OSTEOARTRITIS, OSTEOARTROZA I OSTEOARTROPATIJA – KOJA JE RAZLIKA?

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REVIEW ARTICLE

OSTEOARTHRITIS, OSTEOARTHROSIS AND OSTEOARTHROPATHY – WHAT IS THE DIFFERENCE?

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SAŽETAK

Osteoartritis, osteoartroza i osteoartropatija su oboljenja sa kojima se lekari susreću u praksi svakodnevno. Uobičajena je upotreba sva tri termina, često bez jasne slike zašto se neki od njih koristi. Unazad nekoliko decenija, glavnu razliku između ovih oboljenja lekari su postavljali na osnovu kliničke slike i radiografije. U poslednjih nekoliko godina napravljen je značajan napredak na polju biohemijskih, imunoloških i citohistoloških istraživanja čime je objašnjena patogeneza ovih stanja, omogućeno definisanje razlika između njih i upotreba odgovarajućeg naziva. Naziv artritis (osteoartritis) treba koristiti isključivo za primarno inflamatorne bolesti zglobova - reumatoidni artritis, juvenilni artritis, reaktivni artritis (Rajterov sindrom). Ukoliko se radi o infektivnoj etiologiji, onda i to treba naglasiti – septični (purulentni) artritis, tuberkulozni artritis. Artroza (osteoartroza) se odnosi na promene u zglobu koje nastaju zbog patoloških procesa u samom zglobu, ali koji nisu u osnovi inflamatorni. Artropatija je naziv za oboljenje zgloba nastalo kao posledica oboljenja drugog organa ili sistema.

Ključne reči: osteoartritis, osteoartroza, osteoartropatija

ABSTRACT

Osteoarthritis, osteoarthrosis and osteoarthropathy are diseases which doctors encounter daily in their practice. The use of all three terms is customary, often without a clear justification as to why a particular term is used for a particular case. In the past several decades, doctors mainly differentiated among these diseases based on clinical presentation and radiography. In the past several years, however, significant progress has been made in the field of biochemical, immunological and cytohistological research, which has provided explanations for the pathogenesis of these conditions, enabled defining differences amongst them, and facilitated the use of appropriate terms for each one of these diseases. The term arthritis (osteoarthritis) should be used exclusively for primarily inflammatory joint diseases – rheumatoid arthritis, juvenile arthritis, reactive arthritis (Reiter's syndrome). If the etiology is infectious, this must also be emphasized – septic (purulent) arthritis, tuberculous arthritis. Arthrosis (osteoarthrosis) relates to changes in the joints occurring due to pathological processes within the joint itself, but which, in their basis, are not inflammatory. Arthropathy is a term for joint disease stemming from another diseased organ or system of organs.

Key words: osteoarthritis, osteoarthrosis, osteoarthropathy

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UVOD

Osteoartritis (ili samo artritis), osteoartroza (artroza) i osteoartropatija (artropatija) su vrlo česta stanja sa kojom se većina ortopedskih hirurga, reumatologa i lekara drugih specijalnosti susreću svakodnevno. Uobičajena je upotreba sva tri termina, često bez jasne slike zašto se neki od njih koristi. Ovo često otežava komunikaciju između lekara, posebno u slučajevima saradnje između kolega u različitim državama. Problemi se dodatno umnožavaju kada se uđe u domen medicinskih publikacija, jer je otežana najpre pretraga željene teme, a zatim i razumevanje napisanog [1,2].

Ova situacija verovatno vodi poreklo od pre više decenija kada su klinička slika i nativna radiografija bile glavni vodiči za imenovanje bolesti. I zaista, velika većina oboljenja zglobova je u ovom smislu vrlo slična – bol, otok i ograničenje pokreta, sreću se u različitom stepenu kod svih stanja [3]. Radiografska slika je takođe slična – gubitak zglobnog prostora, manje ili više izražena subhondralna skleroza, osteofiti i subhondralne ciste [4]. Tek poneki parametar, kao što je izraženo crvenilo, supuracija ili značajno izmenjeni osnovni laboratorijski parametri, mogu uputiti na to da se neko stanje definiše kao inflamacija, metabolički ili endokrinološki poremećaj, mada ni tada sa potpunom sigurnošću. Potrebna je detaljna dijagnostika da bi se postavila tačna dijagnoza [5].

