CLINICAL

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PRM MESOTHERAPY *VS* CONVENTIONAL MESOTHERAPY IN CHRONIC LUMBAGO AND LUMBOSCIATICA-RELATED PAIN CONTROL

- RESULTS OF TWO COHORT, CONTROLLED CLINICAL TRIALS

SUMMARY

To ascertain the therapeutic efficacy of some injectable PRM Pain Therapy medicines specifically for cases of non-paretic, chronic lower back pain, 40 patients (23 M; 17 F) were included in a cohort controlled study vs Ketoprofen (KPF), a powerful NSAID also suitable for mesotherapeutic injections over an observation period lasting 6 months (i.e. a treatment period of 1.5 months and a follow-up of 4.5 months). Patients were divided into two Groups according to their clinical and instrumental diagnoses: Group A consisted of cases of non-paretic chronic lumbosciatica, and Group B those with chronic lumbago.

- The patients in Group A (20) were further divided into two comparable Subgroups of equal number, based on their own preference and subject to their signing the written informed consent: 1) Subgroup A1 was treated with KPF subcutaneously (s.c.) in previously selected anatomical points; 2) Subgroup A2 was treated with a cocktail of Guna®-Lumbar + Guna®-Muscle s.c. in the lower back region and Guna®-Ischial + Guna®-Neural s.c. along the course of the sciatic nerve. From the start of the treatment and throughout the follow-up all patients in Group A were given: Guna®-Matrix drops + Guna®-Flam drops. All patients in Group A answered the NRS and SF-36 before therapy, at the end of the treatment period, and again 130 days after stopping the treatment (at the end of the follow-up) to assess a number of significant parameters.

- The patients in Group B (20) were likewise divided into 2 comparable Subgroups of equal number, based on their own preference and subject to their signing the written informed consent: 1) Subgroup B1 was treated with KPF s.c. in previously-selected anatomical points; 2) Subgroup B2 was treated with a cocktail of Guna®-Muscle + Guna®-Neural and Guna®-Lumbar in the same anatomical points as for patients in Subgroup B1. From the start of the treatment and throughout the follow-up all patients in Group B were given: Guna®-Matrix drops + Guna®-Lympho drops.

All patients in Group B completed the Oswestry Low Back Pain Disability Questionnaire (ODI).

The results of this clinical trial demonstrated that, for both the medical disorders considered, both KPF and the specific PRM Pain Therapy injectable medicines are effective when injected in mesotherapeutic form, with an evident superiority of the latter. Unlike KPF, the injectable PRM preparations were safe and well tolerated (no side-effects in Subgroups A2 and B2). The authors analyze the therapeutic core products constituting the single PRM Pain Therapy injectable medicines and conduct a literature review, illustrating the rationale behind the action and usage of these products.

KEY WORDS **CHRONIC LUMBAGO, NON-PARETIC CHRONIC LUMBOSCIATICA, PHYSIOLOGICAL REGULATING MEDICINE, LOW-DOSE MESOTHERAPY, GUNA®-MUSCLE, GUNA®-NEURAL, GUNA®-LUMBAR, GUNA®-ISCHIAL, KETOPROFEN**

LOW BACK PAIN

Despite heavy, tiring working activities having disappeared or been much reduced (Carragee, 2005) and despite the rising number of studies and improvement in our understanding of suitable treatment methods (van Tulder *et* Al., 1997), the disability secondary to lumbago has not diminished in the highly industrialized countries (Andersson, 1999; EULAR, 2005) by comparison with 25 years ago (Roland *and* Morris, 1983). Painful low back disorders restrict a patient's physical and occupational activities, carrying considerable direct and indirect costs; in the United States alone, these costs amount to around $ 50 billion a year (Frymayer *and* Cats-Baril, 1991).

- The lower portion of the spine is the vertebral segment most exposed to mechanical strain, be it of *static* type (in relation to loading), or of *dynamic* type (in relation to movement).

Most of the bending and extending work done by the vertebral column is supported by the lumbar spine. In particular the last two lumbar discs (L4-L5; L5-S1) sustain more than two thirds of this function (Cox, 1991).

The physiopathology of lumbar pain must also take several other implications into account: the width of the posterior longitudinal ligament has a dominant role in containing the discs; it progressively becomes narrower in the cranio-caudal direction in the lumbar stretch, no longer covering the posterolateral area and this consequently increases the risk of disc bulging. In the early stages of arthritis in the lower back, which involves an initial reduction of the inter-vertebral disc, there is an anomalous slipping of one vertebral disc over the other, with a stretching of the longitudinal ligaments and the early formation of osteophytes on the edges of the vertebral bodies, which can develop the characteristic anatomopathological features of *"dripping candle wax"* (FIG. 1). The reduction of the disc modifies the normal relationships between the posterior articular facets, triggering a progressive arthritic degeneration.

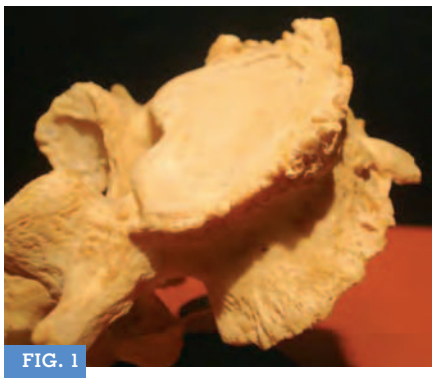


FIG. 1

Imposing formation of marginal osteophytes all along the superior and inferior edges of the body of a lumbar vertebra with "*dripping candle wax*" anatomopathological alterations, "*fish spine*" deformation of the vertebral body, and evident signs of osteoporosis.

