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The Local Effects of Transdermal Nitroglycerine Treatment in Peripheral Vascular Pathology and in Various Other Diseases

G. Lupescu¹, R. Lupescu¹, C. Plavat¹, A. Lopez Collado²

Acting directly on the vascular smooth muscle by releasing NO, transdermal nitroglycerine (NG) induces not only general vasodilator effects, profitable for heart pathology, but also local effects favourable in various non-cardiac diseases: peripheral vascular, dermatologic, rheumatic, surgical. The local effects of NG thus reveal a new therapeutic aspect of this drug known for over a century, maybe as important as those represented by the classical effects of NG in heart diseases. *J Clin Basic Cardiol* 2001; 4: 295–6.

Key words: transdermal nitroglycerine, local effects

Local vasodilation increases O₂ supply and accelerates the elimination of catabolites responsible for pain, pruritus and inflammatory phenomena. The predominant decrease of venous pressure facilitates the resorption of interstitial oedema.

Materials, Methods and Results

Medicinal forms, adequate for the treatment of various diseases have been used (ointment, gel, alcoholic NG solution) with low concentrations of NG that can be applied to an extensive skin area. Local 0.05 % ointment alone was administered in 75 patients (pts) (mean age 54.5 years) with obliterating arteriopathy and intermittent claudication. After two weeks, in 90 % of pts walking perimeter and Master's step-test values increased over 50 % in comparison with baseline. The recolouring time and the venous filling were shortened (in average by 5.2 sec. and 6.3 sec., respectively). Photoplethysmography detected the significant augmentation of digital pulse waves in 82 % of pts (Fig. 1). In various leg ulcers (ischaemic: 17 pts, venous: 21 pts) local 0.05 % NG ointment significantly improved the healing process and shortened the period of cure compared to conventional treatment [1, 2].

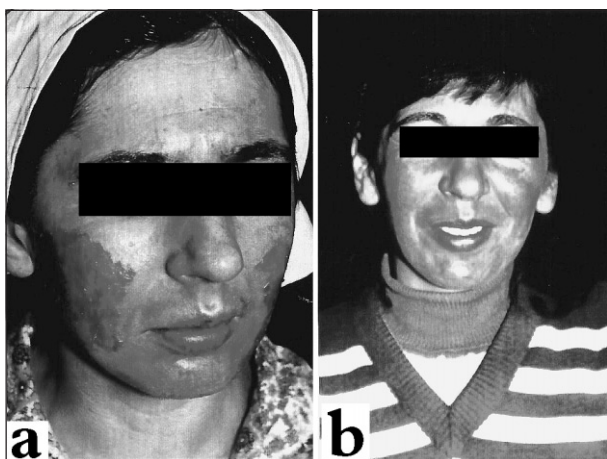


Figure 1. Burns (of second degree) before (a) and after (b) local NG treatment alone. In burns pain often rapidly disappears after local NG ointment administration, aesthetical and functional prognosis is better than with other drugs and hospitalization period is significantly shortened.

In a double blind cross-over study, the efficacy of local 0.05 % NG ointment was proved in 36 pts (mean age 46 years) with profound thrombosis of the inferior limbs. The local NG treatment (associated with conventional therapy) significantly accelerated the diminution of spontaneous pain and the decrease of interstitial oedema ($p < 0.001$ for both symptoms) in comparison with placebo [1, 2].

Another study, performed in a similar way, was carried out on 56 pts (mean age 45 years) with rheumatic and post-traumatic diseases: arthrosis 16 pts, abartricular rheumatism 10 pts, infectious rheumatism 14 pts, algoneurodistrophy 16 pts. The local 0.05 % NG ointment accelerated diminution of pain ($p < 0.001$), decrease of tumefaction ($p < 0.001$) and improvement of joint mobility ($p < 0.005$) [3].

To control hair-shedding, in a double blind study the scalp of 42 pts (mean age 41 years) affected by seborrhoea was gently swabbed with a weak alcoholic solution of NG (0.01 %). The hair fallen daily (counted by a standardized brushing method) significantly decreased in number ($p < 0.05$ %) in the 21 pts treated with alcoholic NG solution in comparison with the other 21 pts treated with alcoholic solution alone [3].

