosti ispitivanja, neposrednom dobijanju rezultata i mogućnosti opservacije velikih površina kože, sa dobrom prezentacijom mikroanatomskih struktura.

U kontrolisanoj, kliničkoj, prospektivnoj studiji beležena je modifikacija ultrasonografskih parametara kože u toku lečenja topikalnom antipsorijatikom, ditranolom. Ispitivanjem je bilo obuhvaćeno 30 bolesnika sa klinički verifikovanom dijagnozom psoriasis vulgaris, kojima je na psorijatične promene aplikovan 1% ditranol u periodu od 21 dan. Promene su merene pre i svakih 7 dana od početka terapije. Kombinovanom primenom A- i B- modusne ehosonografije, merena je širina ulaznog eha, širina hipoehogene trakaste senke ispod ulaznog eha i debljina derma. Dobijeni rezultati bili su parametri za procenu terapijske efikasnosti ditranola. Evaluacija ultrasonografskih karakteristika pokazala je značajnu redukciju vrednosti u toku terapije. Ultrazvučni pregled kože daje dovoljno kvalitativnih i kvantitativnih podataka koji se mogu numerički izraziti i iskoristiti za objektivniju procenu efikasnosti primenjenog postupka lečenja.

Ključne reči: psorijaza, 20-MHz ultrazvuk, ditranol