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GUNA COLLAGEN MEDICAL DEVICES IN THE TREATMENT OF PAIN IN OUTPATIENT CASES OF OSTEOARTHRITIS

SUMMARY

The aim of this study is to evaluate the effects of the administration of Guna Collagen Medical Devices in acute and chronic pain symptoms associated with Osteoarthritis.
The goal of this study is to evaluate how the administration of district-specific MDs can modulate pain and improve functional and motor responses.

– After ascertaining the patient's clinical state and requesting, if possible, the suspension of anti-inflammatory, analgesic or similar drugs, we proceeded with the administration of subcutaneous, locoregional infiltration, according to the Mesotherapy technique.
The infiltrations were carried out on a weekly basis (1 session/week x 12 weeks) in 20 patients suffering from pain related to their osteoarthritic condition of varying clinical entity (from moderate to severe).

The 20 patients presented the following complaints: 5 knee pain, 7 low back pain, 5 neck pain, 3 shoulder-related pain.
The assessment parameters used were the WOMAC questionnaire for knee pain, the VAS scale for pain and the VAS scale for subjective sensation of functional improvement in movement (0-10). The questionnaires were given to the patients before the start of the therapy (T0) and after the 1st, 2nd, 3rd, 6th and 12th week of treatment.
Therapy involved the use of specific Collagen MDs, administered alone without other drugs, using 5 ml syringes, 30G x 12mm needles. At each treatment data were collected according to the WOMAC questionnaire and the two VAS Scales adopted.
At the end of the treatment period, following the processing of the collected data and the observation of the patients for 6 months after the therapy, it was observed a significant reduction in perceived and evoked pain as well as a general improvement in the functional condition of the joints.

KEY WORDS

GUNA COLLAGEN MEDICAL DEVICES, MD-NECK, MD-SHOULDER, MD-LUMBAR, MD-KNEE, NECK PAIN, SHOULDER PAIN, LOW BACK PAIN, KNEE PAIN, JOINT PAIN, OSTEOARTHROSIS

OSTEOARTHRITIS PAIN

Pain accounts for a large part of the professional life of an outpatient doctor; it is a common complaint that goes hand in hand with the most diverse clinical situations, becoming the reason for the medical consultation.
In chronic diseases, pain has a significant impact on the patient's quality of life and can limit, for example, mobility, the capacity to work, psycho-physical well-being, and social relationships.

– In osteoarticular diseases, such as **Osteoarthritis (OA)**, the pain is often difficult to bear.
– It is therefore very important to protect patients from acute pain, and above all from chronic pain, as much as possible.

Various methods are used to classify pain and its extent; that of the IASP (International Association for the Study of Pain) and the WHO, among the most accepted, both stigmatise the major impact that pain has on the quality of life of those who suffer from it.

Certain types of pain can be identified from a classification point of view: acute, chronic, procedural, movement-evoked, referred, and spontaneous pain, etc.

They have in common the nervous pathway and its physio-anatomical hierarchy: there are a number of medical, psychological and psychiatric facets to the pain.
In osteoarticular diseases it is linked to the overactivation of painful type **A Delta** and **c nerve fibres**.

These somatic nociceptive fibres are located in the periosteum, endosteum, joint capsule and peri-articular structures.

It goes without saying that, especially in chronic diseases, there is also a significant psychophysiological-somatomorphic component, with major affective-emotional implications that influence the perceived pain.

– Most of the painful conditions associated with osteoarticular pictures present multifactorial signs and symptoms, often correlated with chronic degenerative diseases, most frequently OA.

In OA, pain symbolises a vast array of distressing clinical conditions.

What these situations have in common is persistent pain that may or may not be related to disease patterns of inflammation and degeneration.
– The joints are subject to acute or chronic inflammatory processes related to an assortment of problems that develop and accumulate over time.
The most common causes are:
– work-related (tiring, repetitive, or sedentary jobs, performed with unnatural postures, etc.)
– morpho-functional disorders (dysplasia, scoliosis, changes in the joint status, etc.)
– traumatic
– iatrogenic/post-operative
– metabolic/food-related/endocrine.

