CLINICAL

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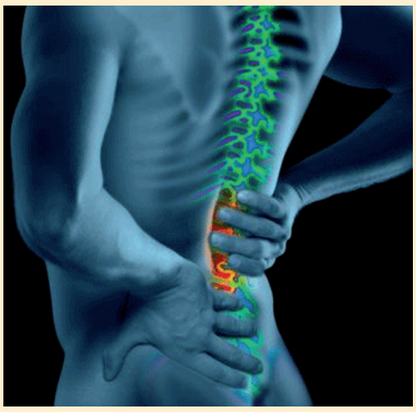
MD-LUMBAR, MD-MUSCLE AND MD-NEURAL IN THE TREATMENT OF LOW BACK PAIN

SUMMARY

– Background
There are still unmet needs in finding optimal drug for the treatment of acute LBP. One of the discussed treatment options is local injection treatment with collagen.
– Methodology
Patients: aged 20-70, suffering from acute LBP with duration < 3 months and with minimum intensity of pain ≥ 40 mm on VAS.
– Outcomes: Pain intensity of difference between the baseline and final visits (VAS). Secondary outcomes: HAQ, Oswestry questionnaire, use of rescue medication, tolerance.
– Therapy: MD-Muscle (1 ml) + MD-Lumbar (2 ml) + MD-Neural (1 ml) or 4 ml of 1 % mesocain in 8 predefined points. Rescue medication: paracetamol < 3 g/daily.
– Results
48 patients were included (36 Collagen MDs vs 12 mesocain). Pain on movement decreased from initial mean 70.1 ± 13.6 to 36.6 ± 23.5 at week 5 ($p < 0.05$) in the MD group and from 70.8 ± 11.5 to 31.9 ± 26.8 in the mesocain group ($p < 0.05$) with no statistical differences between both groups.
Pain at rest decreased from 59.6 ± 16.9 to 28.1 ± 24.1 ($p < 0.05$) in the MD group and from 57.3 ± 16.4 to 25.1 ± 26.9 ($p < 0.05$) in the mesocain group. The differences between the groups were not significant.
Consumption of analgesics tablets (paracetamol 500 mg) was numerically but not significantly lower in the MD group in comparison with the mesocain group (14.4 ± 16.2 vs. 20.4 ± 27.0 NS).
– Conclusions
MD-Lumbar, MD-Muscle, MD-Neural appear to be effective in the treatment of acute low back pain.

KEY WORDS **LOW BACK PAIN, COLLAGEN MEDICAL DEVICE**



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Acute nonspecific low back pain (**LBP**) is defined as LBP not attributed to a recognisable, known, or specific pathology (inflammation, fracture, tumor, radicular syndrome or *cauda equina* syndrome) with a duration of 6 weeks (1).

Acute LBP is usually self-limiting with a recovery rate of 90% within 6 weeks. Peak prevalence occurs between 35 and 55 years and lifetime prevalence is up to 84 %.
– The estimated lifetime prevalence of chronic LBP is about 23%.

Treatment of acute low back pain in primary care aims at: providing adequate information, providing adequate symptom control if necessary, recommending the patient to stay as much as possible active and return early to normal activities, including work (2).

The optimal solution to treat LBP is given by multidisciplinary treatment programmes which usually comprise combination of physical, vocational and behavioural components and adaptation of drug use. The following drugs are recommended for the pharmacological treatment: paracetamol and other analgesics, nonsteroidal antirheumatic drugs (NSAIDs), muscle relaxants, weak and strong opioids, and antidepressants.
– NSAID are most commonly prescribed worldwide for LBP. The administration of NSAIDs may be complicated by NSAIDS induced gastropathy and its serious complications as perforations, ulcerations, and bleeding (PUB) (3).

Introducing COX-2 selective drugs (coxibs) has improved GIT safety profile (4) but has probably increased cardiovascular risk (5); this can be true also for non-selective NSAIDS.
Because of potentially serious adverse events, NSAIDs should be used only for short periods.
There are still unmet medical needs in finding the optimal drug for the treatment of acute LBP.
One of the treatment options is the local injection treatment with collagen.

