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A review on diagnosis and treatment approaches to calcium pyrophosphate deposition disease

Negar Hosseinnejad, Krystyna Zabojska, Aleksandra Cygnarowicz, Aneta Klaudia Wojtas, Urszula Korotko, Aneta Mandziuk, Kinga Witowska, Mariola Turemka, Mikolaj Biskupski, Karolina Sacher

1-Negar Hosseinnejad
The 5 Military Clinical Hospital with Polyclinic SPZOZ in Cracow, Wroclawska Street 1/3, 30-901 Cracow, Poland
negr.h.nejad@gmail.com
https://orcid.org/0009-0002-3552-9513
2-Krystyna Zabojska
Hospital of Our Lady of Perpetual Help in Wolomin, Gdynska 1/3, 05-200 Wolomin, Poland
k.zabojska@gmail.com
https://orcid.org/0009-0002-6962-0497
3-Aleksandra Cygnarowicz
Bonifraters Medical Center sp. z. o. o. Branch in Krakow, Trynitarska 11 St., 31-061 Krakow, Poland
o.cygnarowicz@gmail.com
https://orcid.org/0009-0002-2208-0104
4-Aneta Klaudia Wojtas
Municipal Hospital in Siemianowice Śląskie sp. z o.o., 1. Maja 9 St., 41-100 Siemianowice Śląskie, Poland
aneta.wojtas98@gmail.com
https://orcid.org/0009-0002-6072-1232
5-Urszula Korotko
The Provincial Specialist Hospital in Ciechanów, Powstańców Wielkopolskich 2 St., 06-400 Ciechanów, Poland
urszulakorotko@gmail.com
https://orcid.org/0009-0004-9226-6451

6-Aneta Mandziuk
Independent Public Health Care Facility of the Ministry of Interior and Administration in Białystok/ Fabryczna Street 27 15-471 Białystok, Poland
aneta.mandziuk@o2.pl
https://orcid.org/0009-0001-2787-9479
7-Kinga Witowska
The 5 Military Clinical Hospital with Polyclinic SPZOZ in Cracow, Wroclawska Street 1/3, 30-901 Cracow, Poland
kingawitowska1@gmail.com
https://orcid.org/0009-0003-2389-4887
8-Mariola Turemka
Voivodeship Hospital in Bialystok/Marii Sklodowskiej-Curie 26, 15-278 Bialystok, Poland
mariolaturemka841@gmail.com
https://orcid.org/0009-0001-8219-6515
9-Mikolaj Biskupski
Department of Interventional Cardiology and Cardiac Arrythmias, Teaching Hospital No. 2 of the Medical University of Lodz, Zeromskiego Street 113, 90-549 Lodz
mikolajbiskupskimed@gmail.com
https://orcid.org/0009-0009-8103-4053
10-Karolina Sacher
Silesian Center for Heart Diseases, 41-800 Zabrze, Marii Skłodowskiej-Curie 9, Poland
karolina@saant.pl
https://orcid.org/0009-0001-8875-5912

Abstract

Introduction and purpose of this work

Calcium pyrophosphate disease (CPPD), also known as chondrocalcinosis or pseudogout is an arthropathy related to calcium pyrophosphate crystals' deposition in joints, cartilage, synovial and periarticular tissues, triggering an inflammatory response leading to local articular damage. CPPD mainly affects the large and weight-bearing joints- knees, hips and shoulders. The clinical manifest of CPPD can vary from asymptomatic to symptomatic, involving one or several joints with a possible acute or chronic course. In this extensive review paper, our aim is to outline the current evidence-based knowledge on epidemiology, origins, clinical manifest, diagnostical tools, new guidelines of the American College of Rheumatology (ACR) and the European Alliance of Associations for Rheumatology (EULAR) and current treatment options for CPPD,

Methods:

We performed a systematic electronic search on PubMed, Medline and Google Scholar databases, searching the following terms: "CPPD", "etiology of CPPD", "Epidemiology of CPPD" , " Diagnosis of CPPD" , "CPPD conventional treatment", "biological treatment of CPPD". The search results were limited to publications from 2002 to 2024, as well as key studies and reference books from earlier years, including original papers and randomized, double-blind, placebo-controlled studies.

Brief description of the state of knowledge

Deposition of calcium pyrophosphate (CPP) crystals in joints can lead to an inflammatory response and lead to joint damage. CPPD is the third most common reason of arthritis. Its origin is rather considered to be idiopathic, but there has been research showing the linkage of this disease to genetical background and some metabolic disorders. The treatment is chosen based on the phenotype of the disease, conventional pharmacological treatment includes

NSAIDs, colchicine and corticosteroids. New opportunities to CPPD treatment have appeared thanks to biological medications, blocking the inflammatory mediators and inhibiting the inflammatory process.