- Preparation: Dr. Azaoux's Laboratories - Paris
Private collection.

Chronic low back pain can develop as a result of episodes of acute lumbago, or it may be of sudden onset.
The dull, gravative pain is accentuated by a prolonged erect station, walking or sitting. The pain is always accompanied by a variable degree of restriction of the patient's movements.
Radiculoneuritis occurs in the form of crural pain (involving roots L2 - L3 - L4) or sciatica (involving roots L4 - L5 - S1) (FIG. 2). Sciatica is usually associated with problems of slipped disc, although the compressive-irritative mechanism is not commonly involved. Normally the semi-fluid material constituting the *nucleus pulposus* remains confined inside the *annulus fibrosus*. Due to the formation of fissures (an alteration of the cartilage matrix), the *nucleus pulposus* escapes from the *annulus fibrosus*, causing disc bulging or, when it is more severe, a slipped disc, or giving rise to an oozing of material *drop by drop*, to which the root reacts with a frankly inflammatory response. This mechanism explains five phenomena that every physician sees in daily practice, i.e.:

1) sciatica with no identifiable neural compression;
2) evidence of a slipped disc with no sciatica;
3) sciatica tending to heal spontaneously or after treatment with NSAIDs;
4) surgery to remove the slipped disc can lead to peridural fibrosis, which may be responsible for the chronic irritation of one or more roots;
5) the persistence of painful symptoms even after surgery to remove the slipped disc.

Recent studies have demonstrated that the first cause of lumbago or lumbosciatica *is* ***not so much*** the herniation of the intervertebral disc, but rather a degenerative alteration of the peripheral ring-shaped structures comprising the disc. In fact, discography and CT scans have revealed highly vascularized granulation tissue, rich in mast cells, in the intervertebral discs (FIG. 3).

The mast cell plays a crucial part in the onset and persistence of peripheral pain of hyperalgic type, and it also participates, through the degranulation of specific enzymes, in the degradation of articular cartilage. The outcome is a progressive, profound alteration of the morphofunctional and structural characteristics of the delicate and complex cartilage matrix forming the intervertebral discs, with a consequent increase in the risk of herniation of the *nucleus pulposus* and ultimately of a compression or irritation of the resident nerve roots.

DISC LEVEL	ROOT	WEAKNESS	REFLEX INVOLVEMENT	SENSORY LOSS	PAIN DISTRIBUTION
L3-L4	L4	Quadriceps, tibialis ant.	Knee jerk	Medial knee and shin	Anterior thigh
L4-L5	L5	Extension of big toe	No significant	Big toe	Back of thigh, lateral calf
L5-S1	S1	Gastrocnemius (ankle plantar flexion)	Achiles	Lateral foot and heel	Back of thigh and calf

FIG. 2

The *para-vertebral muscles* of the lumbar spine resist bending actions, while the *oblique muscles* control rotation. When the muscles are contracted and contain numerous TPs, a compressive load comes to bear on the posterior articular facets, giving rise to a further increase in the local pain (FIG. 4).

PATIENTS AND METHODS

- The **primary objective** of these controlled cohort clinical studies was to validate the efficacy of some specific injectable ampoules of PRM Pain Therapy, injected subcutaneously in previously-established points according to an anatomical rationale, often the site of muscle and/or muscle-tendon trigger points, in the low back region or along the course of the sciatic nerve.
- The **secondary objective** was to compare the efficacy of PRM (Physiological Regulating Medicine) mesotherapy *vs* conventional analgesic - anti-inflammatory mesotherapy in the treatment of chronic low back pain with or without signs/symptoms of non-paretic lumbar sciatica.
For all patients the observation period was:

1) THERAPY: from 1 September 2008 to 20 October 2008 (≈ 50 days);
2) FOLLOW UP: from 21 October 2008 to 28 February 2009 (≈ 130 days after completing the last session of treatment for each patient).

The clinical study with PRM injectable Pain Therapy ampoules was not conducted *versus* placebo because, according to the current European standards on the topic, this type of study does not meet the requirements of a *patient-oriented*, or *patient-centered* approach. It is not ethical to treat diseases involving a psychological and/or physical suffering with a placebo. Moreover, the compulsory need to obtain patients' written informed consent (and therefore their agreement to be treated with a placebo) practically cuts off the chances of any practical application of such a solution.

