Physiological tissue changes after administration of micronized Diosmin/Hesperidin, individually or in association with Endermologie®

(Modifications physiologiques tissulaires après administration d'un comprimé micronisé de « Diosmin/ Hesperidin » seul ou en association avec Endermologie®)

Pietro Lattarulo, Pier Antonio Bacci, Sergio Mancini
Physiological tissue changes after administration of micronized Diosmin/Hesperidin, individually or in association with Endermologie®

Pietro Lattarulo *, Pier Antonio Bacci **, Sergio Mancini***

* Neurophysiological Service of Hospital "Policlinico di Monza" - Monza - Italy
** Chairman Leg’s Aesthetic Pathologies Center of Privat Hospital S. Chiara - Florence - Italy
Professor Surgery School University of Siena (Dir. Prof. S. Mancini)
*** Director Surgery School and Surgery Institute - University of Siena - Italy

Abstract (1)
Introduction
Despite the individual use of Endermologie and Diosmin/Hesperidin producing active physiological changes in the cutaneous microcirculation, the possibility of using individual treatments in association has never been taken into consideration. In the cutis treated with Endermologie, microcirculatory changes concern the increase of the blood and lymphatic flow; this effect is no doubt linked to the mechanical stimulation of the cutis and of the subcutis through the contemporary action of positive pressure, suction and the mechanical massage operated by rollers.

Materials and methods
The study was carried out with Optical Probe Videocapillaroscopy (OPVC), Laser Doppler Flow measurements and transcutaneous Oxymetry on 34 subjects, 20 females and 14 males, after having informed them and obtained their consent; their ages ranged from 18 to 42 (average of 30). The phlebotonical drug used is a phlebotropic and venoprotective drug whose active ingredients are micronized Diosmin/Hesperidin.

Results
Molecular activities on microcirculation are conducted through various mechanisms that go from reduction of blood viscosity and capillary permeability to an increase in tcpO2 and the capillary blood flow with reduction of stasis and of anti-inflammatory activity. The data we obtained after Videocapillaroscopic measurements indicate that capillary blood flow rate values and an increase in capillary density virtually overlap both after Endermologie and after intake of 4 tablets of the phlebotonical drug as compared to initial values. After associating the two therapeutic methods, values appear to be almost doubled.

Conclusion
To conclude, the data that we found unquestionably reveals greater combined treatment efficacy in terms of an increase in microcirculatory parameters; the mechanical action of Endermologie, which in our opinion must also be studied neurologically, is more efficacious with the intake of micronized Diosmin/Hesperidin.

Abstract (2)
Introduzione
L’Endermologie è una tecnica non invasiva di massaggio meccanico associato a suzione della cute, che viene sottoposta all’azione fisica di due rulli rotanti. Alcuni autori hanno trovato un incremento della perfusione cutanea e del flusso linfatico, altri un incremento della componente fibrillare collagenica nello strato profondo del derma. Partendo da questo presupposto, abbiamo pensato di valutare gli effetti della terapia fisica Endermologie in associazione con un principio attivo farmacologico che ne potesse potenziare il meccanismo d’azione e quindi l’effetto terapeutico.

Materiali e metodi
Lo studio è stato effettuato dopo ottenimento del consenso informato su 34 soggetti, 20 di sesso femminile, 14 di sesso maschile; l’età era compresa fra 18 e 42 anni (media di 30).
Avendo la necessità di un principio attivo ad azione rapida e in unica somministrazione, abbiamo usato la Diosmina/Esperidina in forma micronizzata. Il protocollo da noi studiato prevedeva la Valutazione strumentale con Videocapillaroscopia a Sonda Ottica (VCSO), Laser Doppler Flussimetria (LDF), Ossimetria Transcutanea (tcpO2) dopo trattamenti, in singolo o in associazione del flebotonico con la terapia endermologica.
Risultati
I dati da noi ottenuti indicano che i valori della velocità del flusso ematico capillare e l'incremento della densità capillare, sono pressoché sovrapponibili sia dopo Endermologie sia dopo assunzione del flebotonico. Pressoché raddoppiati appaiono i valori dopo associazione delle due metodiche terapeutiche. Anche i valori di perfusione (PU) all'LDF e della tcpO2 seguono lo stesso andamento dei precedenti, eccetto un incremento della perfusione di circa 10 volte dopo Endermologie rispetto alla somministrazione del farmaco.

Conclusione
I dati da noi rilevati, dimostrano inequivocabilmente una superiore efficacia della terapia combinata in termini di incremento dei parametri microcirculatori; l'azione meccanica dell'Endermologie, che a nostro parere deve essere studiata anche dal versante neurologico, si potenzia efficacemente con l'assunzione di Diosmina/Eesperidina micronizzate.