U poslednjih 25 - 30 godina napravljen je značajan napredak na polju biohemijskih, imunoloških i citohistoloških istraživanja čime je objašnjena patogeneza ovih stanja, omogućeno definisanje razlika između njih, te upotreba odgovarajućih naziva.

POREKLO

Ustaljeno pravilo u medicinskoj tradiciji je da se inflamacije označavaju nazivima sa nastavkom *–itis*. Opšte poznati, i u svakodnevnoj upotrebi, i van medicinskih krugova, su nazivi kao: apendicitis, prostatitis, encefalitis, itd. Postoje i izuzeci od ovog pravila kao što su pneumonia – inflamacija pluća, flegmona – inflamcija potkožnog tkiva. Ali ono šta je sigurno je da se *–itis* odnosi na inflamaciju [6]. Odatle se i naziv artritis odnosi na različite vrste zapaljenja zglobova. Ukoliko se radi o infektivnom zapaljenju onda je situacija jasna – purulentni (septični) artritis, tuberkulozni artritis, luetični artritis. Problem nastaje kod velike grupe reumatskih bolesti (reumatoidni artritis, juvenilni artritis, ankiloizirajući spondilitis, Rajterov sindrom, SLE, itd.) gde zapaljenje postoji, ali se dugo nije znalo kako nastaje i da li je ono uzrok ili posledica oštećenja zgloba [7].

Poseban problem postoji kod vrlo čestog stanja propadanja zglobova za koje je primećeno da se jav-

INTRODUCTION

Osteoarthritis (or just arthritis), osteoarthrosis (arthrosis) and osteoarthropathy (arthropathy) are very common conditions which most orthopedic surgeons, rheumatologists and doctors of other specialties encounter daily in their practice. The use of all three terms is customary, often without a clear justification as to why a particular term is used for a particular case. This often makes communication amongst doctors more difficult, especially in the collaboration of doctors from different countries. Problems become even more pronounced in the domain of medical publications, rendering the search for the desired topic as well as the understanding of the material written more difficult [1,2].

This situation probably stems from several decades ago, when clinical presentation and native radiography were the main methods defining and naming these diseases. Indeed, a great majority of joint diseases are, in this respect, very similar to each other – different degrees of pain, swelling, and limitation of movement can be found in all of the conditions [3]. The radiographic images are also similar – joint space narrowing, more, or less pronounced subchondral sclerosis, osteophytes, and subchondral cysts [4]. It is only a small number of parameters, such as pronounced redness of skin, suppuration, or significantly altered basic laboratory parameters, that can help in defining a particular state as inflammation, a metabolic, or an endocrinological disorder, though, even then, not with absolute certainty. Detailed diagnostics is necessary for establishing a precise diagnosis [5].

In the last 25 - 30 years, significant progress has been made in the field of biochemical, immunological and cytohistological research, which has provided explanations for the pathogenesis of these conditions, enabled defining differences amongst them, and facilitated the use of appropriate terms for each one of these diseases.

ORIGIN

The established rule in medical tradition is to name inflammations with terms that end in *–itis*. The names in everyday use that are well known, even outside the medical sphere, are terms such as: appendicitis, prostatitis, encephalitis, etc. There are exceptions to this rule, such as pneumonia – inflammation of the lungs, phlegmon – inflammation of the subcutaneous tissue. What is definite, however, is that *–itis* refers to inflammation [6]. This is why the term arthritis refers to different types of joint inflammation. If the inflammation is infectious, then the situation is clear – purulent (septic) arthritis, tuberculous arthritis, luetic arthritis. The problem arises with a large group of rheumatoid diseases (rheumatoid arthritis, juvenile arthritis, ankylosing spondylitis, Reiter's syndrome, SLE, etc.) where inflammation exists, but, for a long time,

lja u toku starenja, ali i u srednjem životnom dobu bez jasnog uzroka, kao i kod mlađih ljudi, kao posledica prethodnog oštećenja zgloba nekim drugim procesom [8]. Ovde zapaljenja nema ili ako ga ima ono se javlja kasnije i nije izraženo. Iz tog razloga ovo stanje nije moglo biti nazvano samo artritis i, da bi se razlikovalo od ostalih, nazvano je osteoartritis. Kasnije, zbog brojnih nedoumica oko postojanja i uticaja zapaljenja u ovom procesu, neki autori su napravili otklon od ovog naziva i počeli da koriste naziv degenerativna bolest zglobova (*degenerative joint disease* – DJD), a drugi, posebno u Evropi, počeli su da koriste naziv artroza.