– **MD-Lumbar** (Guna Laboratories - Milan - Italy) is a medical device composed of collagen and extract of Hamamelis.
– The mechanism of action of locally applied collagen – both structural and functional – is complex.
In the affected tissues the collagen forms a bio-scaffold and long-term action is guaranteed by a patented principle of collagen injectable delivery system.
The Collagen MD replaces the lack of collagen, which is always recurrent in the inflammatory and/or degenerative diseases of the Locomotor Apparatus.
The collagen has also a barrier effect and a lubrication activity.
It is also spasmolytic, it improves function and help decreasing pain (6).

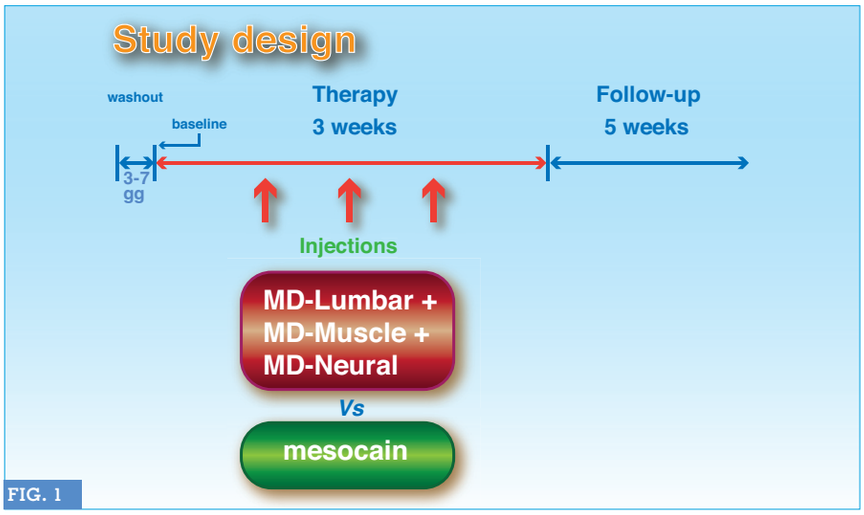

FIG. 1

The extract from Hamamelis has antioxidant and anti-inflammatory efficacy.

– **MD-Muscle** is a medical device composed also by collagen and extract of Hypericum.
This extract has anti-inflammatory, analgesic, and antidepressant activity.

– **MD-Neural** is a medical device made up of a mix of collagen and extract of Colocynthis.
It has spasmolytic and analgesic efficacy with impact on the neuropathic pain.

MD-Muscle, MD-Neural and MD-Lumbar have been tested in different painful conditions of the locomotor system, like osteoarthritis and soft tissue rheumatism including LBP.
In order to get more information about the efficacy of the mix of medical devices, we have suggested a protocol for a randomized, controlled trial to treat acute low back pain.

Collagen has been used in several experimental models of ligament lesions, where it demonstrated the ability of supporting collagen fibrillogenesis in healing collateral ligament in rabbits (7) and also in a group of 10 patients with degenerative cartilage lesions (8).

METHODOLOGY

Design of the study

This single blind, clinical study was designed to evaluate the efficacy and safety of MD-Lumbar, MD-Muscle, and MD-Neural in comparison with mesocain in subcutaneous application in patients with acute low back pain.

FIG. 1 shows the flowchart of the study. After 3-7 days washout, patients were allotted to one of the two groups according to the randomization schedule.
The study was blind for patient but not for the physician.
– The primary outcome measure occurred at week 5, two weeks after the last treatment.

Patients

Patients aged between 20 and 70 years, having signed the informed consent, were included.
They were diagnosed as having acute non-specific LBP with a duration of the disease inferior to 3 months.
The minimum intensity of pain was 40 on scale 0-100.

Main exclusion criteria were: neurologic symptoms longer than 1 month, *cauda equina* syndrome, inflammatory spinal disease, malignant diseases, compression fracture in osteoporosis, recent trauma and therapy with myorelaxants, immunosuppressive drugs and glucocorticosteroids.

– **75 patients** in the MD group; **25 patients** in the control group.

Outcomes

– The primary outcome was the comparison of the difference in pain intensity between the baseline and the final visits obtained by the two study groups.

– Secondary outcomes were functional improvement measured by HAQ, Oswestry questionnaire, comparison of the use of rescue medication and evaluation of tolerance.

