

Efeitos clínicos da acupuntura e infiltração periarticular de corticosteróides no tratamento de gonartrose

Clinical effects of acupuncture and periarticular local infiltration of corticosteroids in the treatment of gonarthrosis

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RESUMO

Introdução: Gonartrose é uma das doenças degenerativas mais comuns. Dor, deficiência e deformidade articular são os sinais clínicos dominantes. **Objetivo do estudo:** Comparar o efeito clínico obtido com três diferentes modelos terapêuticos: 1. Acupuntura; 2. Infiltração local de corticosteróide; 3. Combinação de acupuntura e infiltração local de corticosteróide. **Material e Métodos:** Um estudo clínico prospectivo, aleatorizado, aberto incluiu 21 pacientes do sexo feminino em fase aguda de gonartrose. O diagnóstico foi feito através de exames clínicos e radiográficos. As pacientes foram divididas em três grupos: Grupo I: 7 pacientes com média de idade de $61,0 \pm 6,8$ anos, tratadas através de acupuntura com agulhas (pontas: Du20, Ex31, Ex32, St35, UB40, St44, UB60, Li4, Sp9, UB11), 10 tratamentos. Grupo II: 7 pacientes com $59,0 \pm 10,1$ anos, tratadas com infiltração de Betametasona – Diprofos, no primeiro dia de tratamento com abordagem frontal na parte lateral ou medial do tendão do músculo quadríceps. Grupo III: 7 pacientes, com $58,0 \pm 6,07$ anos, tratadas com uma combinação de infiltração inicial de Betametasona – Diprofos e acupuntura com agulhas, 10 tratamentos. A avaliação dos parâmetros de eficácia foi feita através dos seguintes parâmetros: 1. Dificuldades subjetivas – dor (Escala visual analógica – EVA de 0 a 100 mm); 2. tamanho do joelho, medido através do meio da patela em centímetros; 3. Amplitude de movimento articular (flexão), medida com um goniômetro. Todos esses parâmetros foram medidos no 1º, 8º e 21º dia de tratamento. ANOVA unifatorial, ANOVA de medida repetida e testes post hoc foram utilizados na análise estatística. **Resultados:** 1. Houve significativa melhora nos parâmetros de intensidade de dor e tamanho do joelho dentro dos grupos; ANOVA unifatorial, $p < 0,01$; 2. Não houve melhora significativa no parâmetro de movimento articular dentro dos grupos; ANOVA unifatorial, $p = 0,528$; 3. Houve melhoras significativas em todos os parâmetros (intensidade da dor, tamanho do joelho, movimento articular) nos três grupos; ANOVA de medida repetida, $p < 0,01$. **Conclusão.** O tratamento combinado de acupuntura e infiltração de corticosteróide tem melhor efetividade em intensidade da dor, tamanho do joelho e melhora do movimento articular em comparação com a monoterapia.

PALAVRAS-CHAVE

gonartrose, acupuntura, infiltração local periarticular de corticosteróide.

ABSTRACT

Introduction: Gonarthrosis is one of the most frequently degenerative diseases. Pain, derange of function and deformation of joint are dominating clinical signs. **Aim of the study:** To compare clinical effect obtained with three different therapeutic models: 1. Acupuncture; 2. Local infiltration of corticosteroid; 3. Combination of acupuncture and local infiltration of corticosteroid. **Material and methods:** An open, prospective, randomized clinical study included 21 female patients in acute phase of gonarthrosis. Diagnosis was made by clinical and radiographic examinations. Patients were divided into three groups: I group: 7 patients, average age 61.0 ± 6.8 years, treated with needle acupuncture (points: Du.20, Ex.31, Ex.32, St.35, UB.40, St.44, UB.60, Li.4, Sp.9, UB.11), 10 treatments. II group: 7 patients, average age 59.0 ± 10.1 years, treated with infiltration of Bethametasonum – Diprophos on the first day of treatment with frontal approach on the medial or the lateral side of m. quadriceps tendon. III group: 7 patients, average age 58 ± 6.07 years, treated with a combination of initial infiltration of Bethametasonum – Diprophos and needle acupuncture, 10 treatments. The evaluation of efficacy parameters were performed by following parameters: 1. Subjective difficulties – pain (VAS 0-100 mm); 2. Size