Treći naziv – artropatija, na osnovu opšteg medicinskog shvatanja, mogao bi se odnositi na celokupnu patologiju zglobova. Sufiks *–patija* je naziv za svako patološko stanje, a u praksi se koristi kao naziv za grupu stanja ili naziv za nedovoljno definisana stanja – koagulopatija, hemoglobinopatija, radikulopatija, mijelopatija, encefalopatija, itd. [6]. Tako se i u ortopediji naziv artropatija ustalio za sva stanja nejasnog porekla i razvoja, a koja se na osnovu kliničkog nalaza ne razlikuju značajno od inflamacije i degeneracije.

SAVREMENA RAZMATRANJA

Biohemijska i imunološka istraživanja na polju patogeneze reumatskih bolesti dovela su do savremenog shvatanja da je ovo grupa tzv. autoimunih bolesti - imuni sistem domaćina reaguje protiv sopstvenih ćelija. U slučaju reumatskih artritisa, glavne ciljne ćelije za imuni sistem su u sinoviji zglobova. Dakle, osnovni patološki proces koji se dešava u zglobu je inflamacija [9]. Inflamaciju prati angiogeneza, zatim stvaranje panusa - koji luči enzime (kolagenaza), i promena sastava sinovijalne tečnosti - u kojoj je registrovana ekspresija interleukina 17 (IL-17), glavnog aktivatora mastocita [10].

U okviru ovog složenog imunološkog procesa, praćenog biohemijskim i histološkim promenama, kao drugi korak se dešava oštećenje zglobne hrskavice [11]. Hrskavica se kao avaskularno tkivo ishranjuje iz zglobne tečnosti i vrlo je osetljiva na svaku promenu njenog sastava. Kad se na to doda dejstvo proteolitičkih enzima i inflamatornih ćelija, jasno je zašto vrlo brzo dolazi oštećenja i propadanja hrskavice.

Degeneracija je proces koji se odvija sa starenjem. Zapravo bi se moglo reći da degeneracija jeste starenje. Starenje, koje karakteriše progresivni gubitak funkcije tkiva i organa tokom vremena, predstavlja najveći pojedinačni faktor rizika za osteoartrozu [12].

Raznovrsni genetski mehanizmi upravljaju ovim procesom [13]. Odavno je poznato da je osnovna promena koja se tom prilikom odigrava smanjenje

the way it develops and whether it is the cause or result of damage to the joint had remained unknown [7].

A particular issue is a very common state of joint deterioration which has been noted to occur as a part of the ageing process, but also in middle age, without a clear cause, as well as in young individuals, as the result of previous damage to the joint caused by some other process [8]. There is no inflammation in such cases, or if it does occur, it develops later and is not pronounced. This is why this condition could not merely have been named arthritis; therefore, in order to differentiate it from other conditions, it was named osteoarthritis. Later, due to numerous dilemmas regarding the existence and the influence of inflammation in this condition, some authors strayed away from this term and started to use the term degenerative joint disease (DJD), while others, especially in Europe, started to use the term arthrosis.

The third term – arthropathy, could, based on general medical understanding, refer to overall joint pathology. The suffix *-pathy* is used for every pathological state, and, in medical practice, it is used in terms denoting a group of conditions or in terms naming incompletely defined conditions – coagulopathy, hemoglobinopathy, radiculopathy, myelopathy, encephalopathy, etc. [6]. In the same way, in orthopedics, the term arthropathy has become customary for all conditions of unclear origin and development, which, based on the clinical finding, do not significantly differ from inflammation and degeneration.