In recent years, the medical community is increasingly coming round to the idea that degenerative processes have a multifactorial basis, like in the case of OA, thus abandoning the previous notion which inevitably associated them with ageing.

What all these conditions have in common is that they activate inflammatory processes that are manifested in the form of damaged ligaments, tendons, aponeurosis, planking of the joints and intra-articular cartilage, and affect the collagen component.
In fact, collagen is the main component of all structures that make up the joints (extra and intra).

OSTEOARTHRITIS

OA is defined as degenerative joint disease; it involves the destruction and potential loss of joint cartilage, damage to the subchondral bone, which goes into eburnation, damage to the joint margins with narrowing of the joint space, and the development of osteophytes and geodes on the joint heads.

It is the most common joint disease in the adult population. It is generally diagnosed around the 5th/6th decade of life and is almost omnipresent in multiple joints by the 8th decade, even if not always symptomatic, and can be easily confirmed by radiological diagnostics.

Below the age of 40, OA has repeated/chronic traumatic causes and mainly affects the male gender.
Normally only half of OA patients have symptoms, pain being the most prominent.
OA is damage to the joint cartilage tissue, which is primarily made up of collagen.

OA can be primary, often idiopathic, or secondary (multiple causes that change the microenvironment, metabolism and the characteristics of the joint cartilage).

The bone areas affected by OA are:
– Large joints, 95%: spine 54%; knee 27%; hip 7%; shoulder, elbow, hand and fingers 7%.

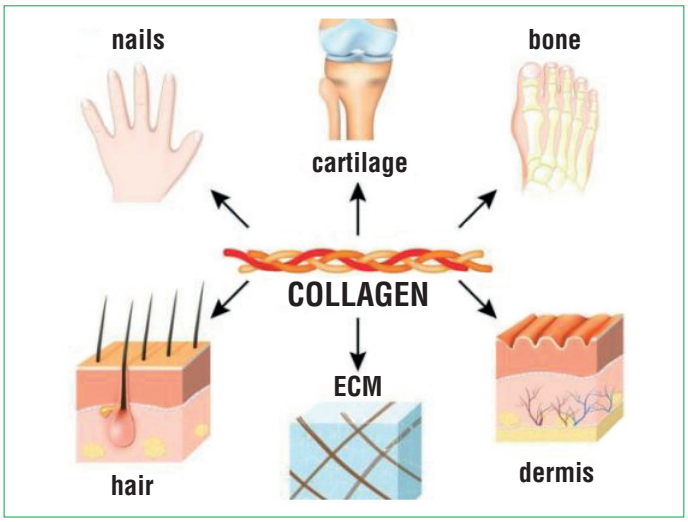
– Small joints, 5%: talus calcaneal joint 4%; metatarsophalangeal joint of 1st finger 1%.

The majority of the joints affected by OA are subjected to a static load (large joints), while the minority are subjected to a dynamic load.
It should be pointed out that, under normal conditions, the joints do not undergo enough friction to damage the bone heads and joint cartilage, whether by habitual use, overuse or trauma.

– The intra-articular hyaline cartilage is not vascularised; it is made up of water and collagen proteins (95%) and chondrocytes (5%).
Since cartilage does not have blood or lymph vessels, the metabolism and health of joints are related to the "squeezing" of joints, i.e. the physiological compression and decompression of hyaline cartilage during movement, which ensures metabolic regulation by diffusion.

The inflammation at the root of OA generates sclerosis and rigidity, thus creating a vicious circle that progressively aggravates the joint damage.
Whatever the cause, one can always

FIG. 1



observe a discrepancy between the physical load and resulting mechanical stress with the capacity of the joints to absorb and cushion this work; there is therefore a progressive thinning of the joint cartilage, exposure of the bone, inflammation of the joint capsules and oedema in the periarticular soft tissue.