Medication

In the active treatment group the patients have received injections of **MD-Muscle** (1 ml), **MD-Lumbar** (2 ml) and **MD-Neural** (1 ml) in 8 predefined points (0,5 ml per point).
– In the control group patients have been administered 4 ml of 1 % mesocain distributed in the same 8 points;

	MD	Mesocain	
Patients	**36**	**12**	
M/F	7/29	4/8	NS
Age	54.2 ± 11.4	56.2 ± 11.6	NS
VAS pain on movement	70.1 ± 13.6	70.8 ± 11.5	NS
VAS pain at rest	59.6 ± 16.9	57.3 ± 16.4	NS
Analgesic treatment before	15/21 (58.3 %)	5/7 (11.3 %)	NS

TAB. 1

General characteristics of the patients included in the 2 treatment groups.

the number of applications was 5 (2/weeks + 1).

Patients have been allowed to use paracetamol (3 g daily *max*) as rescue analgesic medication.
NSAIDs, other analgesics and local treatment with glucocorticoids were not allowed. Newly introduced physical therapy was also not allowed.
Statistical methods for assessment of consumption of analgesics, global assessment and questionnaires, parametric and non-parametric tests were used (T test, ANOVA, Manova analysis of repeated measures, Kruskall-Wallis, Wilcoxon pair test and Mann-Whitney U test).

RESULTS

Here are presented the preliminary results of the *interim* analyses.

– There were altogether **48** patients included and analysed in the study: **36** in the MD group, and **12** in the control group. There were no statistical differences between the two groups as far as sex, age, intensity of pain at rest and pain on movement and usage of analgesics before the study (TAB. 1).

The intensity of pain at baseline was high/about 70 mm on VAS scale 0-100. Pain on movement decreased from initial mean **70.1 ± 13.6** to **36.6 ± 23.5** at week 5 ($p < 0.05$) in the MD group and from **70.8 ± 11.5** to **31.9 ± 26.8** in the mesocain group ($p < 0.05$) with no statistical differences between the two groups (TAB. 2, FIG. 2).

Pain at rest decreased from **59.6 ± 16.9** to **28.1 ± 24.1** ($p < 0.05$) in the MD group and from **57.3 ± 16.4** to **25.1 ± 26.9** in the mesocain group ($p < 0.05$) at week 5. The differences between the two groups are not significant.
The consumption of analgesics tablets (paracetamol 500 mg) was numerically but not significantly lower in the MD group in comparison with the mesocain group (**14.4 ± 16.2** *vs.* **20.4 ± 27.0** NS) (TAB. 3).
The tolerance of the treatment was very good. No serious adverse event was reported in both groups.
The patients evaluated the tolerance of MD as very good in **66.7 %**, as good in **25 %**, and medium in **8.33 %**.
Tolerance of mesocain injections was evaluated as very good in **83.3 %**, good in **7.33 %** and medium in **8.33** % also (NS differences between the groups) (TAB. 4).

DISCUSSION

Management of acute but also chronic

Item	N	MD	Mesocain
VAS, Pain on movement, Visit 1	36/12	70.1 ± 13.6	70.8 ± 11.5
VAS, Pain on movement, Visit 5		46.0 ± 18.5	39.3 ± 26.6
VAS, Pain on movement, Visit 6		39.6 ± 20.5	37.6 ± 28.5
VAS, Pain on movement, Visit 7		36.6 ± 23.5	31.9 ± 26.8
VAS, Pain at rest, Visit 1	36/12	59.6 ± 16.9	57.3 ± 16.4
VAS, Pain at rest, Visit 5		37.3 ± 18.7	33.6 ± 25.8
VAS, Pain at rest, Visit 6		30.0 ± 22.4	29.5 ± 27.1
VAS, Pain at rest, Visit 7		28.1 ± 24.1	25.1 ± 26.9

TAB. 2

Analogic-visual pain scale in the 2 treatment Groups. Score decrease from Visit 1 to Visit 7 (pain on movement and at rest).