CURRENT CONSIDERATIONS

Biochemical and immunological research in the field of the pathogenesis of rheumatic diseases has brought about the current understanding that this is a group of, so called, autoimmune diseases - the immune system of the patient reacts against its own cells. In the different types of rheumatoid arthritis, the main target cells for the immune system are in the synovia of the joints. Therefore, the main pathological process occurring in the joint is inflammation [9]. Inflammation is accompanied by angiogenesis, the formation of pannus – which secrets enzymes (collagenase), and a change in the composition of the synovial fluid – where the expression of the interleukin-17 (IL-17), the main activator of mastocytes, has been registered [10].

As the second step within this complex immunological process, accompanied by biochemical and histological changes, the damage to the joint cartilage occurs [11]. Cartilage, which is avascular tissue, receives its nutrients from the synovial fluid, and is therefore very sensitive to any change in the composition of this fluid. When the effect of proteolytic enzymes and inflammatory cells is added to this, it is clear why cartilage becomes damaged and deteriorates very quickly.

anaboličkih procesa. U zglobovima se ovo odnosi na smanjenje sinteze zglobne tečnosti iz koje se hrskavica ishranjuje, kao i na smanjenje sintetskih procesa u samoj hrskavici - najviše na smanjenu sintezu proteoglikana i glikoproteina - usled čega dolazi do gubitka vode iz matriksa, istanjenja hrskavice, gubitka elastičnosti i plastičnosti i konačno do fibrilacije, fragmentacije i erozije hrskavice [14,15]. Na osnovu ovoga može se zaključiti da je osnovni proces patološki proces u hrskavici, te da taj proces nije inflamacija [16]. Tačni patogenetski mehanizmi osteoartroze i dalje su nepoznati, uprkos savremenom napretku u analizi i dijagnozi [17].

Nakon nekoliko decenija istraživanja, potvrđeno je da inflamacija u obliku sinovitisa postoji u procesu degeneracije. Najnovija istraživanja na ovom polju pokazala su da je ona delom posledica procesa starenja hondrocita, gde dolazi do usporavanja antioksidativnih procesa i povećanja lučenja nekoliko inflamatornih i prodegenerativnih medijatora, što je pokrenuto oksidativnim stresom [18]. Međutim, najvažniji faktori inflamacije su fragmenti hrskavice koji otpadaju sa zglobne površine i direktno, fizički, nadražuju sinoviju, ali i proinflamatorni citokini i MMP (matriksne metaloproteinaze), koji se iz ovih fragmenata oslobađaju direktno na sinoviju [19,20]. Dalje, kao i u reumatskim bolestima, zapaljena sinovija oštećuje hrskavicu i tako se formira začarani krug međusobnog oštećenja. Iz ovoga se jasno vidi da, iako postoji, inflamacija nastaje sekundarno, odnosno kao posledica drugog procesa u zglobu [21].

Postoji veliki broj slučajeva kada se oštećenje zgloba javlja kod mlađih i sredovečnih ljudi. Ovaj proces je vrlo sličan degeneraciji, ali, s obzirom da je rečeno da je degeneracija u stvari starenje, postavlja se pitanje: zašto bi jedan ili nekoliko zglobova starili brže od ostalih organa i sistema? Opet, odgovor je u patogenezi. Naime, zglobovi se „troše" u toku korišćenja. Ovo trošenje ubrzano je povećanim korišćenjem, kao i povećanim mehaničkim stresom – *overuse and overweight*. Povećani mehanički stres najčešće je posledica prekomerne telesne težine. Međutim, i životna aktivnost (sport i rad), kao i neadekvatna biomehanika (displazija acetabuluma, femoroacetabularni impingement, Pertesova bolest, epifizioliza, varus kolena, stanje nakon preloma, itd.) dovode do oštećenja zgloba [8].

Osteoartritis je najčešća bolest zglobova i jedno od glavnih javno-zdravstvenih pitanja tekućeg veka [22]. Zbog rastućeg očekivanog trajanja života, posebno u razvijenim zemljama, njegova globalna prevalenca se brzo povećava, što ga čini bolešću povezanim sa izuzetno visokim ekonomskim opterećenjem [22,23].

