CLINICAL

P. Godek

COLLAGEN THERAPY IN LUMBAR SPONDYLOSIS. DOES THE METHOD OF ADMINISTRATION MATTER?

– A PILOT STUDY

SUMMARY

Objective: Comparison of the effectiveness of collagen injections with three methods of administration in the treatment of low back pain (LBP) in lumbar spondylosis.
Materials and methods: Randomized prospective study, 30 patients with lumbar spondylosis were assigned to 3 groups: subcutaneous (group A, n = 10), periradicular (group B, n = 10), and epidural (group C, n = 10).
Collagen injections were carried out once a week (in total 4 injections).
Assessment: Visual Analogue Scale (VAS) (0-10), Oswestry scale (0-50), Laitinen scale (0-16), One Leg Stence Test (OLST) – time to occurrence of pain in the support limb.
Endpoints: start of therapy (W0), end (W1) and 1 month after its completion (W2).
Results: An improvement was obtained in all the 3 methods of collagen Medical Devices administration. Minimal clinically important difference (MID) i.e. 3 points on the VAS scale was observed in 44% of patients in group A, 40% of patients in group B and 60% in group C. MID on the Oswestry scale determined at 10 points was obtained respectively in 56%, 50% and 20% of patients, while MID for Laitinen scale determined at 4 points was obtained in 56%, 30% and 40% of patients, respectively.
Only in the A group all treated patients achieved a reference value of 30 seconds for OLST.
Conclusions: Subcutaneous administration collagen is not inferior in terms of effectiveness to periradicular and epidural injections in the treatment of LBP in lumbar spondylosis.

KEY WORDS

CHRONIC LOW BACK PAIN, CHRONIC PAIN TREATMENT, CHRONIC PAIN, PAIN CONTROL, MEDICAL DEVICE INJECTIONS

INTRODUCTION

Low back pain (LBP) is one of the 10 most common diseases of civilization, covering, as estimated by WHO, 60-70% of the population in developed countries with an annual prevalence of 15-45% adults and an annual incidence of 5% (1).

The mechanism of pain in the lumbar region is a very complex process. Anatomical pain generators are well known because intervertebral discs, *dura mater*, facet joints, and paravertebral soft tissues have nociceptive innervation. Pain conduction pathways are also well known, but the mechanisms of disturbed "processing" of the pain signal at the level of the dorsal root ganglion, spinal cord or cerebral centers, and the associated sensitization processes leading to pain chronicization are still the subject of intensive study (2).

The experience of Pain Medicine in research on the administration of synthetic drugs on the example of local anesthetics and steroids leads to linear thinking - the precision of access to pain generators and strictly defined dosage are a condition of treatment effectiveness and determine the strength of the therapeutic effect (3).

– For collagen, the same paradigm no longer seems so obvious, because clinical experience shows that some patients have remarkable improvement even after subcutaneous administration of collagen in the lumbar spine, which seems to be away from major pain generators.

Even in the case of very advanced degenerative processes, in addition to reducing pain, it is also reported functional effects such as obtaining upright posture, increasing flexibility and improving overall mobility.
This suggests that collagen is not an ordinary drug that works on a complementary basis with a specific receptor, causing a therapeutic effect proportional to the dose and local availability, but rather it is a catalyst for change, a biologically active substance that triggers a cascade of repair processes. The following arguments support the use of injectable collagen in the treatment of low back pain:
1) inflammatory process associated with discogenic instability is always associated with an increased collagen biodegradation, the supply of exogenous collagen reduces the negative balance of production and biodegradation;
2) collagen fulfills the role of a biological medium (bio-scaffold) for cell colonization producing a tissue signal promoting healing (monocytes, platelets, macrophages, fibroblasts);
3) collagen has spasmolytic and anti-edema effects through the barrier effect;
4) exogenous collagen, provides a substrate for the production of new collagen chains; on the one hand, it contributes to the stabilization of capsule and ligament structures, and on the other, it improves mobility through fascia reorganization (4,5,6).

