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Intra-articular injections – current indications and contraindications

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Abstract

Therapeutic intra-articular injections are becoming an increasingly popular treatment modality for osteoarthritis, in particular in its initial stage. The available literature provides varied reports on the efficacy of drugs being administered directly into the joint cavity. This results from inconsistent research methods and assessment criteria. There is considerable controversy as to the best therapeutic approach in everyday clinical practice. The aim of this paper was to present synthetically information and research results concerning the use of selected therapeutic agents in intra-articular injection treatment. The collected data is supposed to facilitate adjusting treatment strategies to patients' individual needs.

Keywords: intra-articular injections, synovial fluid, joint

Introduction

The technological leap at the turn of the 20th and 21st centuries and constant development of knowledge about the pathomechanisms of diseases allow more accurate management of sources of health problems. Currently, orthopaedists reduce the number of indications for systemic use of anti-inflammatory drugs. Patients are more often offered solutions such as intra-articular topical injections or

drugs to be administered directly in the area of bone and soft tissue damage. Intra-articular injections are becoming increasingly popular nowadays. In terms of anticipated therapeutic results, we can distinguish diagnostic, decompressive and therapeutic intra-articular injections as well as compilations of the above mentioned types.

Because of the issue's complexity, in our report we focus on therapeutic injections. The major advantage of employing such way of treatment is a higher bioavailability of drugs at the spot of injection in comparison to their general application [1]. Anatomically, this results from the avascularity of articular cartilage, which significantly impairs a drug's access to zones of damage [2]. The attempts to overcome this barrier involve long-term administration of high-dose drugs, which leads to an increased risk of systemic side effects, especially in case of chronic conditions. For this reason, intra-articular injections seem to be a safer treatment modality, which offers drug application in the proximity of damaged intra-articular structures [1]. There are many indications for therapeutic intra-articular injections, the most common of which include: traumatic or overload intra-articular injuries, degenerative and proliferative changes, inflammation of different aetiologies, haemorrhages, exudates or pain of unspecified aetiology [1, 3, 4, 5]. According to many authors, however, treatment with direct drug injections into the joint has multiple limitations. It should be remembered that intra-articular injections must not be carried out in the presence of uncontrolled coagulopathy, hypersensitivity to the active ingredient or during general or topical infection. [**Błąd! Nie zdefiniowano zakładki.**] Other absolute contraindications, which must not be ignored, are periarticular fractures and joint instability. [4] For an array of articular and general health problems there are no unambiguous safety criteria to perform therapeutic intra-articular injections. In the case of patients who are on anticoagulant therapy [5], have compromised blood coagulability for other pathological reasons [**Błąd! Nie zdefiniowano zakładki.**], are on immunosuppressive therapy [6] or suffer from diabetes [7], it has to be balanced if the advantages of the treatment outweigh the potential health risks.

General principles of intra-articular injection treatment

The decision to start treatment with therapeutic intra-articular injections must be based on a strong foundation of evidence-based medicine. After establishing

indications for such treatment, an appropriate drug should be chosen. The most commonly used agents include: hyaluronic acid and its derivates [8, 9, 10], glucocorticosteroids [11, 12, 13, 14], platelet-rich plasma (PRP) [15, 16, 17], collagen [18], radioactive isotopes [19, 20] and progenitor stem cells [21, 22]. The drug should be administered in a sterile environment [23]. Injections have to be done in accordance with current guidelines and the procedure can be guided by ultrasonography or fluoroscopy for considerably easier targeting [1]. Undoubtedly, the physician's knowledge and experience are crucial during the procedure. For this reason, injections into the hip or spine should be done by the most qualified persons [**Błąd! Nie zdefiniowano zakładki.**]. In this paper, we intend to focus on three preparations which are most commonly used in intra-articular injection therapies: hyaluronic acid, glucocorticosteroids and platelet-rich plasma [24].