In OA, there is an increasing reduction in the physiological ability of the joint components to slide freely over one another.
– The correct functioning of joints depends on the quality of their cartilage components; if their mechanical and metabolic properties are preserved, the joint is less likely to undergo OA and deterioration, and cause pain.
Over time, many factors contribute to a reduction in the metabolic capacity of collagen to maintain the physiological dynamics of synthesis and degradation.
Being bedridden for a long time, immobility or mobility that is not sufficient to provide mechanical stimuli to the joints give rise to a deficit in the ability to synthesise collagen and therefore in the physiological regeneration of cartilage and successful management of joint lubrication (primarily hyaluronic acid). Movement, in fact, is one of the factors that regulates the metabolism of cartilage and collagen based on mechanical "squeezing" in relation to the static-dynamic load on the joint.

OA has long been considered a degenerative disease with an age-related basis; in recent years, however, the disease tends to be considered within the context of a multifactorial framework that generates a complex aetiology and pathogenesis of the joint damage, with a biochemical-cellular basis involving the chondrocytes, collagen and cartilage.
– It has been observed that one of the main factors that cause OA is the suffering of chondrocytes leading to the release of enzymes and signal molecules, which gradually induce an abnormal turnover of the elements that make up the joint structures.

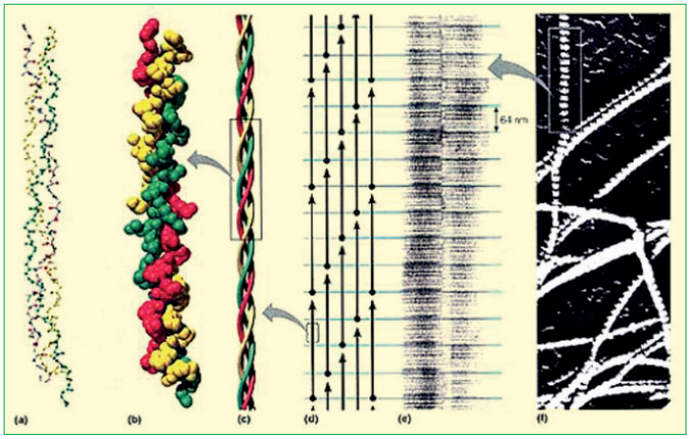


FIG. 2

THE IMPORTANCE OF COLLAGEN

Collagen represents approximately 7% of the weight of an adult organism.
It is so abundant in the human body that it constitutes approximately 30% of the total proteins; it is found almost everywhere (skin, teeth, bones, tendons, joints, serous membrane and vessel walls, etc.) (FIG. 1); it has significant metabolic and connective support functions and also performs biochemical functions associated with tissue homeostasis, such as, for example, a **buffer function**.

– As stated above, the importance of collagen lies in the fact that it is the most widely-represented, versatile and ubiquitous protein-based structure in the body.

Collagen plays an active role, rather than a passive role as a mere structural element; this is because it can adapt its metabolism according to the body weight and pressure to which it is subjected, e.g. FACIT (Fibril Associated Collagens with Interrupted Triple Helices).

Collagen also has **bioconductor** and **biosensor** characteristics, with **piezoelectric** and **vector information transfer** properties.
It also interacts with water to generate ion exchanges: these biophysical properties give collagen a powerful metabolic role in the structures formed from it (FIGS. 2 , 3 , 4).

The basic unit of collagen is tropocollagen, consisting of three laevorotatory peptide helices; this unit is bonded to glucose and galactose, which are connected to specific amino acids.

This basic structure gives collagen its vast range of properties, especially the repetition of specific amino acid triplets; each type of collagen has a specific variation of the amino acid triplets.
Tropocollagen gives rise to procollagen, which polymerises to form protocollagen outside the cell by means of a self-catalytic self-assembly mechanism involving certain oxidases.