– The aim of this study was to check whether the administration of collagen in the immediate proximity of pain generators (periradicular, epidural) improves its effectiveness in comparison with the superficial (subcutaneous) administration of the same dose.

MATERIALS AND METHODS

The study was single-center, prospective, randomized and open.
– Inclusion criteria: adult patients, positive signs and symptoms in a clinical examination, lumbar spondylosis with foraminal stenosis confirmed by X-ray or MRI; no other treatments in the last 6 weeks.
– Exclusion criteria: systemic diseases (inflammatory, infectious or neoplastic), recent injuries, surgery and neurological deficits.

The assignment to **3 groups** with different collagen administration techniques was performed with simple randomization based on a computer-generated randomization list. All injections were always administered by the same physician.
Group A – subcutaneous injections in the line of facet joints, paravertebral, multipoint technique.
Group B – periradicular injections under ultrasound control, in-plane technique.

	All patients, n	Group A	Group B	Group C
N (total)	30	10	10	10
F	19 (63,3)	6	8	5
Age, average (SD)	62,6 (13,7)	62,0 (16,1)	68,1 (13,4)	57,6 (10,2)
Duration of complaints, weeks, average	11,7 (14,2)	6,3 (8,3)	12,1 (11,3)	16,6 (19,9)
Range	1 - 52	1 - 28	3 - 32	1 - 52
Period of disease				
Acute	16 (53,3)	7	4	5
Subacute	4 (13,3)	1	3	-
Chronic	10 (33,3)	2	3	5
Level of foraminal stenosis				
L3/L4	2 (6,7)	2	-	2
L3/L4, L4/L5	1 (3,3)	-	-	-
L3/L4, L4/L5, L5/S1	3 (10,0)	-	2	-
L4/L5	2 (6,7)	1	-	1
L4/L5, L5/S1	8 (26,7)	4	2	4
L5/S1	14 (46,7)	3	6	3
Painful side(s)				
left	9 (30)	3	4	3
right	8 (26,7)	2	4	2
both	13 (43,3)	5	2	5

TAB. 1

Characteristics of the study groups.

Group C – epidural, interlaminar approach injections under ultrasound control.

A collagen mix containing 2 vials of **MD-Neural** and 1 vial of **MD-Lumbar** per session was administered, and if the complains were bilateral, injectate was administered bilaterally in groups A and B.

Frequency of injections: 1/week (4 sessions in total).

Endpoints: W0 (before treatment), W1 (end of therapy - after 4 weeks), W2 (after 1 month of observation).

Control tools: Visual Analogue Scale **(VAS)** (0-10), **Oswestry** (0-50) and **Laitinen** (0-16) questionnaires completed by the patient, **One Leg Stence Test** (OLST) (0-30 seconds) with measurement always carried out by the same physician (7).

Descriptive statistics (mean, standard deviation, frequencies) were calculated in StatsDirect statistical software version 2.8.0. In assessing the effectiveness of treatment, the value of minimal important difference (MID) was used.

A change of MID on the VAS scale was set to 3 points, for the Oswestry scale to 10 points, for the Laitnen scale 4 points, and for the OLST test as a reference value indicating the normal state, a time of ≥30 seconds was used (8,9).

Each patient qualified for the study received very accurately, giving written information about its purpose, injection technique and possible risk of complications. Written consent to participate in the study was obtained from each patient and personal data protection was ensured.

RESULTS

Between May and July 2019, **30 patients** (19 F and 11 M; mean age 62.6) were included in the study.

The average duration of the complaints was 11.7 weeks (range from 1 to 52 weeks).

The study groups were similar to each other except for the duration of the discomfort (mean 6.3 weeks in group A *vs.* 16.6 weeks in group C).