Owing to the fundamental role of the circulatory factor in the clinical evolution of burns we have investigated the local effects of transdermal 0.05 % NG ointment (in 48 pts, 33 men and 15 women, aged 18–45 years), in a randomised study. The 24 pts (group A) received local 0.05 % NG ointment alone and the other 24 pts (group B) received common ointments with cortisone and antibiotics. The area of the burns was approximately equal in the two groups, but no more than 30 %; general treatment and primary toilet were also identical. The demarcation between the burns and the living tissues made up more rapidly in group A (24–36 h) in comparison with group B (48–72 h). After 48 h the beginning of the treatment, 50 % reduction in pain was seen in group A compared to group B.

Local bacterial infection with resistant germs occurred in 7 % of group A and in 10 % of group B. The period of healing was shorter in group A (9–10 days) in comparison with group B (12–14 days). Functional and aesthetical residual problems were 30 % and 50 %, respectively [4]. Collating the results published by us since 1983 [5] we have found that local transdermal NG could induce unexpected beneficial effects in various non-cardiac diseases [3–6]: local vasodilating effects (with positive results in the treatment of chronic arteriopathies, including obliterating vascular disturbances); trophic effects (in ischaemic or venous ulcers, in burns, even

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in ocular cornean ones, frostbite (Fig. 2), miscellaneous wounds, dry and seborrhoeic pityriasis, in scalp seborrhoea, hair shedding, not very extensive vitiligo (in this disease the results, maybe by redistributing the cutaneous pigment, are modest, although superior to other usual drugs), antioedematous effects (in cardiac, traumatic, phlebotic oedema and in chronic venous failure); antipruriginous effects (in eczemas); anti-pain effects (in rheumatic affections, gouty arthritis, neuromyalgia, Zona Zoster) and increases the non-specific resistance of the skin (epidermal mycoses).

Discussion

Although transdermal NG is far from being a panacea, the multitude of its favourable effects is due to the important role of circulation in the pathogenic mechanism of various diseases. It is known that the cutaneous absorption of NG is directly proportional to both the concentration of the transdermal preparation and the surface covered by it. 2 % NG ointment has been used in ischaemic cardiopathy for quite a long time. But this very concentrated drug can be administrated only on very restricted cutaneous areas. In fact, both the classical NG 2 % ointment and the adhesive round discs have been conceived for the treatment of ischaemic heart disease, using only the advantages of the route of penetration into the skin of NG: slow absorption (and controlled in the case of the adhesive patches), prolonged action and short-circuit of the first liver inactiveness. The local effects of NG treatment cause a different problem, a special one, which needs adequate medicinal forms. Maybe the high concentration of the 2 % NG ointment is the factor, which has not favoured the discovery of the local therapeutical effects of NG because the

use of such an ointment on a large cutaneous area may induce serious adverse effects from acute headache to syncope. On the other hand, NG ointment at low concentration seems to be useful for classical indications of the drugs including coronary artery disease and heart failure. Moreover, low concentration NG ointments seem to have advantages as compared to the classical 2 % NG ointment or adhesive patches because:

- 1) they allow a progressive administration considering the tolerance to NG
- 2) the side effects (especially headache) are greatly reduced
- 3) extended thoracic applications may include the areas of pain projection or the eventual irritative spines (radicular etc.) contributing to the start of angina pectoris crises
- 4) in cases of myocardial ischaemia with heart failure the low concentration ointment can be applied both on the chest and the oedema areas quickening the resorption of the oedemas.

Concerning the relation between local and general effects of NG, the direct mechanism of vascular dilation caused by NG on smooth vessel wall (the vasculature representing a major clearing organ of NG) suggests the following assumption regarding the pharmacokinetic and pharmacodynamical effects of this drug [7]. Depending on the penetration route of NG into the human body and the direction of the blood circulation, the action of NG is gradually reduced in accordance with its progressive catabolization by the bloodwalls from the circulatory sections it passes through. In this way, if NG enters the body through the blood capillaries as a consequence of the transdermic, oral or buccal administration, the greatest action of NG can be noticed at the level of capillaries and veins (where the concentration of NG molecules is at a maximum), gradually decreasing at the level of arteries and arterioles. Thus, one can explain why low doses of NG operate predominantly on capillaries and veins while the high doses are of some effect for the arterial system, too (for arteries to a greater extent than for arterioles). The involvement of vasculature in NG metabolism [8–10] constitutes a valuable theoretical base for understanding the local therapeutical effects of transdermal NG.