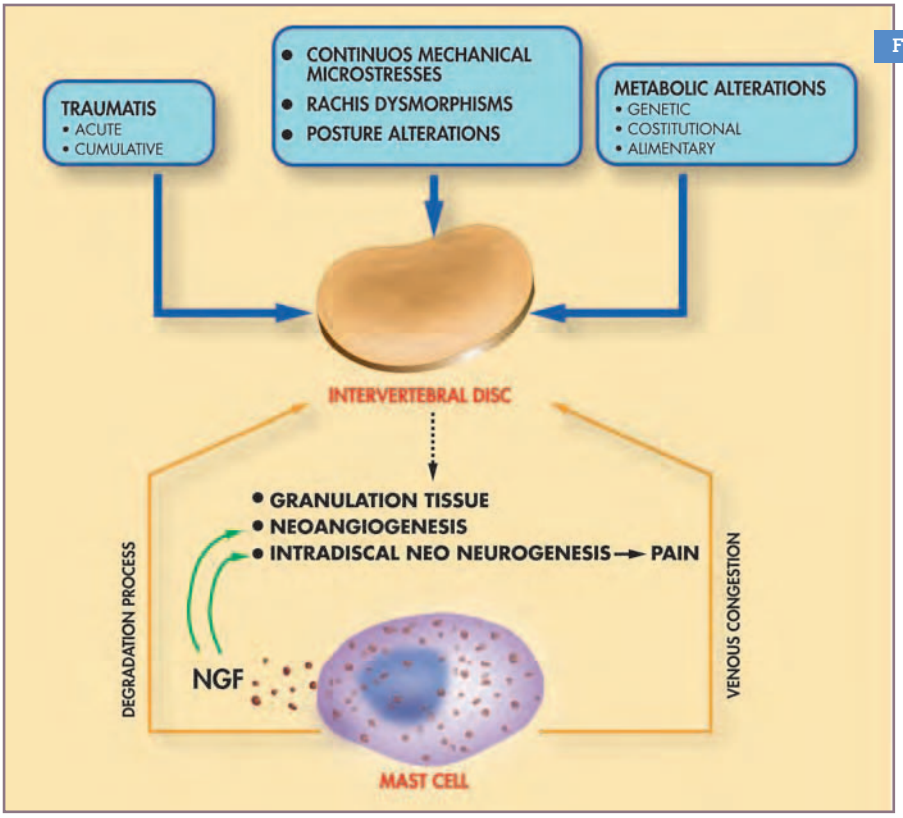


FIG. 3

Role of mast cells in the onset and persistence of pain originating in the vertebral disc.

- Graphics by the authors based on the literature review.

- Until not long ago, it was believed that the intervertebral disc contained no nerve endings and that it was only the peripheral region of the disc that was reached by a few nerve endings, coinciding with the more superficial sheets of the *annulus fibrosus*. It has since been demonstrated that mast cells are capable of synthesizing, storing and releasing NGF (Nerve Growth Factor) inducing neo-neurogenesis and invasion of the normally non-innervated cartilage tissue of the disc by sensory nerve fibers.
- This leads to the introduction of a new concept relating to the genesis of vertebral pain not only extra-disc, but also intra-disc, with interesting therapeutic implications.

The two control Groups (Subgroup A1 and Subgroup B1, *see below*) were treated with local s.c. infiltrations of Ketoprofen (KPF) (2-[*benzoylphenyl*] *propionic acid*).
KPF is a powerful NSAID that is effective, administered locally (Koes *et* Al., 1997) or systemically (UK BEAM Trial Team, 2004), in the treatment of the conditions considered in this trial.
Airaksinen *et* Al. (1993) demonstrated the efficacy of KPF *vs* placebo in the treatment of soft tissue pain of traumatic origin. Cornefjord *et* Al. (2001) showed the effect of KPF on nerve conduction velocity in conditions of experimental root compression.

Group A = patients with non-invalidating chronic lumbosciatica

- The preset number of patients was **20** (12 M; 8 F), with a mean age of 50.9 years.
- Inclusion criteria: patients suffering for more than 3 months of lumbo-crural pain in L4-L5 and/or lumbosciatica in L5-S1, with no tributary muscle functional loss; pregnancy beyond the third month.
- Exclusion criteria: 1) patients suffering from lumbo-crural pain or lumbosciatica for less than 3 months; 2) patients with severely impaired sensory and motor velocity of the sciatic and the external popliteal sciatic nerves (EMG); 3) patients with evidence at discography and CT of major disc bulging or slipped disc. For patients in items 2) and 3), the therapeutic indication is not medical, but surgical, after careful evaluation; 4) patients suffering from liver and/or kidney diseases; 5) patients with gastroduodenal ulcer; 6) pregnancy up to the third month.

According to their individual preferences and after obtaining their written informed consent, the patients in **Group A** were divided into 2 Subgroups (**A1** = for conventional mesotherapy; **A2** = for PRM mesotherapy):