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of knee, measured across the middle of patella with centimeter band; 3. Range of joint motion (flexion), measured using a goniometer. All of these parameters were measured on 1st, 8th and 21st day of treatment. One way ANOVA, repeated measures ANOVA and post hoc tests were applied for statistic analysis. Results: 1. There were high significant improvements in the parameters of pain intensity and size of knee inside the groups; One way ANOVA test, $p=0.000<0.01$; 2. There were no significant improvements in the parameter of joint movement inside the groups; One way ANOVA test, $p=0.528>0.05$; 3. There were high significant improvements in all parameters (pain intensity, size of knee, joint movement) in all three groups; Repeated measures ANOVA test, $p=0.000<0.01$. Conclusion: Combined treatment of acupuncture and local infiltration of a corticosteroid has better effectiveness in pain intensity, size of knee and improvement of motion in comparison with monotherapy.

KEYWORDS

gonarthrosis, acupuncture, periarticular local infiltration of corticosteroid.

Introduction

‘Gon’ means ‘knee’. ‘Arthrosis’ means ‘disorder of the joint’. Gonarthrosis thus means a disorder of the knee joint, generally inferring early joint surface damage of any kind, while ‘gonarthrits’ infers more advanced arthritic destruction.⁽¹⁾ Approximately 25 percent of persons 55 years of age or older have had knee pain on most days in a month in the past year,⁽²⁾ and about half of them have radiographic osteoarthritis in the knee. Pain, function disorder and deformation of the damaged joint, which may be accompanied by effusion and signs of local inflammation, are dominant in the clinical picture. The X-ray shows changes in the advanced phases of the disease which are characterized by shrinking and asymmetry of the joint space, subchondral sclerosis, formation of cysts and osteophytes.⁽³⁾ The therapy is directed towards decreasing the pain and increasing these patients’ quality of life. The therapy may be inoperable and operable. The inoperable therapy includes non-pharmacological therapy (patient education, physical therapy, reflex therapy – acupuncture, occupational therapy) and pharmacological therapy (oral and local application of non-steroid anti-inflammatory medicines, intraarticular and periarticular infiltration of corticosteroids, oral application of glucosamine and chondroitin and intraarticular injections of hyaluronic acid). If all these measures yield no effect, operative treatment is recommended.^(4,5,6)

Osteoarthritis of the knee increases in prevalence with age and is more common in women than in men. This is a leading cause of impaired mobility in the elderly.^(7,8) Taking into consideration that today’s average life span (in the developed countries) is getting longer and longer, the health and social problems entailed by this disease are greater as well. Appropriate medical management requires that physicians be able to diagnose osteoarthritis early, recognize factors that may affect the prognosis or complicate the disease, and make effective use of the many available treatments.⁽⁹⁾

A recent survey of rheumatologists in the US suggested that >95% prescribe corticosteroids “at least sometimes”, and 53% “frequently”.⁽¹⁰⁾ The greater number of scientific studies relate to

intraarticular infiltration of corticosteroids, even though the contraindications of this therapy are well known.^(11,12,13,14) We have not found any data on periarticular infiltration of corticosteroids in the case of gonarthrosis in the medical literature.

Acupuncture has been used as a medical modality of traditional Chinese medicine (TCM) for over 3,000 years in China. In the late 1997, the American National Institutes of Health Acupuncture Consensus Development Panel (NIHCDP) offered a report of the evaluation of the efficacy of acupuncture for 14 medical conditions and concluded that acupuncture is effective for 2 conditions and may be useful for 12 others.⁽¹⁵⁾ For pain, there was strong evidence that real acupuncture is more effective than sham acupuncture; however, for function, there was inconclusive evidence that real acupuncture is more effective than sham acupuncture. Even though the results of 11 studies of acupuncture in the case of osteoarthritis, which Ernst refers to in his review are opposite⁽¹⁶⁾, there is however existing evidence suggesting that acupuncture may play a role in the treatment of knee OA.⁽¹⁷⁾

Aim of the study

The aim of our study was to compare the clinical effects of three therapeutic modalities – acupuncture, periarticular infiltration of corticosteroids and a combination of these two methods.