FIG. 3

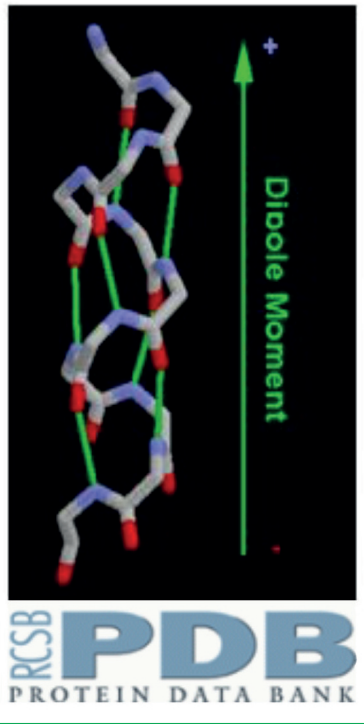
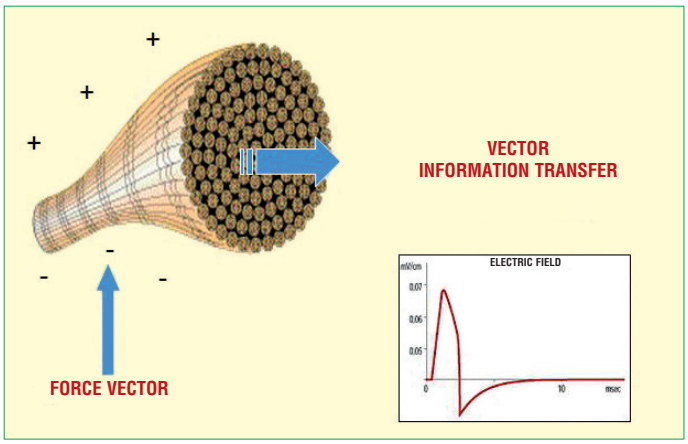


FIG. 4



The individual units of protocollagen are ready to self-assemble in turn, giving rise to mature collagen that has periodicity (true micro-metamerism) (FIG. 2).

GUNA COLLAGEN MEDICAL DEVICES: THE NEW THERAPEUTIC APPROACH TO PAIN IN OSTEOARTICULAR DISEASES

The Guna Collagen Medical Devices (MDs) are an effective therapeutic aid, considering the high concentration of collagen in the structures involved in joint diseases such as OA.

The administration of porcine-derived collagen has beneficial effects on the management/reduction of certain lytic enzymes, the most important being the MMP-9, MMP-13 metalloproteases and Cathepsin K.

– Many studies highlight the importance of MMPs and other lytic enzymes in the genesis and chronic maintenance of joint damage on an enzymatic-inflammatory basis, where a collagen metabolism imbalance favours its degradation rather than neosynthesis. There are other collagenolytic enzymes in addition to MMPs, for example other collagenases and ROS, often in a broader context of low grade inflammation based on many factors.

– There is considerable evidence in the medical-scientific literature (over 40 articles) concerning the positive results shown by the intraarticular and/or periarticular infiltration of Collagen MDs, which improve the response of tissue to MMPs and lead to reparative processes in the joint and periarticular tissue (**www.collagenmd.guna.com**).

– It was therefore decided to use Collagen MDs in selected patients with confirmed OA.

Guna Collagen Medical Devices are injectable medical devices based on highly biocompatible collagen of porcine origin, with the utmost histocompatibility with human collagen.
The molecular selection is of high quality due to the use of tangential-flow filtration, sterilisation of the collagen fibres, and control of the molecular weight.
The collagen obtained in this way is highly pure and bioavailable (TAB. 1).

The Collagen MDs also contain ancillary biological molecules that increase specific joint tropism and the effectiveness of collagen on the intended target area. Their possible uses fall within the context of secondary prevention and therapy.

TAB. 1

Guna Collagen Medical Devices.