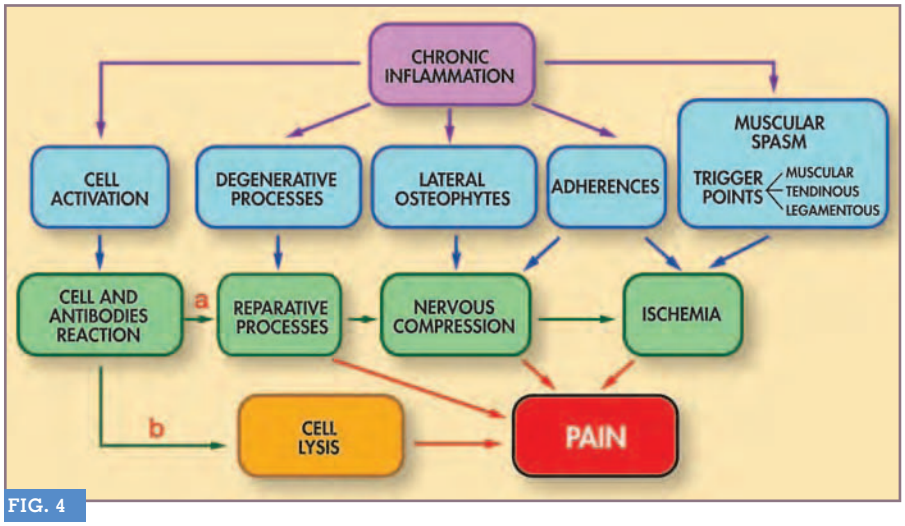
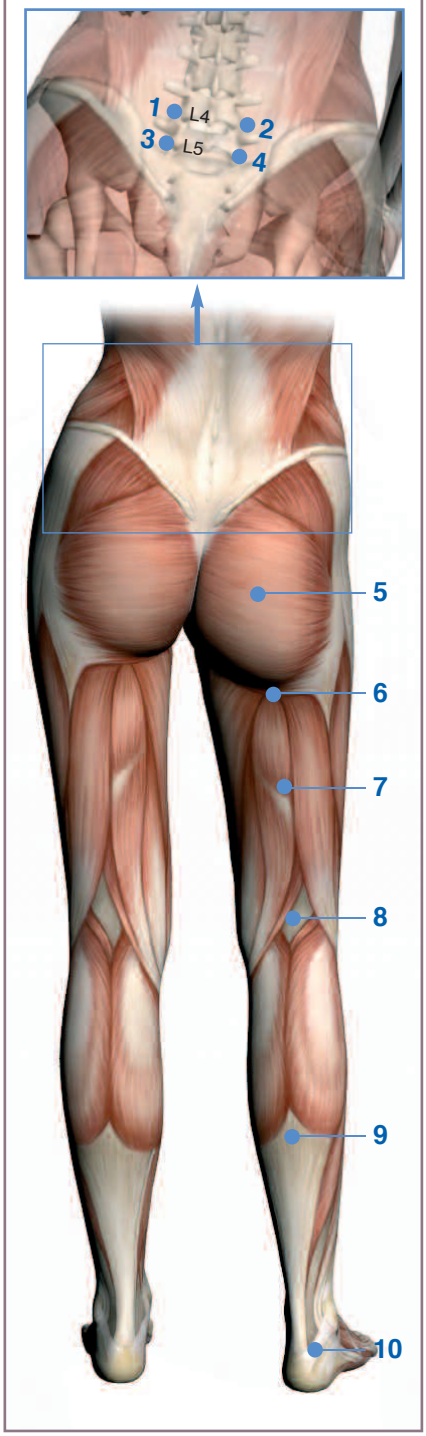


FIG. 4

Genesis of chronic lumbago and lumbosciatica secondary to surgery involving posterior laminectomy.

FIG. 5



Anatomical sites of the points for infiltration with:
- SUBGROUP A1 = POINTS from 1 to 10: 0.4 ml per point of KPF s.c., 4 mm 27 G. needle.

- SUBGROUP A2 =
- **POINTS 1, 2, 3, 4: GUNA®-LUMBAR 1 ampoule + GUNA®-MUSCLE 1 ampoule; s.c. injection of 1 ml of cocktail per point, 4 mm 27 G needle.**
- **POINTS 5, 6, 7, 8, 9, 10: GUNA®-ISCHIAL 2 ampoules + GUNA®-NEURAL 2 ampoules; s.c. injection of 1.3 ml of cocktail per point.**

POINTS 1 and 2: 2-3 cm laterally from the inferior margin of the spinous process of L4.
- They coincide with the acupuncture point U.B. 25.
POINTS 3 and 4: 2-3 cm laterally from the inferior margin of the spinous process of L5.
- They coincide with the acupuncture point U.B. 26.
POINT 5: 6-7 cm laterally from the posterior median line, 1-2 cm under the tip of the coccyx.
- It coincides with the acupuncture point U.B. 54.
POINT 6: point at the midline along the gluteal crease.
- It coincides with the acupuncture point U.B. 36.
POINT 7: on a line connecting the midpoints of the gluteal transverse crease, 10-12 cm below the former.
- It coincides with the acupuncture point U.B. 37.
POINT 8: exact midpoint of the popliteal transverse crease.
- It coincides with the acupuncture point U.B. 40.
POINT 9: Point midway between POINT 8 and the tip of the heel.
- It coincides with the acupuncture point U.B. 57.
POINT 10: 3-4 cm inferiorly and posteriorly to the tip of the external malleolus.
- It coincides with the acupuncture point U.B. 61.

1) **Subgroup A1** (**10** patients; 8 M, 2 F; mean age 49.6 years).
Patients were treated with 8 consecutive sessions of analgesic/anti-inflammatory mesotherapy with KPF, 2 ampoules (2 ml = 100 mg each) injected s.c. with a 4 mm 27 G needle in 10 previously-established points (FIG. 5).
All patients in Subgroup A1 suffered from lumbosciatica in L5 or S1.
- Quantity of KPF per point = 0.4 ml ≈.
- Frequency of applications: twice a week (e.g. on Mondays and Thursdays) for the first 4 applications, then once a week.

2) **Subgroup A2** (**10** patients; 4 M, 6 F; mean age 52.2 years). Patients were treated with 8 consecutive sessions of PRM mesotherapy with the following cocktail:

a. **Guna®-Lumbar** 1 ampoule (2 ml) + **Guna®-Muscle** 1 ampoule (2 ml), injected in four equal aliquots (1 ml) in 4 points in the low back (FIG. 5), using a 4 mm 27 G needle;
b. **Guna®-Ischial** 2 ampoules (4 ml) + **Guna®-Neural** 2 ampoules (4 ml) in 6 points located on the lower limb (FIG. 5), using a 4 mm 27 G needle.
- Quantity of cocktail per point: 1.3 ml ≈.