Conclusions

Up to the present, NG has been almost exclusively used for its general effects, even when transdermally administered, excepting Raynaud's disease and, very recently, the dysfunction of the erection ('blue syndrome'). The local effects of NG, practically unexploited, are frequently quite spectacular and can be successfully used in various non-cardiac diseases and that is why this fact may be considered as an actual rediscovery of NG.

References

1. Lupescu G Jr, Lupescu G, Plavat C. The local effects of transdermal nitroglycerin treatment in peripheral vascular diseases. *Isr J Med Sci* 1996; 32: 982 (abstract).
2. Lupescu G, Lupescu N, Plavat C. The local effects of transdermal nitroglycerin treatment in peripheral vascular diseases. *Eur Heart J* 1998; 19 (Suppl): 189 (abstract).
3. Lupescu G Jr, Lupescu G, Carasel M, Plavat C. Unexpected effectiveness of transdermal nitroglycerin in non-cardiac diseases. *Cardiovasc Drugs Ther* 1997; 11 (Suppl 2): 397 (abstract).
4. Lupescu G Jr, Lupescu G, Giubelan C, Velcea I, Giubelan M. Unexpected effectiveness of transdermal nitroglycerin in burns. *Br J Surg* 1996; 83 (Suppl 2): 81 (abstract).
5. Lupescu G, Lupescu N, Blendea N. Multidisciplinary indications of the transcutaneous treatment with nitroglycerin. *Viata med* 1983; 12: 557–62 (in Romanian).
6. Lupescu G, Lupescu G Jr. Thérapeutique à la nitroglicérine locale. *Arch Un Med Balk* 1987; 5–6: 508–9.
7. Lupescu G Jr, Lupescu G. An assumption regarding the action of nitroglycerin in different vascular areas. *Cardiovasc Drugs Ther* 1997; 11 (Suppl 2): 397 (abstract).
8. Ignarro LJ, Lippton H, Edwards JC, Baricos WH, Hyman AL, Kadowitz PJ, Gruetter CA. Mechanism of vascular smooth muscle relaxation by organic nitrates, nitrites, nitroprusside and nitric oxide: evidence for the involvement of S-nitrosothiols as active intermediates. *J Pharmacol Exp Ther* 1981; 216: 739–49.
9. Fung H-L, Sutton SC, Karnya A. Blood vessel uptake and metabolism of organic nitrates in the rat. *J Pharmacol Exp Ther* 1984; 228: 334–41.
10. Fung H-L. Pharmacokinetics and pharmacodynamics of organic nitrates. *Am J Cardiol* 1987; 60: 4H–9H.

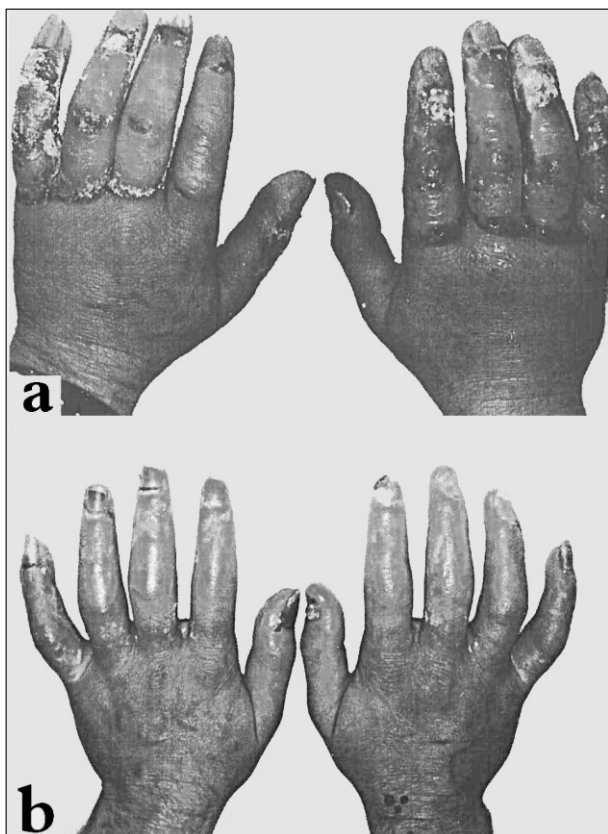


Figure 2. Frostbites (of third degree at the risk of digital spontaneous amputation) before (a) and after (b) local NG treatment alone.

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