The detailed characteristics of the study

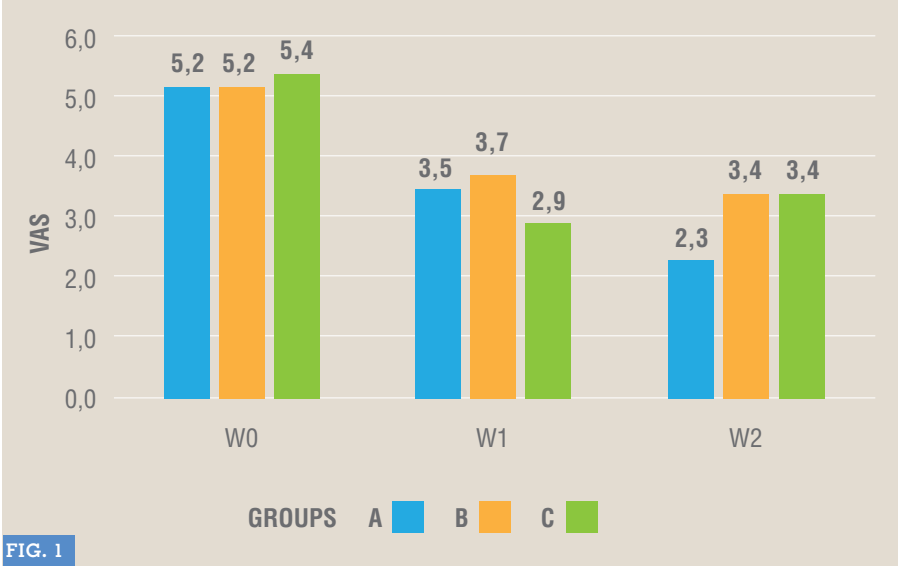

FIG. 1

Average Visual Analogue Scale (VAS) values at control points.

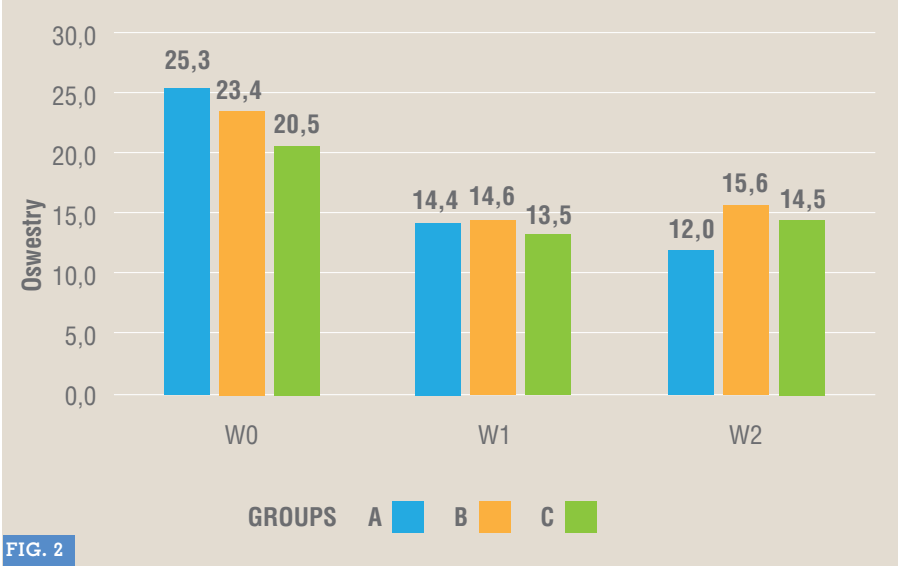

FIG. 2

Average Oswestry questionare values at control points.