All patients in Subgroup A2 suffered from lumbosciatica in L5 or S1.
None of them had lumbo-crural pain.
- Frequency of applications: the same as for Subgroup A1 (*see above*).

For **all** patients in Group A: treatment at home with **Guna®-Matrix** (20 drops, twice a day, at 9 a.m. and 9 p.m.) + **Guna®-Flam** (20 drops, twice a day, at 9 a.m. and 9 p.m.). For details on Guna®-Matrix, *see* Milani, 2007 *b*.

All patients in Group A (Subgroups A1, and A2) completed the **NRS** (Numerical Rating Scale) and the **SF-36**. The NRS is easy to administer and is associated with a better compliance than Visual Analog Scales at all ages (0 = least possible pain; 10 = intolerable pain). The SF-36 is considered an extremely reliable test (Brazier *et* Al., 1992).

Both tests were administered before starting the therapy, immediately after completing the last treatment and then approximately 130 days (4 months) after completing the cycle of treatment (follow-up). The follow-up tests was completed for 17/20 patients in Group A (85%), i.e. Subgroup A1: 8/10 patients (80%); Subgroup A2: 9/10 patients (90%).

The results are shown in TABLES 1. and 2.

- The study demonstrated the efficacy of both types of mesotherapy (conventional allopathic and PRM), **and of the PRM mesotherapy, in particular, in the treatment of non-invalidating chronic lumbosciatica**.

In particular, in Subgroup A2 (PRM):

- the NRS score went from 7 before treatment to 5 immediately after completing the cycle of treatment, dropping further to 3.8 at the follow-up;

- the SF-36 score went from 23.1 before the treatment to 83.9 immediately after completing the full cycle of therapy, settling at 78.4 at the follow-up.

We believe that the better results obtained

in Subgroup A2 in the treatment of non-invalidating chronic lumbosciatica are attributable to the particular nature and formulation of the PRM injectable ampoules employed.

The patients in Subgroup A2 (PRM) received a therapy divided into two parts:
1) lumbar spine area
(**Guna®-Lumbar** + **Guna®-Muscle**);
2) sciatic nerve area
(**Guna®-Ischial** + **Guna®-Neural**),
according to the principle of **anatomical specificity** of the PRM Pain Therapy injectable formulations.

IN THE LUMBAR SPINE AREA:

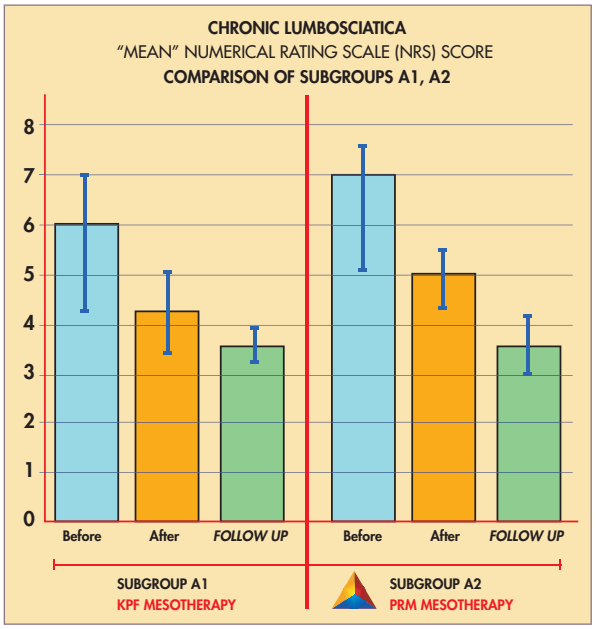
Guna®-Lumbar

According to the rationale behind the formulation and structure of **Guna®-Lumbar**, the presence of anti-IL1α4C and anti-IL1ß 4C guarantees a powerful anti-inflammatory and analgesic effect (*in* Milani, 2006; Milani, 2007 *a*).
Low-dose, low-titer anti-inflammatory cytokines have been the object of basic research (Amadori *et* Al., 2007; Gariboldi *et* Al., 2009). The presence of beta-endorphin 4C also guarantees a reduction of the painful symptoms due to an upregulation of the specific receptors. Intervertebral disc 4X has an anti-degenerative action on the intervertebral discs and, more in general, an anti-neuralgic effect. According to Materia Medica, the reduction in low back pain is further guaranteed by *Bryonia* 4X, *Alumina* 8X, and *Phosphoricum acidum* 6X.

Hamamelis 6X regulates venous peridiscal congestion and *Natrium sulph*. 8X has an effective action on the small vertebral joints, such as the articular facets.