Materials and Methods

An open, prospective, randomized clinical study included 21 female patients in acute phase of gonarthrosis. Diagnosis was made by clinical and radiographic examinations. Patients were divided into three groups: **I group** - 7 patients, treated with needle acupuncture (Du.20, Ex.31, Ex.32, St.35, UB.40, St.44, UB.60, Li.4, Sp.9, UB.11), 10 treatments, 5 days/week. **II group** - 7 patients, treated with infiltration of bethametason dinatrium phosphate (2mg/ml) + bethametason dipropionat (5mg/ml) - Diprophos®, 1ml on the first day of treatment with frontal approach on the medial or the lateral side of m. quadriceps tendon. **III group** - 7 patients, treated with a combination of initial infiltration of Diprophos® and needle acupuncture, 10 treatments, 5 days/week. The evaluation of efficacy was performed using the following parameters: 1. Subjective difficulties (pain) measured by Visual Analogue Scale - VAS (0 – 100 mm), 2. Size of knee measured across the middle of patella by centimeter band, 3. Range of joint motion (flexion) measured using a universal goniometer with a 360-degree scale. These parameters were measured on 1st, 8th and 21st day of treatment. One way ANOVA, repeated measures ANOVA and post hoc tests were used for statistic analysis.

Results

There were no significant differences between the groups created according to age, the initial intensity of pain, and the range of joint motion – flexion (table 1), but there were differences according to the size of the knee.

Table 1.
Overview of patients according to age, initial pain and flexion.

GROUP	N	AGE	PAIN	FLEKSIJA
		MEAN ± SD (yrs)	MEAN ± SD (VAS)	MEAN ± SD (degree)
I	7	61,29 ± 6,80	7,5 ± 0,5	77,14 ± 11,13
II	7	59,71 ± 10,14	7,79 ± 0,86	80,71 ± 15,39
III	7	58,71 ± 6,07	8,14 ± 0,38	72,14 ± 7,56
One way ANOVA		F=0,19; p = 0,83	F=1,93; p = 0,175	F=0,93; p = 0,412

After 8 and 21 days, the groups did not differ in the degree of joint motion range – flexion (table 2).

Table 2.
ROM (flexion) after the 8th and the 21st days.

GROUP	N	MEAN ± SD (degree)	MEAN ± SD (degree)
		8th day	21st day
I	7	87,14 ± 8,09	93,57 ± 8,02
II	7	99,29 ± 12,05	93,57 ± 10,29
III	7	90,71 ± 10,32	97,86 ± 4,88
One way ANOVA		F=3,1; p = 0,07	F=0,66; p = 0,528

After 8 days, a significant difference in the intensity of pain between all three groups was measured (One way ANOVA < 0,01; post hoc tests < 0,05). 21 days later, the statistically considerable difference in the intensity of pain between the groups was maintained (One way ANOVA < 0,01), and using post hoc tests, a difference between I and III was discovered, as well as between II and III (p<0,05), whereas between I and II there was no considerable difference (table 3).

Table 3.
Pain intensity after the 8th and the 21st days.

GROUP	N	MEAN ± SD (VAS)	MEAN ± SD (VAS)
		8th day	21st day
I	7	5,43 ± 0,53	4,29 ± 0,39
II	7	1,86 ± 1,11	4,14 ± 0,94
III	7	4,07 ± 0,53	2,29 ± 0,57
One way ANOVA		F=37,97; p < 0,01	F=19,1; p < 0,01
postHoc tests		p < 0,05	I e II: p > 0,9 I e III: p < 0,01* II e III: p < 0,01*

Using sorting inside the groups, after the 8th and 21st days, statistically important differences for each observed parameter were found; Repeated measures ANOVA test, p<0.01. (Figures 1,2,3).