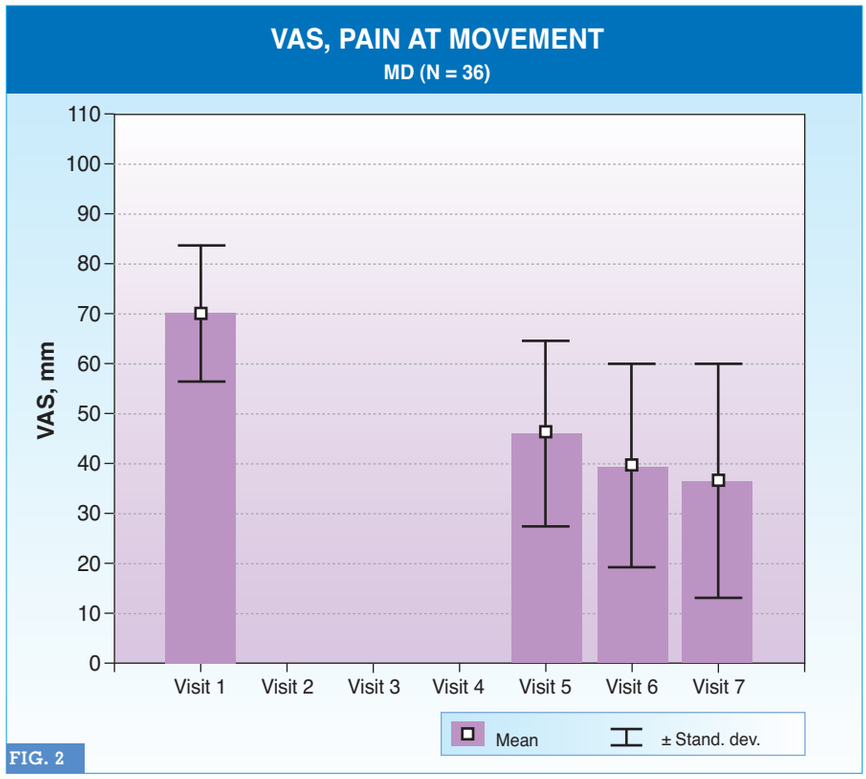

FIG. 2

back pain remains still a challenge with not yet available optimal drug.
MD local injections are new and very innovative, based on physiological regulation (Physiological Regulation Medicine).

MD injections were tested in 7 controlled trials, which has been part of submission dossier (6). Tested conditions were lumbar and neck pain, knee, hip and hand OA, sciatica, neuropathic pain, shoulder pain, wound healing.

The studies have shown good efficacy and no serious adverse events.
MD injections have also no drug interactions and can be used concomitantly with other drugs, which is of great advantage especially for old people or patients with polymorbidities.

– The results of our study suggest that the mix of the 3 tested MD is effective in the treatment of acute LBP.

Our results must be interpreted with caution, because of many limitations. Firstly, the study is still on going with aim to recruit 100 patients; here we are presenting the *interim* analysis of 48 patients.
– Nevertheless, some preliminary clinical findings can be already discussed.

The patients mean improvement of pain is around 30 mm on VAS which is definitively much more than minimal, clinically important improvement of pain, which is about 15-20 mm.
The onset of pain relief is relatively quick in less than 2 weeks.
– **Analgesic efficacy of MD seems to be at least good as of mesocain.**
Long term treatment focused on restructuralization and stabilization of connective tissue by MD injections can be achieved only by MD injections. MD injection treatment is of course much more physiological in long term therapy in comparison with local anaesthetics providing the immediate anaesthetic and analgesic effect.

The other positive point is the very good tolerance of MD local treatment and good adherence to therapy.
It is commonly accepted that generally adherence to treatment in chronic painful conditions of the Locomotor Apparatus is an important issue.

CONCLUSIONS

▶ MD-Lumbar, MD-Muscle, and MD-Neural appear to be effective in treatment of acute low back pain.

▶ MD-Lumbar, MD-Muscle, and MD-Neural are well tolerated.

▶ MDs might be effective and a safe choice in the therapy of acute back pain. ■

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Item	N	MD	Mesocain	Stat. signif. of diff.
Paracetamol consumption during Visits 1 - 6 (no. of. tbl.)	36/12	**14.4 ± 16.2**	**20.4 ± 27.9**	Unpaired T-test, NS

TAB. 3
Paracetamol consumption.

Item	MD	Mesocain	Stat. signif. of diff.
Tolerance, Visit 6, Very good	24 **(66.7 %)**	10 **(83.3 %)**	Chi-square test, NS
Tolerance, Visit 6, Good	9 **(25.0 %)**	1 **(8.33 %)**	
Tolerance, Visit 6, Medium	3 **(8.33 %)**	1 **(8.33 %)**	

TAB. 4
Therapy tolerance (patients' evaluation). Evaluation took place at the end of Visit 6.

Paper presented at the
26th Congress of Biological Medicine
26th May 2012, Milan - Italy

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