Guna®-Muscle

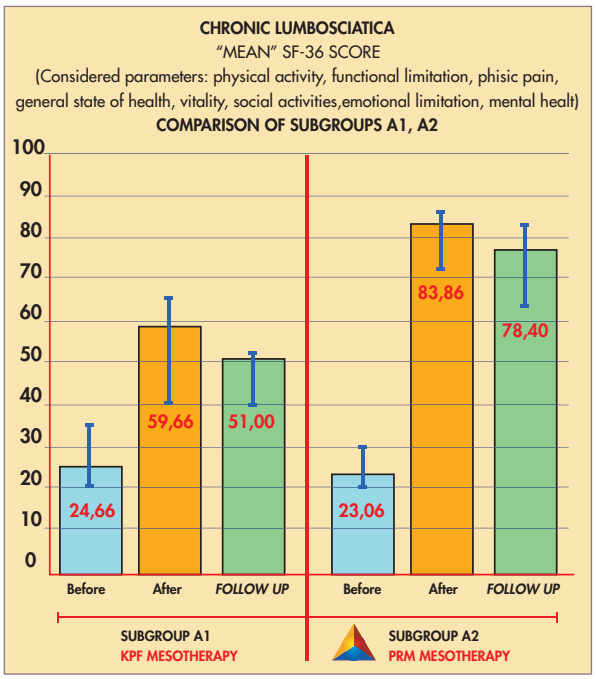
Guna®-Muscle has been the object of clinical experimentation (Milani, 2006; Hermann *et* Al., 2008) and detailed clinical considerations (Milani, 2008). Because of the presence of its 5 constitutive core ingredients, i.e. (i) spastic or cramp-like pain (*Colocynthis* 4X; *Cuprum sulphuricum* 4X), (ii) sprain pain (*Hypericum* 4X), (iii) contusive pain (*Arnica* 4X; *Belladonna* 6X), (iv) muscular rheumatism (*Colchicum* 6X; *Lithium benzoicum* 8X), and (v) anti-degenerative core (*Muscle tissue* 4C; *Procain chloride* 2X), it is the specific low-dose, low-titer medicine for TP management, always involved and active in the low back muscles in cases of lumbosciatica.



TAB. 1

- **Subgroup A1. The mean NRS score dropped from 6 before the treatment to 3.8 at the end of the follow-up, 130 days after completing the cycle of treatment (difference 2.2).**

- **Subgroup A2. The mean NRS score dropped from 7 before the treatment to 3.5 at the end of the follow-up, 130 days after completing the cycle of treatment (difference 3.5).**



TAB. 2

- **Subgroup A1. The mean SF-36 score rose from 24,66 before the treatment to 51.0 at the end of follow-up, 130 days after completing the cycle of treatment (difference 26.34).**

- **Subgroup A2. The mean SF-36 score rose from 23.06 before the treatment to 78.4 at the end of the follow-up, 130 days after completing the cycle of treatment (difference 55.34).**

IN THE SCIATIC NERVE AREA:

Guna®-Ischial

According to the recommendations (Guna Method, Therapeutic Guide; 2007), **Guna®-Ischial** is the injectable medicine explicitly formulated for sciatica, lumbosciatic pain, nerve pain in the lower lumbar spine, leg nerve pain due to the post-surgery treatment of disc herniation in L4 - L5 - S1, etc. In addition to the formulation containing an anti-inflammatory core (anti-IL 1α 4C; anti-IL 1ß 4C) and an analgesic PNEI core (beta endorphin 4C), there are also 3 antineuralgic cores:

- primary neuralgic pain: *Gnaphalium* 4X, *Arsenicum album* 6X, *Rhododendron* 6X, *Aconitum napellus* 8X. *Lachesis* 8X (which is also effective in the treatment of reflexed neuralgic pain); and

- secondary neuralgic pain: *Rhus tox.* 4X; *Cimicifuga* 4X (this is also effective in the treatment of reflexed neuralgic pain).

Guna®-Neural

In **Guna®-Neural**, the presence in the anti-degenerative core of Neurothophin (NT) 4 4C gives this medicine a very important and specific neurotrophic effect.
NT4 is a small protein that ensures the survival of the peripheral neurons and combats retrograde neuronal degeneration. Studies on *low-dose* NT4 have been conducted by Malzac (2002) and Milani (2009).
It is worth adding that some of the components of the four PRM drugs used in the patients in Group A2 have been the object of tests in quality basic research, e.g. *Arnica* (van Haelen *and* Fastré, 1968; 1972; 1973. Macedo *et* Al., 2004); *Belladonna* (Poitevin *et* Al. 1983); *Aconitum* (Pennec *and* Aubin, 1984); *Lachesis* (Enbergs *and* Arndt, 1993); *Rhus tox.* (Wenquin *et* Al., 2000); *Arsenicum album* (Lira-Salazar *et* Al., 2006).

Group B = patients with chronic low back pain

- The preset number of patients was **20** (11 M; 9 F); mean age 44.8 years.
- Inclusion criteria: 1) patients suffering from monolateral, bilateral lumbago, or iliac crest pain according to Caillet (1977) and Maigne (1997) for more than 3 months; 2) pregnancy beyond the third month.
- Exclusion criteria: 1) patients suffering from the types of pain stated in the inclusion criteria, but for less than 3 months; or patients with spondylolysthesis or congenital alterations of the lumbosacral spine; 2) patients suffering from liver and/or kidney diseases; 3) pregnancy up to the third month; 4) patients with gastroduodenal ulcer.

According to their personal preferences and after obtaining their written informed consent, patients in **Group B** were divided into 2 Subgroups (**B1** = for conventional mesotherapy; **B2** = for PRM mesotherapy):

1) **Subgroup B1** (**10** patients; 6 M, 4 F; mean age 43.2 years).
Patients were treated with 8 consecutive sessions of analgesic/anti-inflammatory mesotherapy with Ketoprofen (KPF) 2 ampoules (2 ml = 100 mg each) injected s.c. with a 4 mm 27G needle in 8 previously-established points (FIG. 6).
It should be noted that, in addition to the above-stated characteristics, KPF has proved effective (Metscher *et* Al., 2001) and superior in therapeutic efficacy to Diclofenac in the symptomatic treatment of acute low back pain (Zippel *and* Wagenitz, 2007).
- Quantity of KPF in each point: ≈ 0.5 ml.
- Frequency of applications: twice a week for the first 4 (e.g. Mondays and Thursdays), then once a week for the other 4.