Hyaluronic acid

Hyaluronic acid is one of a group of organic compounds called glycosaminoglycans. In the human body, it is the major component of the synovial fluid [25]. It exhibits hygroscopic properties and is the predominant component of the hyaline cartilage. Hyaluronic acid makes it possible for diffusion to satisfy the nutritional needs of the articular cartilage. It provides a mechanical barrier to protect the surface of the hyaline cartilage from excessive pressures during physiological joint loading. It also reduces friction and tangent forces to the articular surfaces between bones [26, 27]. Hyaluronic acid preparations and its derivates are injected transcutaneously into the joint cavity during early osteoarthritis to protect the cartilage from further deterioration [10]. As proven by experiments and everyday practice, they are safe and well tolerated by patients [28]. However, the disadvantages of this treatment modality include short duration of pain relief and no microscopically observed effect of articular cartilage regeneration. Concerning the high costs of such therapy, the results of treatment are disproportionately limited [5]. In 2015, a meeting of experts from different countries was organised to summarise the current state of knowledge and to adopt a position on viscosupplementation [10]. The indication for hyaluronic acid injections into the knee joint is pain in the course of mild to moderate degenerative and proliferative changes. It is not recommended using hyaluronic acid as a method of last resort. Drug injections cause a subjective decrease in pain and complement

nonsteroid anti-inflammatory therapies [10]. Clinical studies showed a major decrease in the analgesic efficacy of hyaluronates as early as at six weeks after injection. However, some studies confirmed the positive anodyne effect as long as at 26 weeks after injection [10]. The knee joint is most commonly accessed and treated through a lateral approach at the level of the base of the patella [10]. Experts did not confirm unambiguously the positive impact of hyaluronic acid in the treatment of glenohumeral joint arthritis. Unfortunately, the amount of workmanly research is small [29, 30]. The use of hyaluronic acid in patients with talocrural joint arthritis seems to be advantageous in treating early to moderate stages of the disease. In advanced arthritis, no positive impact on pain levels and inhibiting the progression of pathological changes was demonstrated [10]. In the affected hip joint, the application of hyaluronic acid can yield temporarily favourable outcomes, but only in the initial arthritis stage. In advanced forms of coxarthrosis, hyaluronates were not reported to have any therapeutic impact on pain intensity and disease progression [31]. Migliore et al. pointed out that ultrasound-guided injections provided a longer therapeutic effect [32].

Glucocorticosteroids

Glucocorticosteroids are drugs with anti-inflammatory and immunosuppressive properties. They inhibit an inflammatory response, including joint inflammation, by using different mechanisms. As such they do not exhibit analgesic effects. They exert a systemic influence on protein and fat metabolism as well as affect the cardiovascular and central nervous systems. During treatment, it should be remembered that glucocorticosteroid interact with many drugs from different groups and cause multiple side-effects [33]. Knee joint injections may alleviate pain and increase joint mobility in chronic and acute osteoarthritis. Hepper et al. reported a positive effect of intra-articular knee steroid injections, but with short-term benefits of up to approximately 4 weeks [12]. Arden et al. showed a significantly longer duration of up to 26 weeks [13]. In their study published in 2012, Yavuz et al. demonstrated higher efficacy of methylprednisolone in comparison to betamethasone, with the treatment effect of both drugs being significantly smaller at 12 weeks after injection [14]. It is difficult to clearly define the duration of the analgesic effects of corticosteroid injections in the treatment of knee osteoarthritis. Frozen shoulder patients were reported to experience positive effects of treatment at one month after

intra-articular steroid injection [34]. An even more rapid response was observed in patients with arthritis of the first carpometacarpal joint. Positive effects of glucocorticosteroid treatment were evident as early as in the first weeks after injection and pain decreased in 68% of the examined patients during a two-year follow-up period [35]. Relatively long-term therapeutic effects were observed in hallux rigidus patients. In such cases, steroid injections were effective up to 3 months from the beginning of the treatment [36].

