

BIOREVITALIZATION AND COSMETIC SURGERY OF THE FACE: SYNERGIES OF ACTION

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Summary

Polydeoxyribonucleotide (PDRN) is used in aesthetic medicine as a skin revitalizing agent as well as to correct depressed scars and striae distansae.

The purpose of this study is to evaluate the effect of PDRN in stimulating skin biorevitalization of the face in women who underwent to a complete face-lift or a mini lifting procedure, not only to improve the cosmetic appearance but also to create more suitable conditions to better tolerate surgery. 15 female patients with an age ranging from 28 and 58 years (mean age 46) who had to undergo to a mini lifting procedure (10 patients) and a complete face-lift (5 patients) were treated in four sessions preoperatively, once a week, with intradermal administration of PDRN. Four more sessions, again on a weekly basis, were carried out starting from day 15 post-operatively. During the week before surgery and the two weeks following it, a home therapy consisting of one i.m. PDRN vial a day was offered to the patients. In all treated patients scar healing was normal, with no evidence of diastase and/or delayed scarring. Moreover the skin showed a good eutrophication and the suture stitches were removed a few days earlier than in the case of the traditional protocol (on day 10 instead of day 12). The patients' subjective evaluation was positive in all cases and extremely positive in 35% of them. The results of the study reveal a trophic and revitalizing action of PDRN on the skin which is therefore useful to improve the cosmetic appearance of the face and to create those conditions that assure a better tolerability of the stress due to surgery, and to reduce the healing time.

Riassunto

Il Polidesossiribonucleotide (PDRN) viene utilizzato in medicina estetica sia come rivitalizzante della cute che nella correzione di cicatrici depresse e di striae distensae. Scopo di questo studio è la valutazione dell'effetto del PDRN nel favorire la biorivitalizzazione della cute del volto in pazienti sottoposte ad intervento chirurgico di lifting completo o minilifting, non solo per migliorare l'aspetto estetico ma anche al fine di creare un ambiente più adatto a tollerare l'intervento chirurgico.

15 pazienti di sesso femminile di età compresa fra i 28 e 58 anni (media 46) che si sottoponevano ad un intervento di minilifting (10 pazienti) e lifting completo (5 pazienti) sono state trattate in quattro sedute pre-operatorie, una volta alla settimana, con infiltrazioni intradermiche di PDRN.

Altre quattro sedute, a cadenza settimanale, sono state eseguite successivamente all'intervento, a partire dal quindicesimo giorno postoperatorio.

Nella settimana prima dell'intervento e nelle due settimane successive, le pazienti hanno effettuato una terapia domiciliare con PDRN, una fiala intramuscolare al giorno.

In tutti i casi trattati la cicatrizzazione è stata normale, senza evidenze di diastasi e/o ritardi di cicatrizzazione. Inoltre la cute ha mostrato una buona eutrofizzazione ed i punti di sutura sono stati rimossi qualche giorno prima rispetto al protocollo tradizionale (10° giornata vs 12°).

Il giudizio soggettivo delle pazienti è stato positivo in tutti i casi, ed estremamente positivo nel 35% delle pazienti.

I risultati dello studio depongono a favore di un'azione trofica e rivitalizzante della cute da parte del PDRN, utile pertanto sia al fine di migliorare l'aspetto estetico, sia di creare un ambiente favorevole in grado di meglio sopportare le sollecitazioni dovute all'intervento chirurgico, riducendo anche il tempo di guarigione.

INTRODUCTION

Polydeoxyribonucleotide (PDRN) is the active ingredient of a preparation used in medicine as wound healing, antidystrophic and skin revitalizing agent. It consists of low molecular weight DNA fractions and it is constituted by polymers of deoxyribonucleotides whose length ranges from 50 and 2000 base pairs. PDRN therefore supplies deoxyribonucleotides, deoxyribonucleosides as well as purine-pyrimidine bases. Many studies in international literature show that nucleotides and nucleosides stimulate cell growth of several types of cells (1-7), they also promote and accelerate the synthesis of nucleic acids (8-9), and wound healing of both cutaneous and mucous tissues (10-13). These effects seem to be attributed both to the stimulation of salvage pathways, for the neosynthesis of nucleic acids with a low energy consumption (14-19), and by the activation of type A2 purinergic receptors (8, 20-22).