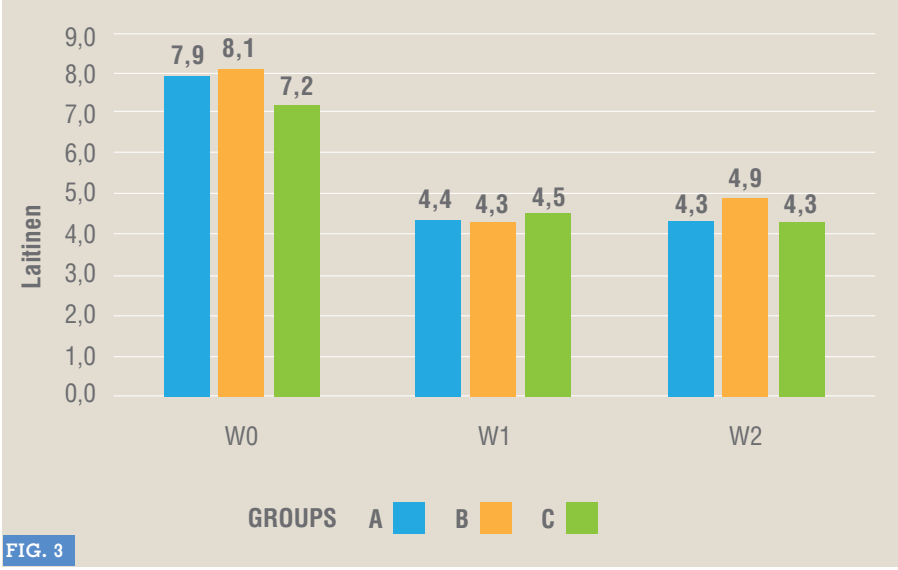

FIG. 3

Average Laitinen questionare values at control points.

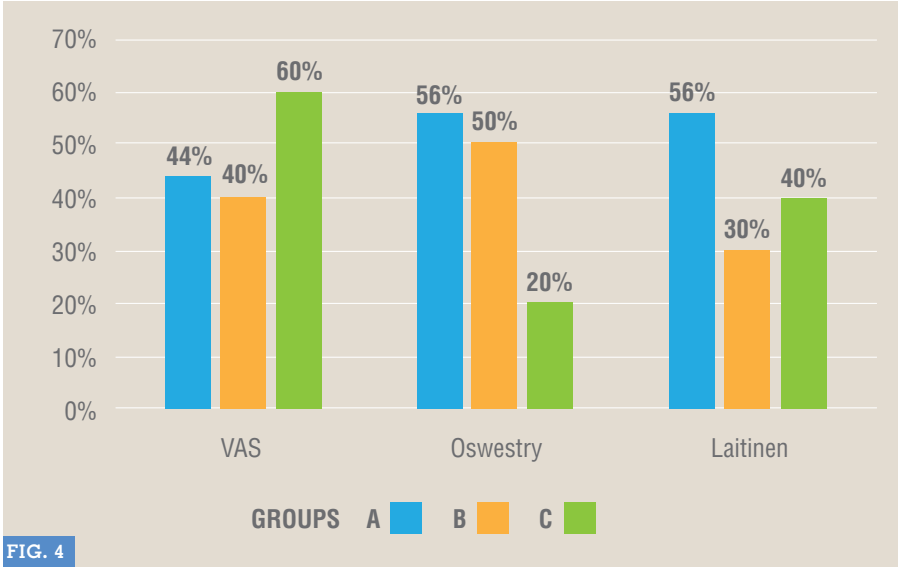

FIG. 4

Percentage of patients achieving minimal clinically significant difference (MID) in individual study groups.