	GUNA Medical Device	COMPOSITION
BODY DISTRICT SPECIFIC	**MD-NECK**	Collagen + Silica
	MD-THORACIC	Collagen + *Cimicifuga*
	MD-LUMBAR	Collagen + *Hamamelis*
	MD-SHOULDER	Collagen + *Iris*
	MD-HIP	Collagen + Calcium Phosphate
	MD-KNEE	Collagen + *Arnica*
	MD-SMALL JOINTS	Collagen + *Viola*
	MD-POLY (Multi-articularity)	Collagen + *Drosera*
	MD-ISCHIAL (Sciatica)	Collagen + *Rhododendron*
TISSUE-SPECIFIC	**MD-MUSCLE**	Collagen + *Hypericum*
	MD-NEURAL	Collagen + *Citrullus*
	MD-MATRIX (Extra-Cellular Matrix)	Collagen + Citric acid, Nicotinamide
	MD-TISSUE (Soft tissues)	Collagen + Ascorbic acid, Magnesium gluconate, Pyridoxine hydrochloride, Riboflavin, Thiamine hydrochloride

Another reason for deciding to use the Collagen MDs was the lack of side effects. They are very safe, easy to handle, quick and straightforward to use, and therefore also suitable for an outpatient setting.
– Moreover, they are well tolerated by patients according to the literature.

MATERIALS AND METHODS

Twenty patients (13 M and 7 F) suffering from OA were enrolled in this trial.

All patients were diagnosed in a specialist consultation prior to being recruited for the trial.
– The patients (60-85 years) were divided into groups according to the area affected by the arthritic damage and pain.

Patients M: **5** with **Gonarthrosis**, **5** with **Lumbar Spondyloarthritis**, and **3** with **Cervical Spondyloarthritis**.

Patients F: **3** with **Shoulder OA**, **2** with **Lumbar Spondyloarthritis**, and **2** with **Cervical Spondyloarthritis**.

– After signing the informed consent form (purpose, methods, treatment procedure and products for the study concerned), all patients underwent **infiltrative Mesotherapy treatment** on a weekly basis for 12 consecutive weeks, at which times the specific MD for the affected area was administered.

Questionnaires were issued to the patients on the 1st, 2nd, 3rd, 6th, and 12th weeks.

All the patients filled in 2 VAS (Visual Analogue Scale) questionnaires, one for the pain and the other for the assessment of perceived subjective improvement.
The 5 M patients suffering from Gonarthrosis also filled in the WOMAC (Western Ontario and McMaster Universities Arthritis Index).
To take part in the study, the patients were asked to discontinue any ongoing therapies where possible, to avoid affecting the outcome of the results.

PATIENTS M

• **Gonarthrosis Group**:
5 patients, average age 70.8 years (min. 60 - max. 82), with previous diagnosis of confirmed Gonarthrosis.
– Treatment: MD-Knee.

• **Lumbar Spondyloarthritis Group**:
5 patients, average age 72.4 years (min. 61 - max. 85), diagnosed with Lumbar Spondyloarthritis with disc problems, osteophytic processes and straightening of the lumbar spine.
– Treatment: MD-Lumbar.

• **Cervical Spondyloarthritis Group**:
3 patients, average age 73.3 years (min. 68 - max. 79), with a diagnosis of confirmed Cervical Spondyloarthritis.
– Treatment: MD-Neck.

PATIENTS F

• **Scapulohumeral OA Group**:
3 patients, average age 68.3 years (min. 68 - max. 72), with a clinical picture that was variable but attributable to a process of Scapulohumeral Osteoarthritis.
– Treatment: MD-Shoulder.

• **Lumbar Spondyloarthritis Group**:
2 patients, average age 67.5 years (min. 66 - max. 69), with a confirmed diagnosis of Lumbar Spondyloarthritis.
– Treatment: MD-Lumbar.

• **Cervical Spondyloarthritis Group**:
2 patients, average age 69 years (min. 67- max. 71), with a confirmed diagnosis of Cervical Spondyloarthritis.
– Treatment: MD-Neck.