In various *in vitro* studies PDRN showed its trophic action on several cell types (23) and its effect on the growth of human fibroblasts in primary cultures (24-27). It also stimulates the secretion activity of collagen proteins and of other proteins of the extracellular matrix (24). Thellung (28) demonstrated that PDRN acts by activating A2 purinergic receptors. In fact he showed that by pre-treating cell cultures of fibroblasts with DMPX, an A2 receptor antagonist, the effect on both cell proliferation and metabolic activation is reduced in a statistically significant way, which is proved by a dramatic decrease of intracellular calcium release, while the A1 receptor antagonist has no effect.

The results of *in vitro* studies can reasonably explain the therapeutic effect of PDRN that was highlighted in several clinical studies, with respect to postphlebotic ulcers (33), burns (34), depressed scars (29-30), skin repair areas

explanted by means of dermatomy (35-36), and corneal reepithelisation after Photorefractive Keratectomy (PRK) (37).

This study was carried out by evaluating the action of PDRN as an agent promoting the bio-revitalization of the face not only to improve its cosmetic appearance, which is fundamental, but also to create more suitable conditions to better tolerate a lifting or a mini-lifting.

PATIENTS AND METHODS

From June 2002 and September 2003 (for a total of 18 months) 15 female patients with an age ranging from 28 and 58 years (mean age 46) were involved in the study using the following exclusion criteria: smokers, women suffering from autoimmune diseases or treated with systemic drugs with cutaneous trophic action. Patients presented skin phototypes II and III according to Fitzpatrick classification. The material used was Polydeoxyribonucleotide (PDRN, Placentex Integro, Mastelli), a dose of 1 vial (3 ml) was administered in each session. The protocol required the enrollment of patients with an indication for a mini lifting procedure (due to ptosis of the middle and lower third of the face and neck, total = 10 patients) and for a complete face-lift (due to ptosis of the whole face and the neck, total = 5 patients).

Four sessions were carried out pre-operatively once a week and infiltrations were stopped one week before the scheduled date of surgery. They were carried out according to these techniques: a "crescent-like" infiltration on the frontal region, a "net-like" infiltration on the chin region, and a "micropomphus-like" one on the pre and retro-auricular anterior cervical region.

After surgery, starting from day 15 post-operatively four more sessions were carried out once a week on the same previously treated areas using the same infiltration techniques.

In the periods when patients were not treated with subcutaneous infiltrations, (the week before and the two weeks after surgery), a home daily treatment with one intramuscular vial of PDRN was offered to them (fig 1).

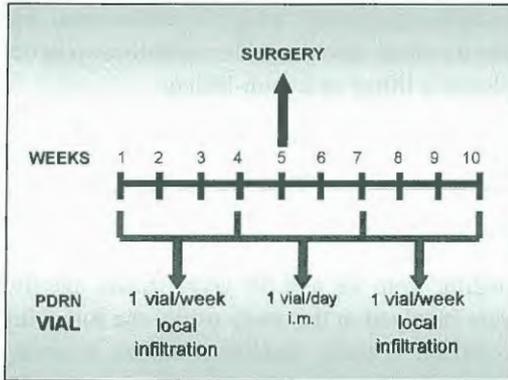


Fig. 1 Protocol of treatment. PDRN local infiltration, once a week: four sessions pre-operatively, and, 15 days after surgery, four more sessions of infiltrations. PDRN, daily intramuscular administration: in the week before and in the two weeks after surgery.

RESULTS

In this personal experience no complications occurred with respect to infections and hematomas either pre or post-operatively. When undermining the tissues intra-operatively, a good elasticity of the skin tissues was observed offering better traction and anchoring of the skin flaps. All treated cases showed normal wound healing with no evidence of diastase and/or delayed scarring. Conversely, suture stitches were removed a few days earlier than in the case of the traditional protocol (day 10 vs day 12). The skin showed a good eutrophication and a post-operative satisfactory outcome due to a better traction on the skin. In this case history the scarring adjustment was good, with no clinical evidence of pathological scars especially hypertrophic ones (fig 2-3).



Fig. 2 Patient before treatment.



Fig. 3 Patient after treatment. The patient has been submitted to temporal lifting procedures associated to PDRN administration.

DISCUSSION

Evidence of the effect of skin biorevitalization and eutrophication was previously shown by several researchers who used infiltrations of PDRN for various applications in aesthetic medicine.