Degeneration is a process that develops with ageing. In fact, one could say that degeneration is ageing. Ageing, characterized by progressive loss of tissue and organ function over time, is the most prominent individual risk factor for osteoarthrosis [12].

Various genetic mechanisms drive this process [13]. It has long been known that the main change within it is the reduction of anabolic processes. In the joints, this refers to the reduction in the synthesis of synovial fluid, which provides nutrients for the cartilage, as well as the reduction of the processes of synthesis within the cartilage itself – primarily reduced synthesis of proteoglycans and glycoproteins – which results in loss of water from the matrix, thinning of the cartilage, loss of elasticity and plasticity, and finally, in fibrillation, fragmentation and erosion of the cartilage [14,15]. Based on this, it can be concluded that the main process is the pathological process within the cartilage and that this process is not inflammation [16]. The exact pathogenetic mechanisms of osteoarthrosis remain unknown, despite the modern-day developments in analysis and diagnosis [17].

After several decades of research, it has been confirmed that inflammation in the form of synovitis is present within the process of degeneration. The latest research in this field have shown that this is partially the result of the process of chondrocyte ageing, whereby antioxidative processes are slowed down and the secretion of several inflammatory and prodegenerative mediators is increased, which is triggered by oxidative stress [18]. However, the most important factors of inflammation are the fragments of cartilage which come away from the surface of the joint and directly, mechanically, irritate the synovia, as well as proinflammatory cytokines and MMP (matrix metalloproteinases), which are released from these fragments directly onto the synovia [19,20]. Furthermore, as in rheumatic diseases, the inflamed synovia damages the cartilage, thus completing a vicious cycle of mutual injury. This clearly demonstrates that, although it does exist, inflammation occurs as a secondary process, i.e., as the result of a different process within the joint [21].

There is a large number of cases where joint damage occurs in young and middle-aged individuals. This process is very similar to degeneration, however, as it has been stated that degeneration is, indeed, ageing, the question arises as to why one or a few joints should age more quickly than other organs or systems of organs. Again, the answer lies in pathogenesis. Namely, joints get "worn" during use. This deterioration is accelerated by increased use as well as by increased mechanical stress – *overuse and overweight*. Increased mechanical stress is most frequently the result of excess body weight. However, activity (sports and work relat-

Osnovna patološka promena u ovim slučajevima je u subhondralnoj kosti. Jedan od važnih zadataka ove kosti je da bude podloga zglobnoj hrskavici i omogući njenu ulogu u prihvatanju, amortizovanju i prenosu sila koje deluju u zglobu. Ukoliko se ova uloga naruši – zadebljavanjem i deformisanjem pod većim pritiskom usled težine tela, promenom oblika usled preloma ili druge bolesti ili mikrofrakturama – to se direktno odražava na hrskavicu koja, kao i kod degenerativnog procesa, propada, što dovodi do zapaljenja sinovije i ponovo nastaje već spomenuti začarani krug. Međutim, ni u ovom procesu inflamacija nije glavni pokretač, već samo jedna od karika u lancu bez koje bi se proces svakako odvijao, ali verovatno nešto sporije.

Konačno, dolazimo do velike grupe bolesti različitih organa i sistema organa koje u okviru svoje kliničke slike imaju i oštećenje zglobova. Među njima najznačajnije su: *diabetes mellitus*, hemofilija, različite neuropatije (*tabes dorsalis, syringomyelia*, paralize, itd.) i brojne metaboličke bolesti (giht, pseudogiht, alkaptonurija, hemosideroza). Tipičan primer artropatije je Šarkoov zglob (najčešće kao neuroartropatija ili dijabetska artropatija) [24]. Zajedničko za sve ove bolesti je da se osnovni patološki proces nalazi izvan zglobova, a da su oni oštećeni sekundarno. Mehanizmi oštećenja su različiti. Kod neuropatija to je neadekvatno delovanje mišićnih sila, dakle u osnovi je mehaničko oštećenje [25]. Kod *diabetes mellitus*-a to je kombinacija neuropatije i ishemije. Kod hemofilije to su ponovljena krvarenja u zglobu što dovodi do poremećaja ishrane hrskavice, kao i do oslobađanja proinflamatornih faktora raspadom krvnih ćelija [26]. Kod metaboličkih bolesti to je nakupljanje određenih materija u zglobovima što dovodi do direktnog oštećenja hrskavice i inflamacije sinovije [27]. Dakle, kod ovih procesa oštećenje je posledica više mehanizama, uključujući i inflamaciju.