RESULTS, DISCUSSION AND CONCLUSION

At the end of the 12 weeks of treatment, all 20 patients had completed the therapeutic cycle.
The data collected were processed using the statistical method of mean distribution (FIG. 5), a statistical study of simple modality, effective and highly suited to an outpatient experiment.
– This statistical study is based on the average of the values collected in order to eliminate or reduce errors relating to min. and max. distribution values; this enables an objective, fairly reliable assessment of the results obtained in the population in question.

As shown by the results in TABS. 2 and 3, there was a gradual, contained improvement in the first 3 weeks of treatment (reduction in perceived pain, and a modest improvement in overall subjective perceived pain).
– The improvement and elimination of pain are fundamentally different **after the 6th week of treatment** by infiltrative mesotherapy when compared with the initial conditions; the results obtained are maintained up to the 12th week, with further improvements.

Based on the data obtained at the end of the 12th week, we can confirm that the treatment had a very positive effect on the pain and the general well-being of the patients.

The very low invasiveness and speed of administration of the MDs also resulted in almost total adherence to the therapy, generating good feedback, and satisfaction from the patients.
The infiltrative treatment using Guna Collagen MDs is certainly of great im-

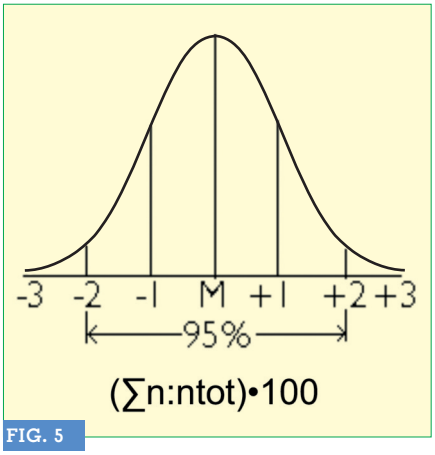


FIG. 5

Average distribution of statistical values; distribution bell curve with summation.

portance in the treatment of OA and pain.

This area is increasingly appealing to practitioners, since there is a gradual increase in joint diseases in the population.

– There are many strategies for managing OA (viscosupplementation, PRP, oral collagen, etc.), but, among the infiltrative treatments, Guna Collagen Medical Devices stand out in terms of quality and safety.

Based on our experience and the literature, we can confirm that they have unique characteristics that are ideal for the treatment and management of OA, including in an outpatient setting (very important aspect).

Guna Collagen Medical Devices have an excellent formulation profile.

They are highly purified products combined with ancillaries that enhance their therapeutic action; no adverse effects have been reported in 10 years, and they have a broad range of applications (13 MDs can be combined in various ways, if necessary).

– Moreover, their therapeutic effect can be detected after fewer sessions, and last for longer periods, than other therapeutic strategies. They can also be administered to patients with comorbidi-

A

	WOMAC baseline	WOMAC 1st week	WOMAC 2nd week	WOMAC 3rd week	WOMAC 6th week	WOMAC 12th week
1	59	59	55	53	45	38
2	56	55	52	53	46	32
3	53	53	50	49	38	20
4	51	50	50	48	41	28
5	52	52	51	49	41	26
	54.2	**53.8**	**51.6**	**50.4**	**42.2**	**30.8**

	VAS baseline	VAS 1st week	VAS 2nd week	VAS 3rd week	VAS 6th week	VAS 12th week
1	9	8	8	7	5	4
2	9	9	9	8	6	4
3	8	7	7	8	7	5
4	8	7	6	6	5	3
5	7	7	6	6	5	3
	8.2	**7.6**	**7.2**	**7**	**5.6**	**3.8**

	VAS baseline	VAS 1st week	VAS 2nd week	VAS 3rd week	VAS 6th week	VAS 12th week
1	0	0	2	2	5	7
2	0	1	2	3	5	6
3	0	1	1	2	3	7
4	0	2	2	3	5	8
5	0	1	1	2	4	8
	0	**1.0**	**1.6**	**2.4**	**4.4**	**7.2**