Summary
Early diagnosis of CPPD, distinguishing it from other forms of arthritis and identifying the possible co-occurring diseases such as gout, rheumatoid arthritis and osteoporosis can help the clinicians to apply the proper treatment without delay. Most patients suffering from CPPD seniors burdened with different comorbidities, this is why it is very important to choose the right treatment, which prevents exacerbation of the inflammatory process and ensures high quality of life for the patients.
Key words:
Calcium Pyrophosphate deposition disease, pharmacological treatment, biological medications, non-pharmacological treatment, criteria of CPPD diagnosis.

Aetiology and epidemiology:
A crystal deposition arthropathy of unknown origin- Calcium Pyrophosphate deposition disease -is a common aetiology of arthritis caused by the deposition of calcium pyrophosphate crystals in particular tissues, especially hyaline cartilage and fibrocartilage causing inflammation and joint damage. The crystals lead to activation of the immune system resulting in acute inflammatory response. [1]

It can clinically manifest in a wide range, from being asymptomatic to presenting as acute or chronic inflammatory arthritis. The inflammation commonly applies damage to larger, weight bearing joints, such as knees, hips and shoulders, but can also affect smaller joints- wrists and ankles. Though it is considered to be idiopathic, evidence suggests that there are associations between CPPD and genetical background- Some mutations, such as in ANKH were noted in familial forms of the disease and other metabolic disorders,[2][3] specifically primary hyperparathyroidism [4][5], hereditary hemochromatosis [6] or hypomagnesemia [7]. The population of patients affected by CPPD mostly consists of individuals [8] over 65 years of age, of whom 30–50% are over the age of 85 [9]. In this population of patients, the disease will commonly appear with a milder course[10].

Symptoms:
Symptoms can vary depending on the manifestation of the disease [11], the acute onset of the disease may be represented as monoarticular or oligoarticular arthritis. The vigorous inflammatory response to CPP crystals manifests as tangible temperature rise around the affected joint, erythema and swelling in and around the affected joint, which are signs of. CPPD can also lead to systemic symptoms such as fevers and chills. The length of the acute episode may vary from few weeks to few months [12]. It is worth mentioning that a large number of patients with an onset of CPPD had predispositions including osteoarthritis, trauma, surgery, or rheumatoid arthritis.

Diagnosis:
-Crystal analysis:
The gold standard in facilitating diagnosis of CPPD is synovial fluid aspiration and analysing the sample under polarizing light microscope (PLM). An analysis with the help of a PLM not only allows identifying the crystals' morphology, but also defines their birefringence [13]. The radiographic findings can be suggestive of chondrocalcinosis, but they are not diagnostic.

Therefore, synovial fluid analysis unambiguously confirms the diagnosis [14] [15]. The crystals are visible as slightly positive birefringent rhomboidal crystals, thin bars and parallelepipeds [16]. As much as this method seems to be straight at the point, there are some factors that need to be meticulously scrutinized in order to be able to detect the crystals, as in some cases they do not demonstrate birefringence , may be phagocytized and found inside vacuoles or be sparsely distributed, which obligates the analyst to allocate extra time for an accurate diagnosis, this is why the experience and dedication of the analyst plays a key role[17].

-Imaging diagnostics

In diagnosis of CPPD the urge for imaging techniques is inevitable. Each of the techniques can reveal CPP deposit in different stages of advancement. For instance, joint sonography can show early signs of cartilage alteration and in later stages can even detect joint's calcification in course of CPP deposition. Studies have shown that the findings from ultrasonographic examinations are highly reliable, providing more details, bilateral US assessment of knees, wrists and hips appeared to have excellent accuracy of >90% [18]and high feasibility [19]. additionally, ultrasound examination is a non-invasive, readily available bedside technique, which can bring the clinician valuable findings not only for diagnosing the disease, but also as a screening tool.

Chondrocalcinosis in course of CPPD can be seen as dense deposits of crystals outlining the contours of the articular cartilage in a radiograph. An X-ray graph can detect 40% of clinically important CPPD [20] In spite of this, a conventional radiograph can still be very helpful in excluding other differential diagnoses.