NAŠA TAČKA GLEDIŠTA

Iz svega navedenog jasno je da postoji velika sličnost među opisanim procesima. Inflamacija uvek postoji kao faktor, više ili manje izražen. Određena istraživanja za cilj imaju da pokažu da je ona ključni faktor u svim bolestima. Već su spomenuti citokini i MMP koje luče hondrociti, i IL-17 kojeg luči sinovija. Tu su još IL-15 [28] i sistem komplementa, čije su vrednosti povišene u zglobnoj tečnosti, čak i u degenerativnom oštećenju [29]. Kristali mokraćne kiseline u gihtu i CPPD (Ca-pirofosfat dihidrat) u pseudogihtu prisutni su i u degenerativnom procesu i reaguju sa NALP-3 inflamazomom, intracelularnim proteinskim kompleksom, koji aktivira IL-1ß i IL-18, takođe proinflamatorne faktore [30,31].

ed), as well as inappropriate biomechanics (acetabular dysplasia, femoroacetabular impingement, Perthes' disease, epiphysiolysis, varus knee, state after fracture, etc.) result in joint damage [8].

Osteoarthritis is the most frequent joint disease and one of the main public health issues of the century [22]. Due to increased life expectancy, especially in developed countries, its global prevalence is rapidly rising, making it a disease linked to a very high economic burden [22,23].

The fundamental pathological change in these cases occurs in the subchondral bone. One of the most important roles of this bone is to be the basis for the joint cartilage and to facilitate its role in receiving, buffering and transferring the forces acting in the joint. If this role is disrupted – through thickening and deforming under increased pressure caused by body weight, through change in shape caused by fracture or other disease, or due to microfractures – this directly reflects on the cartilage, which, just like in the degenerative process, deteriorates leading to synovial inflammation, and the aforementioned vicious cycle is formed again. However, in this process, inflammation is again not the main trigger, but merely one of the components of the chain without which the process would definitely still occur, but probably somewhat more slowly.

Finally, there is a large group of diseases affecting different organs and systems of organs, which in their clinical presentation also include joint damage. The most significant amongst them are the following: *diabetes mellitus*, hemophilia, different neuropathies (*tabes dorsalis, syringomyelia*, paralyses, etc.), and numerous metabolic diseases (gout, pseudogout, alkaptonuria, hemosiderosis). A typical example of arthropathy is Charcot joint (most commonly as neuropathy or diabetic arthropathy) [24]. A common feature for all of these diseases is that the main pathological process occurs outside the joints and that the damage to the joints occurs as a secondary outcome. The mechanisms of damage vary. In neuropathies it is the inadequate action of the muscular forces, i.e., mechanic damage is at the basis of the disease [25]. In *diabetes mellitus*, it is a combination of neuropathy and ischemia. In hemophilia it is repeated bleeding in the joint, which leads to a disruption in the nourishment of the cartilage as well as the release of proinflammatory factors resulting from the breakdown of blood cells [26]. In metabolic diseases it is the accumulation of certain substances in the joints, which leads to direct cartilage damage and synovial inflammation [27]. Therefore, in these processes, the damage is the result of multiple mechanisms, including inflammation.

Najnovija teorija govori o tzv. „adipokinima", citokinima koje stvara masno tkivo i za koje se smatra da imaju uticaj na nastanak inflamacije u procesu oštećenja zglobova kod gojaznih ljudi [32,33,34].