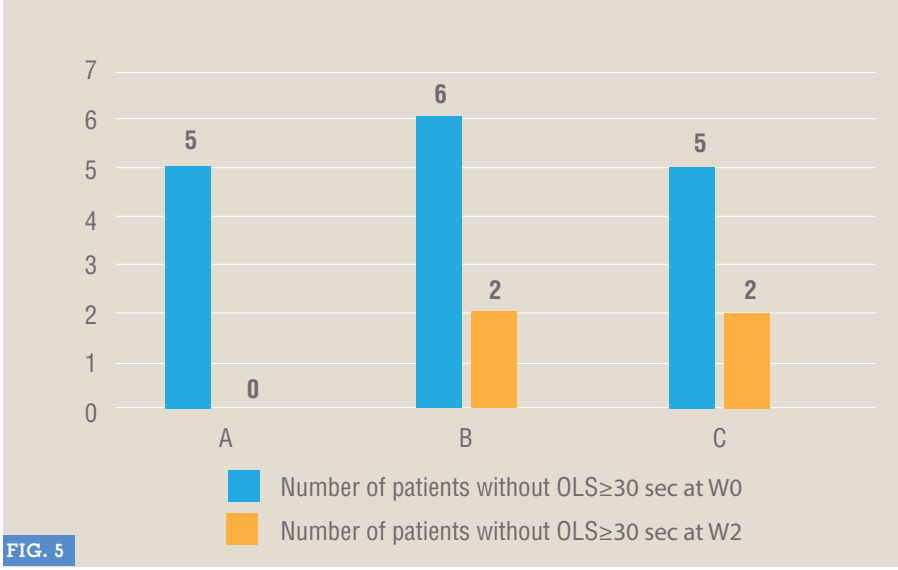

FIG. 5

Number of patients without OLST ≥30 seconds at control points W0 and W2.

group are presented in TAB. 1.
All patients who started the study received a full dose of treatment and had a W1 control visit.
One person (from group A) was not included in the W2 follow-up visit because of surgical treatment in the field of lower limb arterial surgery during the observation period.
The changes in the mean VAS values and scoring of the Oswestry and Laitinen scales in individual groups are shown in FIGG. 1, 2, 3.

The percentage of patients who obtained the accepted values of MID was analysed in all groups.
The highest percentage of MID change on the VAS scale was obtained in group C (60%), while the highest percentage of MID change on the Oswestry and Laitinen scale was obtained in group A (56%) (FIG.4).
In the OLST functional test, the number of patients who did not reach the OLST reference value (≥30 seconds) at the W2 checkpoint in each group was recorded (FIG. 5).

There were no side effect of Collagen Medical Devices in the studied groups of patients.

There were two cases of mild punctional syndrome with transient headaches in the epidural group and one worsening of pain in group A during the treatment alone (between dose II and III); this event did not require discontinuation.

DISCUSSION

Improvement was observed in all groups treated with collagen injections.

– The highest percentage of patients achieving minimal clinically significant change in the Oswestry and Laitinen scales was observed in the subcutaneous supply group, and the VAS scale in the epidural supply group.

The advantage of the study is its randomized and prospective nature. At the same time, the small number of patients studied remains the biggest limitation. As a consequence, classical statistical analysis was abandoned in favor of calculating the percentage of patients reaching MID in terms of endpoints.
The study should be considered as a pilot study and may be the basis for estimating the size of the sample of a proper, randomized clinical trial in the assessment of the effectiveness of collagen therapy.

Pavelka *et* Al. compared the effectiveness of subcutaneous injections of a mix containing collagen MD-Lumbar, MD-Muscle, and MD-Neural with mesocaine in a group of 48 patients, obtaining comparable effects over a 5-week observation period. The authors emphasize the good safety profile of the preparations (10,11).
Additive injections have a completely different application of collagen injections in the experimental treatment of low back pain, where the authors hope to restore the structural framework of the fibrous ring of the intervertebral disc, but these studies do not go beyond the phase of the animal model and *in vitro* (12,13).
To the author's knowledge, however, there are no publications that would re-

port the use of collagen in periradicular or epidural administration as an option for conservative treatment of LBP.
The explanation of collagen principle of operation in such an application should be subject to further research, as it may be a very interesting option for the treatment of LBP with a stiffness component.

CONCLUSIONS

1) Collagen administred by injection shows a high safety profile.
2) Regardless of the method of administration, paravertebral collagen injections show an analgesic effect and also improve mobility in patients with foraminal stenosis in the course of lumbar spondylosis in the short observation period.
3) Collagen administered subcutaneously form seems to be of particular interest as a therapeutic option in patients with foraminal stenosis in the course of lumbar spondylosis, showing no less analgesic effect and functional improvement than in periradicular and epidural injections, with no risk associated with the technique of administration.
4) Due to the limited size of the study group, the obtained results should be treated as preliminary. They require confirmation in randomized clinical trials on a larger group of patients.

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author
Piotr Godek, MD
– Sutherland Medical Center
Warsaw, Poland