B

	VAS baseline	VAS 1st week	VAS 2nd week	VAS 3rd week	VAS 6th week	VAS 12th week
1	9	9	8	8	5	4
2	8	7	7	6	4	2
3	9	9	8	8	6	4
4	7	7	5	6	3	1
5	6	5	5	5	3	2
	7.8	**7.4**	**6.8**	**6.6**	**4.2**	**2.6**

	VAS baseline	VAS 1st week	VAS 2nd week	VAS 3rd week	VAS 6th week	VAS 12th week
1	0	1	1	2	4	7
2	0	2	2	3	5	8
3	0	1	2	2	4	7
4	0	1	1	2	6	8
5	0	2	2	3	5	8
	0	**1.4**	**1.6**	**2.4**	**4.8**	**7.6**

C

	VAS baseline	VAS 1st week	VAS 2nd week	VAS 3rd week	VAS 6th week	VAS 12th week
1	9	9	9	8	6	3
2	9	8	7	7	5	2
3	8	8	8	7	5	2
	8.6	**8.3**	**8**	**7.3**	**5.3**	**2.3**

	VAS baseline	VAS 1st week	VAS 2nd week	VAS 3rd week	VAS 6th week	VAS 12th week
1	0	1	1	2	4	7
2	0	0	1	1	5	8
3	0	1	2	2	6	8
	0	**0.7**	**1.3**	**1.7**	**5**	**7.6**

TAB. 2

Patients M (13) divided according to disease.

A – Gonarthrosis (5) – from left to right: WOMAC score for Gonarthrosis, VAS for perceived pain and VAS for perceived subjective improvement.

B – Lumbar Spondyloarthritis (5) – left: Perceived pain score on VAS; right: Perceived subjective improvement on VAS.

C – Cervical Spondyloarthritis (3) – left: Perceived pain score on VAS; right: Perceived subjective improvement on VAS.

A

	VAS baseline	VAS 1st week	VAS 2nd week	VAS 3rd week	VAS 6th week	VAS 12th week
1	8	8	7	7	4	2
2	9	8	8	7	3	1
3	8	7	7	7	4	2
	8.3	7.6	7.3	7	3.6	1.6

	VAS baseline	VAS 1st week	VAS 2nd week	VAS 3rd week	VAS 6th week	VAS 12th week
1	0	0	1	1	3	7
2	0	1	2	2	4	8
3	0	2	2	2	4	8
	0	1	1.6	1.6	3.6	7.6

B

	VAS baseline	VAS 1st week	VAS 2nd week	VAS 3rd week	VAS 6th week	VAS 12th week
1	7	7	6	6	4	2
2	8	7	7	6	4	2
	7.5	7	6.5	6	4	2

	VAS baseline	VAS 1st week	VAS 2nd week	VAS 3rd week	VAS 6th week	VAS 12th week
1	0	2	2	3	5	8
2	0	2	3	4	6	9
	0	2	2.5	3.5	5.5	8.5

C

	VAS baseline	VAS 1st week	VAS 2nd week	VAS 3rd week	VAS 6th week	VAS 12th week
1	9	9	8	7	4	2
2	9	9	9	7	5	2
	9	9	8.5	7	4.5	2

	VAS baseline	VAS 1st week	VAS 2nd week	VAS 3rd week	VAS 6th week	VAS 12th week
1	0	2	3	2	4	8
2	0	2	2	3	5	8
	0	2	2.5	2.5	4.5	8

TAB. 3

Patients F (7) divided according to disease.

A – Scapulohumeral Arthritis (3) – left: Perceived pain score on VAS; right: Perceived subjective improvement on VAS.
B – Lumbar Spondyloarthritis (2) – left: Perceived pain score on VAS; right: Perceived subjective improvement on VAS.
C – Cervical Spondyloarthritis (2) – left: Perceived pain score on VAS; right: Perceived subjective improvement on VAS.

ties who are undergoing specific individual therapies, depending on the case. ■

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The author would like to thank the editors of the websites from which the images are taken:

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