Ipak, moramo reći sledeće: inflamacija je jedan od osnovnih patoloških procesa koji je dešava svakodnevno u ljudskom organizmu. Mnogi procesi su praćeni inflamacijom. Ona se dešava neposredno nakon preloma kosti. Da li onda treba naziv fraktura promeniti u *fracturitis*? Svaka rana na koži je praćena inflamacijom. *Vulneritis*? Ali da li je to presudno sa kliničke tačke gledišta? Mi mislimo da nije. Osnovni patogenetski proces i posledične terapijske procedure su ono na osnovu čega treba dati naziv oboljenju. Reumatoidni artritis je bolest inflamatorne patogeneze. Uspešno se može lečiti tokom više godina različitim antiinflamatornim lekovima. I zato je to artritis, isto kao i juvenilni artritis, ankiloizirajući spondiloartritis, itd.

Diabetes mellitus, hemofilija, giht i pseudogiht se leče, svaka bolest na svoj način. Kod nekih od njih antiinflamatorni lekovi imaju važnu ulogu, s obzirom da je i inflamatorni faktor jak, ali glavnu terapiju predstavlja nešto drugo – ono šta deluje na glavni patogenetski mehanizam.

Konačno, brojni terapijski pokušaji da se proces artroze leči antiinflamatornim lekovima, čak i onim najsavremenijim anti-IL-1 i anti-TNF medikamentima, doživeli su potpuni neuspeh [35,36]. Ovo, naravno, nije razlog da se antiinflamatorni lekovi ne koriste, ali njihova uloga je u simptomatskoj terapiji, a ne u uticaju na tok bolesti [37].

ZAKLJUČAK

Na osnovu svega navedenog iznosimo sledeći predlog:

- Naziv artritis (osteoartritis) treba koristiti isključivo za primarno inflamatorne bolesti zglobova - reumatoidni artritis, juvenilni artritis, reaktivni artritis (Rajterov sindrom). Ukoliko se radi o infektivnoj etiologiji, onda i to treba naglasiti – septični (purulentni) artritis, tuberkulozni artritis.
- Artroza (ustaljena skraćenica OA može da ostane, ali treba da se odnosi na naziv osteoartroza) se odnosi na promene u zglobu koje nastaju zbog patoloških procesa u samom zglobu, koji nisu u osnovi inflamatorni. I tu treba biti precizan:
  1. Primarna artroza – nastaje na prethodno neizmenjenom zglobu:
     a) degenerativna –nastaje u procesu starenja
     b) idiopatska – nastaje brže od prirodnog procesa starenja, ali bez jasnog uzroka.

OUR PERSPECTIVE

From all that has been stated, it is clear that there is a great similarity among the above-described processes. Inflammation always exists as a more or less pronounced factor. Certain studies are aimed at demonstrating that it is the main factor in all of the diseases. Cytokines and MMP, secreted by chondrocytes have already been mentioned, as well as IL-17 secreted by the synovia. Also, there are the IL-15 [28] and the system of complements, whose values are elevated in the synovial fluid, even in degenerative damage [29]. Crystals of uric acid in gout as well as CPPD (Ca-pyrophosphate dihydrate) in pseudogout are also present in the degenerative process and react with NALP3 inflammasome, the intracellular protein complex, which activates IL-1ß i IL-18, also proinflammatory factors [30,31]. The newest theory describes the so called "adipokines", cytokines secreted by adipose tissue, which are considered to have influence on the development of inflammation in the process of joint damage in obese people [32,33,34].

However, the following must be noted: inflammation is one of the main pathological processes occurring on a daily basis in the human body. Many processes are accompanied by inflammation. It occurs directly after bone fracture. Consequently, should the term fracture be changed to *fracturitis*? Every skin wound is followed by inflammation. *Vulneritis*? Is this, however, crucial from the clinical point of view? We think that it is not. The main pathogenetic process and the resulting therapeutic procedures are what a disease should be based on. Rheumatoid arthritis is a disease of inflammatory pathogenesis. It can successfully be treated over a number of years with anti-inflammatory drugs. This is why it is termed arthritis, just like juvenile arthritis, ankylosing spondyloarthritis, etc.

Diabetes mellitus, hemophilia, gout, and pseudogout can be treated, each disease in its own way. In some of these, anti-inflammatory drugs have an important role, since the inflammatory factor is strong, however, the main therapy is something else – the treatment that affects the main pathogenetic mechanism.