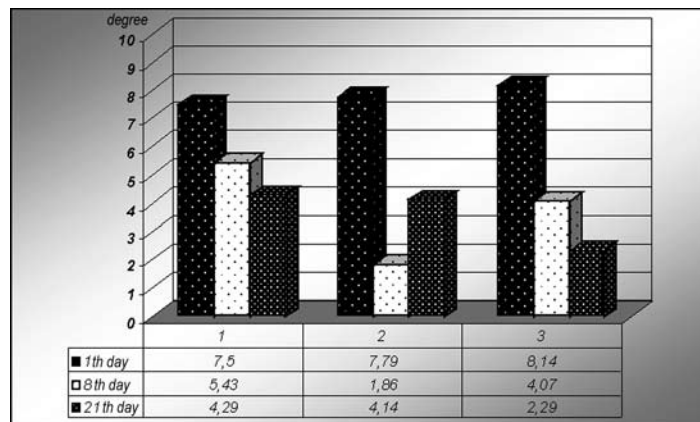


Figure 1.
Changes in the pain intensity inside the groups during the observation period.

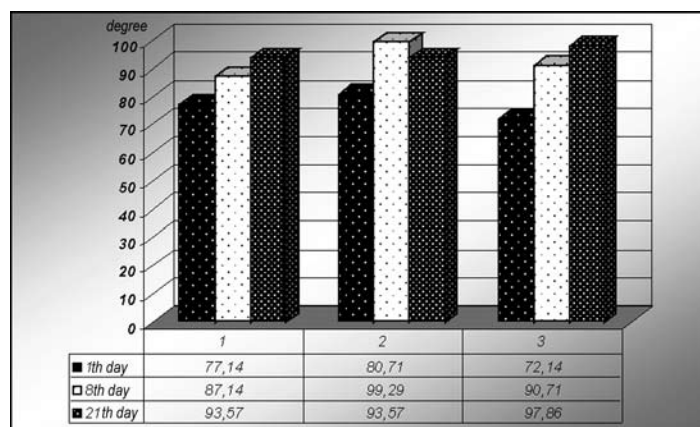


Figure 2.
Changes ROM (flexion) of the knee inside the groups during the observation period.

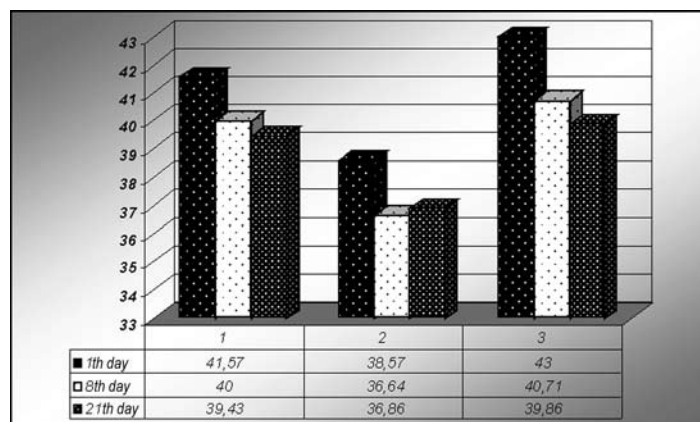


Figure 3.
Changes in the knee size inside the groups during the observation period.

Discussion

Gonarthrosis is, like other variants of OA, included in non-inflammatory rheumatic diseases of the bone-joint system, which affects all joint structures (including the subchondral bone), where the cartilage of the joint undergoes the greatest damage.