Introduction
Endermologie is a noninvasive mechanical treatment of tissues associated with suction of the cutis, which undergoes the physical action of two rotating rollers. The technique came into being in France and developed in Europe. Initially it was used in the treatment of traumatic and burn scars (1). It was then used to relieve exhaustion after muscular fatigue (2). Lastly it was successfully introduced in the treatment of the localized Adiposity. Since then a great deal of work has been done to clarify what mechanism triggers off the Endermologie effect on tissue: some authors found an increase in cutaneous perfusion and lymphatic flow (3), others an increase in the collagenic fibrillary component in pigs' endepidermis after a complete therapeutic cycle (4) others an recovering of interstitial matrix and the collagenic component associated with secondary venolymphatic actions (5). To date this method has been successfully used in "single-treatment" in the field of Aesthetic Medicine and Surgery; these results are sustained by an increase in microcirculatory perfusion induced by the physical action of Endermologie on the dermis. The best results are borning after the utilisation in the integrated protocol of treatment named BIM.ED (6).

Based on this assumption, we thought of assessing the effects of physical Endermologie treatment in association with a pharmacological active ingredient that could strengthen its action mechanism and, therefore, its therapeutic effect in the venolymphatic system. As a fast-acting single-dose active ingredient was required, we used Diosmin/Hesperidin in micronized form (Arvenum 500 Stroder / Daflon 500 Servier). It is a venotoic and venoprotective drug whose purified flavonic fractions are 90% Diosmin and 10% Hesperidin. Drug micronization enables quick, efficacious intestinal absorption. The drug reduces blood viscosity (7), increases tcpO2 (8), reduces capillary permeability (9), and increases flow speed and stasis reduction (10-11-12-13-14-15).

Materials and methods
The study was carried out with Optical Probe Videocapillaroscopy (OPVC), Laser Doppler Flow measurements and transcutaneous Oxymetry on 34 subjects, 20 females and 14 males, after having informed them and obtained their consent; their ages ranged from 18 to 42 (average of 30). All subjects were clinically studied to exclude vascular and/or internist pathologies that could affect the assessment outcome of the study proposed (macro and/or microvascular disorders, liver/kidney pathologies). All subjects were non-smokers and had not taken drugs for at least four months.

The study protocol included the following points:

a) Instrumental measurements with Optical Probe Visuocapillaroscopy (OPVC), Laser Doppler Flow Measurements (LDF), transcutaneous Oxymetry (tcpO2). (15-16)
b) Individual Endermologie session, administration of four tablets of Diosmin/Hesperidin in a single bolus, Endermologie and Diosmin/Hesperidin in association.

The pattern followed was as follows:
Day 0 = OPVC, LDF, tcpO2, basal; 
Day 4 = Endermologie treatment; 
Day 8 = Diosmin/Hesperidin 4 tablets; 
Day 12 = Endermologie + Diosmin/Hesperidin 4 tablets; 

“Dynamic” instrumental measurements were taken 30 minutes after treatment; the intake of Diosmin/Hesperidin took place 30 minutes before treatment individually and/or in association. An individual operator trained to use the machine performed Endermologie (LPG - System's) on a limb for 20 minutes. (17-18).
All instrumental measurements were taken in standard conditions (21°C and absence of machine noise, and after the subject had rested in a supine position). The OPVC (Moritex, Alfa Strumenti) equipped with optical fibres and a microtelecamera was conducted enlarged 100x and 200x in order to obtain detailed morphological information; the areas examined (lower limbs) were marked with a demographic pencil; the cutaneous surface examined was dampened beforehand with cedar oil to avoid light from reflecting on the horny layer.

Parameters taken into consideration with the OPVC were:
  a) Red globule flow rate in the most significant observation field
  b) Modification of capillary density

To quantize the red globule flow rate, 200x optics were used and the following score was adopted:
  0 = blood stasis;
  1 = to and fro movement;
  2 = rectilinear movement;
  3 = quick rectilinear movement.

As for capillary density, 100x optics were used and the following score was adopted:
  0 = no increase;
  1 = slight increase (20%);
  2 = good increase (60%);
  3 = excellent increase (> 80%).

Laser Doppler Flow Measurements and transcutaneous Oxymetry (tcpO2) were conducted with a Perimed PF 5040 (Swedish) instrument. (19-20)

Oxymetry setting parameters were calibrated at 21 degrees, 156 mmHg of atmospheric O2. The detector electrode was preheated to 44°C and positioned on the subject's cutis.

The Laser Doppler followed the same parameters; the probe was fixed to the cutis in the vicinity of the electrode for tcpO2. Quantization of values obtained was expressed in Perfusion Units (PU) for the Laser Doppler, and in mmHg for the tcpO2.

