

## The role of injection collagen therapy in the course of rheumatic diseases

Maria Maślińska

Early Arthritis Clinic, National Institute of Geriatrics, Rheumatology and Rehabilitation, Warsaw, Poland

**Key words:** collagen injection, inflammatory rheumatic diseases, pain

The main two aims collagene therapy in rheumatology are supporting pain treatment in inflammatory diseases and element of multimodality of pain treatment in non-inflammatory diseases.

In inflammatory rheumatic diseases can coexist the different type of pain such as nociceptive pain, neuropathic pain, nociplastic pain as well as inflammatory pain. This last pain ententity resulting from the activity of the inflammatory process, and special inflammatory environment i.e. pro-inflammatory cytokines, especially interleukin-6 (IL-6), tumor necrosis factor (TNF), IL-1 or chemokines, can be seen as a possible combination of other types of pain. Inflammatory processes can be involved in previously mentioned types of pain as a combination of the previously mentioned types (Table I) [1].

Residual pain results from chronic pain initiated by the inflammatory process, e.g. in rheumatoid arthritis (RA), but remains because it results from other mechanisms/causes, such as: a fibromyalgia component, low mood/depression, damage that is no longer amenable to anti-inflammatory therapy. In such case, the necessary and supportive treatment should be analyzed in detail.

Currently in RA is presented the concept of dual role of collagen which may imply an approach to collagen therapy. A controversial finding of collagen and arthritis hypothesis was reported: intravenous injection of CII could potentially suppress a collagen induced arthritis (CIA) model by increasing a crucial anti-inflammatory mediator of CIA, IL-4 [2]. The antiarthritic mechanism of collagen

and its peptides has been suggested. Collagens of different molecular weights are absorbed in the large intestine and transported to arthritic joints via the circulation as tripeptides to treat arthritis. It was assumed that the administration of collagen by various routes (intra-articular injections, intra-tendon local injections, intra-muscular injections, peri-articular injections, mesotherapy) may have an impact on pain relief, stimulation of healing, the use of glucocorticosteroids (reduction or even elimination) and remove factors generating pain beyond the inflammation resulting from inflammatory rheumatic disease [3]. In one study polymerized-collagen increased the time to total knee arthroplasty by at least 60 months, modifying the disease course, improving functional disability, and decreasing pain [4]. Another revealed that collagen injection can induce in tenocytes an anabolic phenotype by stimulating tenocyte proliferation and migration and collagen type I synthesis, maturation, and secretion, thus favoring tendon repair. In particular, based on its effect on gluteal tenocytes, collagen could be effective in the discouraging treatment of greater trochanteric pain syndrome. Collagen acting as a mechanical scaffold, could be an effective medical device used as a novel therapeutic, regenerative and rehabilitative approach to favor tendon healing in tendinopathies [5].

The study by Nitecka-Buchta et al. [6] confirmed that intramuscular injection of collagen is a more efficient method for reducing myofascial pain within masseter muscles than intramuscular injection of lidocaine. The usefulness of mesotherapy was touched upon in other abstracts. To summarized available studies the collagen

**Table I.** Factors that need to be taken into account in the analysis of pain, i.e. causes, type, time and effects

Cause	Type	Duration	Effects
Inflammation	Nociceptive	Acute < 12 weeks	Increasing scoring in disease activity assessment (e.g. DAS, DAS28), despite of decrease of inflammatory markers or/and joint involvement Functional impairment Glucocorticosteroids use Abnormal movement patterns
Damage/deformation	Neuropathic	Chronic > 12 weeks	
Overload	Nociplastic		
Functional impairment			
Abnormal movement patterns			

DAS – Disease Activity Score.

injection therapy in rheumatic diseases is of particular importance in the treatment of diseases without significant systemic inflammation, such as degenerative disease (e. g. osteoarthritis).

Administration/injection methods may be different depending on the problem: damage, local inflammation, pain syndrome. There are also positive data in the case of the use of collagen therapy in inflammatory diseases accompanied by other causes of pain, damage, residual pain, pain in periarticular tissues. Also the effectiveness of collagen therapy in the treatment of tendinopathy and myofascial pain has been demonstrated.

In conclusion such therapy may be a complementary method in the treatment of rheumatic diseases and may also delay surgical interventions in osteoarthritis.

## References

1. Cook AD, Christensen AD, Tewari D. et al. Immune Cytokines and Their Receptors in Inflammatory Pain. *Trends Immunol* 2018; 39: 240–255, DOI: 10.1016/j.it.2017.12.003.
2. Elango J, Zamora-Ledezma C, Ge B, et al. Paradoxical Dual Role of Collagen in Rheumatoid Arthritis: Cause of Inflammation and Treatment. *Bioengineering (Basel)* 2022; 9: 321, DOI: 10.3390/bioengineering9070321.
3. Mary Ann Liebert. *Tissue engineering: Part B* 2017; 23, DOI: 10.1089/ten.teb.2016.018.
4. Borja-Flores A, Macías-Hernández SI, Hernández-Molina G, et al. Long-Term Effectiveness of Polymerized-Type I Collagen Intra-Articular Injections in Patients with Symptomatic Knee Osteoarthritis: Clinical and Radiographic Evaluation in a Cohort Study. *Adv Orthop* 2020; 2020: 9398274, DOI: 10.1155/2020/9398274.
5. Buda M, Dlimi S, Parisi M, et al. Subacromial injection of hydrolyzed collagen in the symptomatic treatment of rotator cuff tendinopathy: an observational multicentric prospective study on 71 patients. *JSES Int* 2023; 7: 799–804, DOI: 10.1016/j.jseint.2023.06.009.
6. Nitecka-Buchta A, Walczynska-Dragon K, Batko-Kapustecka J, et al. Comparison between Collagen and Lidocaine Intramuscular Injections in Terms of Their Efficiency in Decreasing Myofascial Pain within Masseter Muscles: A Randomized, Single-Blind Controlled Trial. *Pain Res Manag* 2018; 2018: 8261090, DOI: 10.1155/2018/8261090.