Finally, numerous therapeutic attempts to treat the process of arthrosis with anti-inflammatory drugs, even with the most up-to-date anti-IL-1 and anti-TNF medicaments, have been completely unsuccessful [35,36]. This, of course, is not a reason for anti-inflammatory drugs to not be used at all, but, their role is in symptomatic treatment, and not in achieving an effect on the course of the disease [37].

CONCLUSION

Based on all that above-stated, we make the following suggestions:

2. Sekundarna artroza – nastaje na terenu patološkog procesa u samom zglobu. Najčešći uzroci su trauma, Pertesova bolest, epifizioliza, avaskularna nekroza, ostehondralni defekt.

Artropatija je naziv za oboljenje zgloba nastalo kao posledica oboljenja drugog organa ili sistema. Postoje: neuroartropatija, ishemijska artropatija, hemofilična artropatija, dijabetska artropatija, metaboličke artropatije (giht, pseudogiht, ohronoza – alkaptonurija, hemosideroza).

Ova nomenklatura je u svakodnevnoj upotrebi u našoj bolnici već nekoliko godina i iz svakodnevne prakse možemo reći da je svaka nejasnoća ili nesigurnost po pitanju dijagnoze na ovaj način izbegnuta.

Istraživanja koja su započeta treba nastaviti, posebno u pravcu ispitivanja povezanosti mehaničkog stresa i inflamacije. Postoje indicije da abnormalni mehanički stres može biti pretvoren u unutarćelijske signale koji za posledicu imaju pojačano stvaranje medijatora inflamacije [38,39]. Potrebno je dalje istraživanje antiinflamatornih lekova, jer, iako ne mogu zaustaviti bolest, ovi lekovi su vrlo važni u ublažavanju simptoma. Međutim, dok se ne dogodi neko revolucionarno otkriće, predlažemo da se u svakodnevnoj kliničkoj praksi držimo naziva koji će nam omogućiti bržu i tačniju dijagnostiku i olakšati komunikaciju među lekarima, kao i između lekara i pacijenata, kojima će biti lakše objasniti njihovo stanje i dati odgovor na pitanje: zašto njegov komšija svoju bolest zglobova već godinama uspešno leči lekovima, a on mora da bude operisan?

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- The term arthritis (osteoarthritis) should be used exclusively for primarily inflammatory diseases of the joints – rheumatoid arthritis, juvenile arthritis, reactive arthritis (Reiter's syndrome). If there is an infectious etiology, this also needs to be stated – septic (purulent) arthritis, tuberculous arthritis.
- Arthrosis (the established acronym OA can remain but should refer to the term osteoarthrosis) relates to changes occurring in the joint as the result of pathological processes within the joint itself, which are not, in their essence, inflammatory. There, also, one must be precise:
  1. Primary arthrosis – develops on a previously unchanged joint:
     a) degenerative – occurs during the ageing process;
     b) idiopathic – occurs more quickly than the natural ageing process, but without a clear cause.
  2. Secondary arthrosis – occurs at the site of a pathological process within the joint itself. The most frequent causes are trauma, Perthes' disease, epiphysiolysis, avascular necrosis, osteochondral defect.

Arthropathy is a term for joint disease which has developed as the result of the disease of another organ or system of organs. There are: neuroarthropathy, ischemic arthropathy, hemophilic arthropathy, diabetic arthropathy, metabolic arthropathies (gout, pseudogout, ochronosis – alkaptonuria, hemosiderosis).

This nomenclature has been in everyday use in our hospital for a number of years and from everyday practice we can say that any unclarity or uncertainty as to diagnosis is avoided in this way.

Research in this area should be continued, especially in the direction of studying the link between mechanical stress and inflammation. There are indications that abnormal mechanical stress can be transformed into intracellular signals which result in increased production of inflammation mediators [38,39]. Further research of anti-inflammatory drugs is necessary because, even though they cannot stop the illness, these drugs are very important in lessening the symptoms. However, until a revolutionary breakthrough occurs, we propose that in everyday clinical practice we should adhere to terms that will enable more efficient and more precise diagnostics and facilitate communication amongst doctors, as well as communication between doctors and patients, to whom it will be much more easy to explain their state and answer the question as to why their neighbor has been managing joint disease successfully with medication for years while they have to undergo a surgical procedure.

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