Results
Optical Probe Videocapillaroscopy (OPVC) (Tab. 1)

* Average values scored in basal conditions
  BASAL FLOW = 1.75
  CAPILLARY DENSITY = 0.75

* Average values found after Endermologie
  FLOW = 2.50 (+0.75)
  CAPILLARY DENSITY = 2.25 (+1.50)

* Average values found after Diosmin/Hesperidin
  FLOW = 2.00 (+0.25)
  CAPILLARY DENSITY = 2.25 (+1.50)

* Average values found after Endermologie + Diosmin/Hesperidin
  FLOW = 2.75 (+1.00)
  CAPILLARY DENSITY = 3.00 (+2.25)

Laser Doppler Flow Measurements and transcutaneous Oxymetry (Tab.2)

* Perfusion and basal tcpO2 values
  PU= 9.63
  TcpO2 = 60.69

* Values after Endermologie
  PU = 27.90 (+18.27)
  TcpO2 = 75.74 (+15.05)
Discussion and conclusions

Some years ago new noninvasive instrumental methods were developed and perfected enabling the entire cutaneous microcirculation to be studied both clinically (microangiopathies and focused treatment) and purely investigatively (microcirculatory changes in response to various pharmacological, physical, etc. stimuli). Laser Doppler Flow Measurements and transcutaneous Oxymetry enable us to quantify, through perfusion analysis of metabolic activity, microcirculatory changes in response to various stimuli; Visuocapillarioscopy instead provides a direct morphological pattern of microcirculation enabling us to appreciate the finest capillary damage. These instruments are the most avant-garde in the complete study of microcirculation. As they are highly sensitive to the outside environment, it is indispensable to observe certain environmental and patient parameters for correct data interpretation.

Despite the individual use of Endermologie and Diosmin/Hesperidin producing active physiological changes in the cutaneous microcirculation, the possibility of using individual treatments in association has never been taken into consideration: the former with physical-mechanical action and the latter with purely pharmacological action. In the cutis treated with Endermologie, microcirculatory changes concern the increase of the blood and lymphatic flow; this effect is no doubt linked to the mechanical stimulation of the cutis and of the subcutis through the contemporary action of positive pressure, suction and the mechanical massage operated by rollers. Our experience has taught us that these effects are protracted for approximately two hours after individual stimulation. (21-22-23-24). It is quite a long time considering that stimulus is physical-mechanical: we think that an autonomic indirect neuromechanism maintaining this effect could come into play.

The phlebotonical drug used is a phlebotropic and venoprotective drug whose active ingredients are micronized Diosmin/Hesperidin. Molecular activities on microcirculation are conducted through various mechanisms that go from reduction of blood viscosity and capillary permeability to an increase in tcpO2 and the capillary blood flow with reduction of stasis and of anti-inflammatory activity. The data we obtained after Videocapillaroscopic measurements indicate that capillary blood flow rate values and an increase in capillary density virtually overlap both after Endermologie and after intake of 4 tablets of the phlebotonical drug as compared to initial values. After associating the two therapeutic methods, values appear to be almost doubled.

LDF and tcpO2 perfusion values (PU) follow the same trend, except for an approximately tenfold perfusion increase after Endermologie as compared to drug administration. An increase in tcpO2, which peaks after associating the two therapeutic methods, reflects a marked increase in the blood flow rate and capillary density; in turn, the latter is linked to the opening of shunts and consequential "virtual" capillary perfusion.

To conclude, the data that we found unquestionably reveals greater combined treatment efficacy in terms of an increase in microcirculatory parameters; the mechanical action of Endermologie, which in our opinion must also be studied neurologically, is more efficacious with the intake of micronized Diosmin/Hesperidin.

This means that, in our opinion, even though the study is based on the investigation of physiological changes after individual treatment, the association of these two methods can form a therapeutic protocol in pathologies for which Endermologie and the Diosmine micronised Esperidine are proposed, certainly enhancing their efficacy and reducing treatment time. Moreover, there are no demonstrated side effects, making these treatments far more popular with patients. The best results with Endermologie are possible only if the methodology is used with precise and good methodology. Badly used the Endermologie cause the alteration of the connettival structure with the slackening of the tissues.
Optical Probe Videocapillarioscopy (Tab.1)

Valori medi in condizioni basali, in singolo e in associazione
(Average values in individual and associated basal conditions)

Laser Doppler Flow Measurement and Transcutaneous Oxymetry (Tab.2)

Valori medi in condizioni basali in singolo e in associazione
(Average values in individual and associated basal conditions)

* N.B. The phlebotonical drug used in this study is named "ARVENUM 500".
Bibliography

1) - Castigliola M., unpublished data - Data Center LPG System's - Lyon - 1995
2) - Portero A., unpublished data - Data Center LPG System's - Lyon - 1996
5) - Bacci P.A. - Il lipolinfedema: riflessioni e osservazioni cliniche, Flebologia Oggi, Torino Minerva Medica, N.2,pag.10.21,1997
11) - Allegra C., Bartolo M., Carioti B, Cassiani D. : Effectiveness of Daflon 500mg on microlymphatics proceedings of the World Congress for microcirculation, Munich, August 1996
13) - Bacci P.A. - Price en charge de l'oedeme de l'insuffisance veineuse cronique - Angiology Today - n.34, 23,4-1998
14) - Albergati F., Bacci P.A., Lattarulo P.: Valutazione degli effetti microcircolatori dopo terapia della matrice extracellulare in pazienti affette da flebolinfedema agli arti inferiori, pag.20, Atti 1° Congresso Nazionale Medicina Estetica SMIME, Milano 1999

***************************