The pain mechanism in gonarthrosis is complex and still insufficiently explored. Bone damage, inflammation of the synovia, stretching of the joint capsule and bursitis are most often listed as pain sources.^(18,19,20) Over the past years, there have been more and more pieces of evidence for the inflammatory component present in patients with OA, i.e. gonarthrosis (releasing of cytokines and metalloproteinases in the joint, hypertrophy of the synovia, infiltration of mononuclear cells).⁽²¹⁾ Some inflammation products (bradykinin, histamine) stimulate nociceptors directly, whereas others (prostaglandins, leukotrienes, interleukin 1 and 6) make the primary afferent nociceptors respond to mechanical or other stimuli.⁽²²⁾ Although the hyaline cartilage is the most damaged in advanced gonarthrosis, due to the non-existence of nociceptors in it, it is not considered as a pain source.

The pathogenetic process starts with the disturbing of the metabolism of the chondrocytes, increased production of metalloproteinases (e.g. collagenases, stromelysin), which damage the cartilage matrix. Even though chondrocytes produce inhibitors of proteases (including tissue inhibitors of metalloproteinases – TIMP 1 and 2), their quantity is insufficient to stop the proteolytic effect. In the further course, there is fibrillation and erosion of the cartilage surface, accompanied by releasing of proteoglycan and fragments of collagen in the synovial fluid. All this leads to a chronic inflammatory reaction of the synovia, accompanied by releasing of cytokine (interleukin factor 1, tumor necrosis factor alpha, metalloproteinase) by the synovial macrophages. They diffuse back into the cartilage and directly destroy the tissue, but also induce chondrocytes to produce proteolytic enzymes further. Apart from the listed ones, it is likely that other pro-inflammatory molecules may play a specific role in the inflammation development (nitrogen oxide – NO, inorganic free radicals). All these processes change the joint architecture, as a result of which augmented bone formation occurs in order to increase its stability.⁽²³⁾ In the greater number of these patients, the system markers of the inflammation, such as the C reactive protein, have also been increased.⁽²⁴⁾ Moreover, increased values of hyaluronic acid in the serum have been found too in some patients (which is also a characteristic of inflammatory arthropathies such as RA).

Corticosteroids (mineralocorticoid - aldosteron and glucocorticoid - cortizon) are a group of hormones which are produced in the organism in the cortex of the suprarenal gland under the influence and control of the hypothalamus and the hypophysis. Glucocorticoids, in physiological conditions, play a role in the regulation of the glucose metabolism (gluconeogenesis). However, an anti-inflammatory effect of this hormone has been noticed, which lead to synthesizing of a large number of medicines with an increasingly stronger anti-inflammatory effect used in different areas of medicine.⁽²⁵⁾

According to findings to date, the anti-inflammatory effect of corticosteroids is founded upon the control over the mRNA synthesis under the direct influence of nuclear steroid receptors. The consequences of this function of corticosteroids are numerous – decreasing of the synthesis of IL-2 (the growth factor of T lymphocytes), preventing lymphocytes from migrating into the seat of the inflammation, lessening of the production of other lymphokine activators of macrophages, inhibition of phospholipase A2 (which decreases the production of arachidonic acid).⁽²⁵⁾ It has also been proved that, in in vitro conditions, the synovial cells decrease the secreting of hyaluronic acid under the influence of corticosteroids.⁽²⁶⁾

Experiments with animals have showed that corticosteroids, administered both systemic and intraarticularly, may directly influence the cartilage and thus influence the disease course.^(27,28,29) It has been proved that, depending on the dose of the medicine, a decrease of the level of stromelysin (proteolytic enzyme of the cartilage), as well as a reductions of interleukin 1 β and the oncogenes c-for and c-myc, which are important for the process of synthesis of metalloproteinase, happens.⁽²⁹⁾ This decrease in the synthesis of metalloproteinases after the injection of corticosteroids has also been confirmed by examining the OA patients.⁽³⁰⁾

However, some authors state that not only do corticosteroids not have protective effect on the cartilage⁽³¹⁾, but they may induce worsening of the condition by provoking a greater loss of proteoglycan.⁽³²⁾ Others state that these processes are in general a reflection of the basic disease (ex. Charkot – like acceleration of the damaging of the hip joint cartilage in the case of OA after the injection of corticosteroids) and not of the direct action of the treatment.⁽³³⁾ Nonetheless, the majority of the authors do not recommend more than 3-4 injections into the joint over the period of one year.