2) **Subgroup B2** (**10** patients; 5 M, 5 F; mean age 46.4 years).
Patients were treated with 8 consecutive sessions of PRM mesotherapy with the cocktail:
a) **Guna®-Lumbar** 2 ampoules (4 ml)

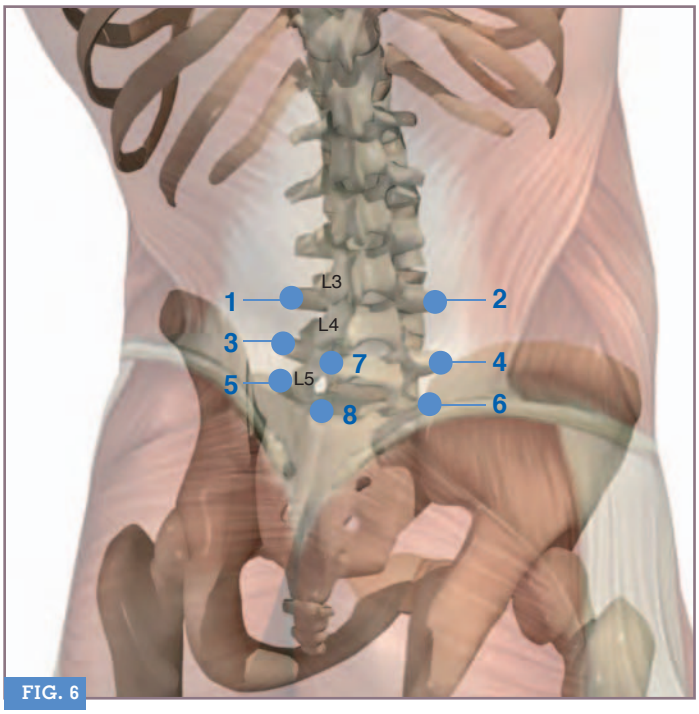


FIG. 6

Anatomical sites of the points for infiltration with:
- **SUBGROUP B1 =**
  - **POINTS from 1 to 8: 0.5 ml per point of KPF s.c., 4 mm 27 G needle.**
- **SUBGROUP B2 =**
  - **POINTS 1, 2, 3, 4, 5, 6: cocktail of GUNA®-MUSCLE 2 ampoules + GUNA®-NEURAL 2 ampoules, 1,3 ml per point, s.c., 4 mm 27 G needle.**
  - **POINTS 7, 8: GUNA®-LUMBAR 2 ampoules, 2 ml per point, i.d., 4mm 27 G needle.**

POINTS 1 and 2: 2-3 cm laterally from the inferior margin of the spinous process of L3. They coincide with the acupuncture point U.B. 24.
POINTS 3 and 4: 3-4 cm laterally from the inferior margin of the spinous process of L4. Points 3 and 4 are located more externally than the acupuncture point U.B. 25.
POINTS 5 and 6: 2-3 cm laterally from the inferior margin of the spinous process of L5. They coincide with the acupuncture point U.B. 26.
POINT 7: Interspinous space L4-L5. It coincides with the acupuncture point D.U. 3.
POINT 8: Interspinous space L5-S1.

intra-dermal (i.d.) at the level of the inter-spinous spaces L4 - L5 and L5 - S1 (2 ml of cocktail for each of the points infiltrated) (FIG. 6).

b) **Guna®-Muscle** 2 ampoules (4 ml) + **Guna®-Neural** 2 ampoules (4 ml) in 6 previously established points (3 on each side) (FIG. 6).

The Guna®-Muscle + Guna®-Neural cocktail was injected 1,3 ml at each point s.c. with a 4 mm 27G needle.

- Frequency of applications: same as for Subgroup B1 (*see above*).

For **all** patients in Group B: treatment at home with **Guna®-Matrix** (20 drops, twice a day at 9 a.m. and 9 p.m.) + **Guna®-Lympho** (20 drops, twice a day at 9 a.m. and 9 p.m.).

All patients in Group B (Subgroups B1 and B2) completed the *Oswestry Disability Index* (**ODI**) Version 2.0 (also called the Oswestry Low Back Pain Disability Questionnaire) (*in* Fairbank *et* Al., 1980; Fairbank *and* Pynsent, 2000), which includes 10 sections (1 - Pain Intensity; 2 - Personal Care; 3 - Lifting; 4 - Walking; 5 - Sitting; 6 - Standing; 7 - Sleeping; 8 - Sex Life; 9 - Social Life; 10 - Travelling), each consisting of six questions that the patient answers by attributing a score from 0 to 6.

The interpretation of the **degree of disability** is simple to calculate, by inputting the sum of the points scored in each section in the following formula:

total points / 50 x 100 = % disability.

Example: ODI score 32; 32/50x100= 64% disability (D) where:
0% - 20% = minimal D; 21% - 40% = moderate D; 41% - 60% = severe D; 61% - 80% crippled D; 81% - 100% = these patients may be in bedbound or exaggerating their symptoms.
Careful evaluation is recommended.
The ODI was administered before starting the therapy, immediately after completing the last treatment, and 130 days after completing the cycle of treatment (end of follow-up).