Platelet-rich plasma

Biological treatment by using autologous growth factors has found its application in patients with intra-articular lesions. The most popular treatment option is the use of therapeutic intra-articular injections where preparations of autologous leukocyte- and platelet-rich plasma (L-PRP) are administered [15]. Platelet-rich plasma contains numerous growth factors and some other cytokines. They are released from platelets and may stimulate tissue repair processes [16]. An undeniable advantage of employing platelet-rich plasma is the simple, cheap and non-invasive way of applying large numbers of autologous cells with healing mediators to the injured area. These substances also decrease pain and limit the intensity of inflammation. The clinical outcomes are promising and include pain alleviation, improved joint functionality and better life quality [37]. In clinical studies, it turned out that better results were obtained in young patients with early to moderate osteoarthritis [38]. Unfortunately, there is no reliable data to show if PRP causes osteophytes to regress or articular cartilage or other structures to regenerate. Although more level I and II evidence-based research into platelet preparations is needed, PRP appears to be a validated treatment modality for early to moderate joint osteoarthritis because it is simple to obtain, cheap and widely available and its efficacy was confirmed by encouraging preliminary results [39]. Promising results were published in 2010 by Kon et al. In their study, 115 patients were treated with PRP for gonarthrosis. At 6 and 12 months, a crucial improvement was achieved when compared to the control group [17]. In 2011, Filardo et al. analysed a similar-sized group, but with a longer follow-up period of 2 years. There was no doubt that the positive therapeutic effect of PRP decreased during the follow-up, but it was still significantly higher than in the placebo group [40].

Discussion

In 2014, Ayhan et al. collected and summarized the available information on therapeutic knee joint injections [24]. Hyaluronic acid and glucocorticoids injections provided similar clinical effects up to 4 weeks, but after that period hyaluronic acid proved more effective in reducing pain and joint stiffness [28, 41]. Therapies with platelet-rich plasma and hyaluronic acid were compared in a total of 150 patients and it turned out that PRP patients obtained better results in reducing pain and joint stiffness up to 6 months after injection. Furthermore, differences in favour of PRP were significant in young patients with chondromalacia or early osteoarthritis [42]. No significant differences in the efficacy of PRP and hyaluronic acid treatment were recorded in advanced osteoarthritis patients over 50 years of age [43, 44]. It is recommended that glucocorticosteroid therapy be used for the shortest time possible. However, where surgery is contraindicated, steroid intra-articular injections seem to be justified in acute or chronic synovitis unless they are carried out immediately before surgical treatment [24]. Hyaluronic acid injections are most commonly performed in patients above 60 years of age who do not accept surgical treatment [24]. Autologous platelet-rich plasma appears to be the best treatment option in patients under 60 years of age with mild osteoarthritis and a BMI under 30. Patients above 60 years of age with moderate arthritis or a BMI above 30 can still be treated with PRP, but it is recommended that a supplementary hyaluronic acid injection be performed at 2 to 4 weeks afterwards [24].

Summary

As medicine develops and new therapies arise, the available treatment algorithms require frequent adjustments to include valuable reports and clinical studies. Physicians should not depend only on their own experience and limit themselves to previously known treatment methods. On the contrary, they are obliged to analyse and introduce systematically newer methods to prevent or manage changes caused by body wear, such as degenerative diseases. This is possible only after a thorough analysis of the literature. Intra-articular injections are becoming increasingly common and every physician should know the main advantages and disadvantages of this treatment modality. According to many authors, therapeutic intra-articular injections are very useful in inhibiting the progression of degenerative disease and improving the quality of live [**Błąd! Nie zdefiniowano zakładki.**, **Błąd! Nie zdefiniowano**

zakładki., **Błąd! Nie zdefiniowano zakładki.**, **Błąd! Nie zdefiniowano zakładki.**, **Błąd! Nie zdefiniowano zakładki.**, **Błąd! Nie zdefiniowano zakładki.**, **Błąd! Nie zdefiniowano zakładki.**, **Błąd! Nie zdefiniowano zakładki.**]. However, further research is needed to develop the best criteria that may be used to triage patients to different forms of intra-articular injections.

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Conflict of interest statement

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