The systematic review prepared and maintained by The Cochrane Collaboration from 2006 which covered 1721 patients in 26 trials has showed that the IA administering of corticosteroids, as compared to a placebo, is more efficient in the pain control and the over-all condition of the patient during the first week, whereas there is no evidence of a more significant amelioration of the functions in that period; that the effect with regard to decreasing the pain is maintained during the second and the third weeks, but the effect is lost later.⁽³⁴⁾

As we have mentioned at the beginning, we have not found data on periarticular administering of corticosteroids in the available literature. Taking into consideration that the coating layers of the joint (synovial membrane, joint capsule) are listed as sources of the pain in gonarthrosis, as well as the supposed pain mechanism (inflammatory component), it is justifiable to expect corticosteroids administered in a periarticular way to have a positive clinical effect.

The western medicine starts to accept acupuncture as a treating method at the beginning of the 70's, when the first studies in accordance with the recognized scientific methodology were conducted and published. The researches to date have confirmed that neurohumoral mechanisms which include the peripheral nervous system (All fibers and the spinal cord), the brain stem and the

hypothalamus, are activated by stimulating acupunctural points. It has been showed that a greater number of neurotransmitters are included in the mechanism of acupunctural analgesia – apart from the endogenous anesthetics, which were first proved and best explored, they are dopamine, serotonin, but also the adrenocorticotropic hormone (stress-related hormone).^(35,36,37) Using a functional magnetic resonance it has been proved that acupuncture causes measurable changes in the respective parts of the brain (by performing stimulation of points on the foot, which has traditionally been linked to sight, a part of the occipital cortex is activated the same way as if the eye was stimulated by light; the stimulation of the close sham point has not provoked such a reaction.⁽³⁸⁾ Furthermore, acupuncture, given in the early phase, may diminish the exudative reaction by blocking the vascular permeability and decreasing the adherence of leukocytes to the vascular endothelium in a degree comparable to the oral administering of aspirin and indomethacin.⁽³⁹⁾ A multicenter study which involved 570 patients with gonarthrosis showed that acupuncture, compared to sham acupuncture and education control group, ameliorates the function and decreases the pain in these patients.⁽⁴⁰⁾

In the group of our examinees, after a week, all three methods gave satisfactory clinical effects, especially with regard to pain, but also regarding to the size and function of the knee (degree of flexion). The best results were observed in the II group of patients (periarticular administering of a corticosteroid). Here, it has to be taken into consideration that the periarticular local administering of corticosteroids is less stressful and brings far less risk for the patient (pain, cartilage damage, infection). After the 21st day, these effects are further present in all three groups. However, it is interesting that in II group there has been a slight deterioration in all observed parameters in relation to the first measuring, whereas the patients who had acupuncture or a combination of these two methods had better results (in regard to the first measuring). The III group patients showed the best results in the control of pain after the 21st day, while groups I and II did not considerably differ statistically. It is important to mention that group I (acupuncture) continued to show a tendency of improvement, i.e. pain lessening (in regard to the first measuring), whereas group II (periarticular corticosteroids) showed a tendency of deterioration. Group III (combination of periarticular corticosteroid and acupuncture), apart from the very good final effect, also showed a tendency of improvement. It is likely that corticosteroids have provided a good initial effect, whereas acupuncture contributed to the lastingness of the effect and the positive tendency during the observation period.

Although the number of patients involved in this research was relatively small, we reckon that the tendencies showed during the observation period are encouraging, as a result of which we consider that it is necessary to continue with further researching.

Conclusion

Acupuncture, periarticular local instillation of corticosteroids, as well as their combination may be successfully used in the

treatment of pain, functional disorder and knee size in the case of gonarthrosis.

Combined therapy of periarticular local administering of corticosteroids and acupuncture has, in our group of patients, given better clinical results in comparison with monotherapy.

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