The follow-up tests were completed for 18/20 patients in Group B (90%), i.e. Subgroup B1 = 9/10 patients (90%); Subgroup B2 = 9/10 patients (90%).

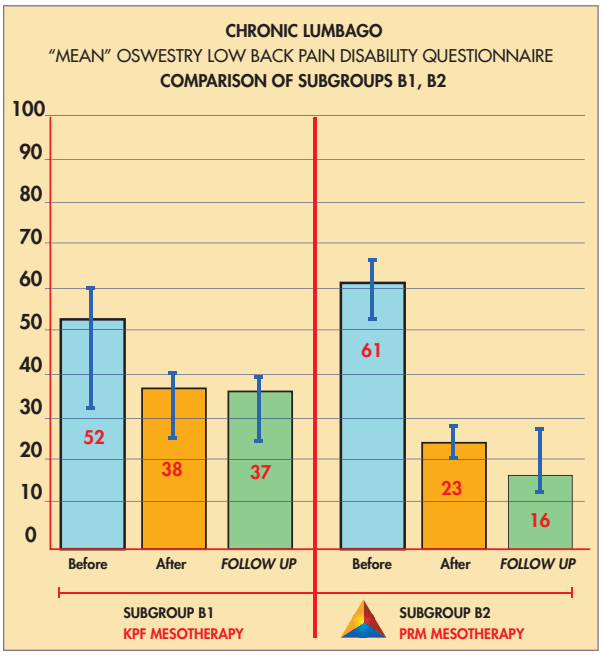
The results are given in TABLE 3.

The study demonstrated the efficacy of both treatments, and a **much better outcome for the patients in Subgroup B2** (PRM).

CONCLUSIONS AND COMMENTS

This cohort controlled clinical study compared two mesotherapeutic techniques, i.e. conventional (Subgroups A1; B1) *vs* PRM (Subgroups A2; B2), applied to the same injection points for the **treatment of chronic non-invalidating lumbosciatica** and **lumbago**. Both conditions were chronic at the time of the patients' inclusion since they had been suffering from the disorder for more than 3 months. The two Subgroups (1, 2) of patients with each of the two conditions considered were comparable in terms of number and severity of disease, so the results were comparable. Both the Subgroups in each of the two Groups received the same treatment at home, which remained the same throughout the follow-up, so that any differences in the results could depend exclusively on the conventional or PRM mesotherapy, and were consequently comparable.
The clinical assessment was done by the patient alone to avoid any interpretation bias on the part of the physicians involved in the study.
- Neither of the treatments revealed any relevant side-effects, except for three patients (one in Subgroup A1, and two in Subgroup B1) who suffered from transient nausea during the 3rd, 4th and 7th sessions, respectively. One of the known side-effects of KPF is nausea.
Tolerability and compliance were excellent in both Groups.
During the treatment, none of the patients in either Group needed any other type of pharmacological or physical therapy.
The study demonstrated that conventional and PRM mesotherapy are both highly effective in the treatment of chronic lumbosciatica and lumbago.
- This was particularly evident in the patients treated with PRM mesotherapy, when compared between the findings at the baseline and at the end of the follow-up.

- Subgroup A2: there was a reduction in



TAB. 3

- **Subgroup B1. The mean ODI score dropped from 52 before the treatment to 37 at the end of the follow-up, 130 days after completing the cycle of treatment (difference 29%).**

- **Subgroup B2. The mean ODI score dropped from 61 before the treatment to 16 at the end of the follow-up, 130 days after completing the cycle of treatment (difference 73%).**

The improvement in the ODI score in Subgroup B2 was 2.5 greater than in Subgroup B1.

the mean NRS score from 7 to 3.5, with a difference of 3.5 (50% of the initial value) and rise in the mean SF-36 score from 23.06 to 78.40, with a difference of 55.34 (a more than 200% improvement over the initial value). This diversity in the results depends exclusively on the different parameters considered by the two scales: the SF-36 also contemplate parameters such as general state of health, social activities and vitality, that are not included in the NRS, but are very important for patients.

- Subgroup B2: there was a reduction in the mean ODI from 61 to 16, with a difference of 45 (73% of the initial value), which means that, on average, each patient who initially had moderate-severe low back pain was experiencing minimal, well-tolerated symptoms after approximately 3 months of treatment and follow-up.

- Since the results achieved by the PRM Pain Therapy were compared with those obtained with a powerful NSAID (KPF), we believe that the outcome of this study - demonstrating the superiority of PRM mesotheraphy *vs* conventional mesotherapy - is of interest, given the former's ease of application and safety. Subgroup B2 also included two pregnant patients (in their fifth and sixth months of gestation) suffering from chronic lumbago due to lumbar hyperlordosis, who completed the therapy and successfully delivered at term.

The PRM Pain Therapy injectable drugs guarantee a specificity of action on single anatomical parts.

Thanks to their composition and the rationale for their use, they can be variously mixed together or with other *low-dose*, *low-titer* injectable drugs according to the physician's preference and personal experience.

- Our data enable us to conclude that, in adults with non-invalidating chronic lumbosciatica and chronic lumbago, the PRM Pain Therapy injectable ampoules forming the object of this study are effective, safe, and well tolerated. ■

A. Ruocco and N. D. Lima contributed equally to this paper.

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