PDRN was used in a clinical trial on 20 patients with severe post-acneic scars. Intradermal administrations on the scar lesion were repeated once a week for a period of 8 weeks. The results were satisfactory in almost all patients. In 5 cases, in

particular, a flattening of the prominence of the lesion was achieved and 6 months after the end of the treatment the results had not changed (29). Rantuccio (30) treated another 20 patients presenting depressed scars with the same infiltrating method and obtained a flattening of some scars and a reduction of others, with a marked improvement of the general appearance.

As far as the treatment of skin striae is concerned, Rossi (31) treated 30 patients whose mean age was 32,8 years by administering PDRN intradermally, with the micropomphus technique along the whole length of the stria. Infiltrations were carried out every 2 weeks for a total of 7-8 sessions. An improvement was obtained in all the cases especially in the more recent striae. The one-year follow-up showed no regression of the obtained cosmetic results. Always in the treatment of striae, Follador (32) used a protocol that associated local application of 70% glycolic acid with PDRN therapy, administered by intralesional infiltrations and combined with intramuscular treatment for the 3-5 days preceding the out-patient sessions for a total of 9-10 sessions. This treatment was administered to 14 patients. Results were good in all the cases and excellent in 6 of them.

The results obtained in this trial confirmed the effectiveness of PDRN in stimulating skin revitalization that improved both the cosmetic appearance and the quality of scarring in lifting and minilifting surgery. Results were mainly based on the positive judgement (and on the extremely positive judgement in 35% of the cases) expressed by the patients who underwent surgery, as well as on the evaluation of the surgeon who worked on a skin which was considered more trophic, elastic and more able to tolerate the stress due to surgery, thus reducing the healing time. In fact, suture stitches could be removed two days earlier than in the case of standard surgery.

The combination of local infiltration therapy with systemic administrations seems to be an important factor for the final outcome.

Integrating the results of this study with the previous clinical trials carried out by various researchers in the field of esthetic medicine, we can conclude that PDRN showed a valid and sure eutrophicating and revitalizing effect on the skin of treated patients.

- 31) **Rossi E (1987)** Come cancellare le smagliature. Impiego di un estratto di placenta intralesionale nelle smagliature cutanee. *Diagnosi & Terapia* **8**: 5-6
- 32) **Follador E (1997)** Protocollo terapeutico con PDRN iniettabile e acido glicolico nel trattamento di striae distensae (smagliature) ed esiti cicatriziali depressi di natura post-acneica. Esperienza personale e primi risultati. XVIII Congresso Nazionale della Società di Medicina Estetica, *La medicina Estetica*, **21**: 33-34
- 33) **Magi G., Nardojanni V., Antonelli P., Cardini P., Rovere V. (1991)** Valutazione clinica dell'effetto del polidesossiribonucleotide nelle lesioni trofiche degli arti inferiori di soggetti vasculopatici cronici. *Minerva Angiologica*, **16(2)**: 437-440
- 34) **Viganò M., Klinger M., Colonna M., Blandini D., De Angelis A., Crabai P. (1990)** Utilizzo di un polidesossiribonucleotide (PDRN) nelle ustioni di grado intermedio. *Giornale Italiano di Ricerche Cliniche e Terapeutiche*, **11(5)**: 90-93
- 35) **Rubegni P., De Aloe G., Mazzatenta C., Cattarini L., Fimiani M. (2001)** Clinical Evaluation of the Trophic Effect of Polydeoxyribonucleotide (PDRN) in Patients Undergoing Skin Explants. A Pilot Study. *Current Medical Research and Opinion* **17(2)**: 128-131
- 36) **De Aloe G., Rubegni P., Biagioli M., Taddeucci P., Fimiani M. (2004)** Skin graft donor site and use of polydeoxyribonucleotide as a treatment for skin regeneration: a randomized, controlled, double-blind, clinical trial. *Wounds* **16(8)**: 258-263
- 37) **Lazzarotto M., Tomasello EM, Caporossi A. (2004)** Clinical evaluation of corneal epithelialization after photorefractive keratectomy in patients treated with polydeoxyribonucleotide (PDRN) eye drops: a randomized, double-blind, placebo-controlled trial. *Eur J Ophthalmol.* **14(4)**: 284-289.

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