Computed tomography (CT) scanning despite of effectively identifying the crystals deposits, is not commonly used for CPPD diagnosing. On the other hand, MR imaging seems to be insensitive to even widespread presence of calcium pyrophosphate crystals in knee joint. [21]

As mentioned earlier, CPPD can represent symptoms variably, thus defining a fixed diagnostical criteria has been challenging. In the table below, the guidelines for diagnostic criteria of CPPD disease are represented. [Citation from the Primer on Rheumatic Diseases (1997)]

Criterion I	Demonstration of calcium pyrophosphate crystal deposition in tissue or synovial fluid by definitive means (eg, characteristic radiographs, diffraction analysis, or chemical analysis)
Criterion IIa	Identification of monoclinic or triclinic crystals showing no or weakly positive birefringence by compensated polarized light microscopy
Criterion IIb	Presence of typical radiographic calcifications
Criterion IIIa	Acute arthritis, especially of knees or other large joints
Criterion IIIb	Chronic arthritis, especially of knee, hip, wrist, carpus, elbow, shoulder, or metacarpophalangeal (MCP) joint, particularly if accompanied by acute exacerbation

Interpretation:

- Definite disease - Criterion I or IIa plus IIb must be fulfilled

- Probable disease - Criterion IIa or IIb must be fulfilled
- Possible disease - Criterion IIIa or IIIb should alert the clinician to the possibility of underlying calcium pyrophosphate deposition

The new guidelines of the American College of Rheumatology (ACR) and the European Alliance of Associations for Rheumatology (EULAR)- classification criteria for Calcium Pyrophosphate Deposition (CPPD) disease were released in 2023 [22]:

The CPPD classification criteria should be applied in the following order:		
1. Entry criterion: Ever had at least one episode of joint pain, swelling, or tenderness[+]		
2. Absolute exclusion criteria: All symptoms are more likely explained by an alternate condition (such as rheumatoid arthritis, gout, psoriatic arthritis, osteoarthritis, etc.)		
3. Sufficient criteria: 1. Crowned dens syndrome[*] or 2. Synovial fluid analysis demonstrating CPP crystals in a joint with swelling, tenderness or pain.[**]		
An individual is classified as CPPD if the entry criterion is met, exclusion criteria are not met, and at least one sufficient criterion is fulfilled. If none of the sufficient criteria are present, an individual is classified as CPPD disease if the sum of the criteria below is >56 points.		
Items can be scored if they were ever present during a patient's lifetime. If a patient fulfills >1 item in a given domain, only the highest weighted item will be scored. Imaging of at least one symptomatic joint by CR, US, CT, or DECT is required.		
Domains and levels		**Points**
A	Age at onset of joint symptoms (pain, swelling, and/or tenderness)	
	≤60 years	0
	>60 years	4
B	Time-course and symptoms of inflammatory arthritis	
	No persistent[1] or typical[2] inflammatory arthritis	0
	Persistent inflammatory arthritis[1]	9
	1 typical acute arthritis episode[2]	12
	More than 1 typical acute arthritis episode[2]	16
C	Sites of typical episode(s)[2] of inflammatory arthritis in peripheral joints	
	1st MTPJ	-6
	No typical episode(s)	0
	Joint(s) other than wrist, knee or 1st MTPJ	5
	Wrist	8
	Knee	9
D	Related metabolic diseases[3]	
	None	0
	Present	6
E	Synovial fluid crystal analysis[4] from a symptomatic joint	
	CPP crystals absent on ≥2 occasions	-7
	CPP crystals absent on 1 occasion	-1
	Not performed	0
F	OA of hand/wrist on imaging (defined as present if the Kellgren	

	and Lawrence score is ≥ 2)	
	None of the following findings or no wrist/hand imaging performed	0
	Bilateral radio-carpal joints	2
	≥2 of the following: STTJ OA without 1st CMCJ OA; 2nd MCPJ OA; 3rd MCPJ OA	7
G	Imaging evidence of CPPD in symptomatic peripheral joint(s)[5]	
	None on US, CT, or DECT (and absent on CR or CR not performed)	-4
	None on CR (and US, CT, DECT not performed)	0
	Present on either CR, US, CT, or DECT	16
H	Number of peripheral joints with evidence of CPPD on any imaging modality[5] regardless of symptoms	
	None	0
	1	16
	2-3	23
	≥4	25

[+]In a peripheral joint or axial joint such as C1/C2 in the case of crowned dens syndrome
[*]Crowned dens syndrome is defined by the following (A) clinical and (B) imaging features. Both (A) and (B) must be present.
(A) Clinical features: Acute or sub-acute onset of severe pain localized to the upper neck with elevated inflammatory markers, limited rotation, and often fever. Mimicking conditions such as polymyalgia rheumatica and meningitis should be excluded.
(B) Imaging features: Conventional CT with calcific deposits, typically linear and less dense than cortical bone, in the transverse retro-odontoid ligament (transverse ligament of the atlas), often with an appearance of two parallel lines in axial views. Calcifications at the atlanto-axial joint, alar ligament, and/or in pannus adjacent to the tip of the dens are also characteristic. DECT features include a dual-energy index (DEI) between 0.016-0.036 [23]

[**]Sufficient criteria are also met if CPP crystals are demonstrated in histopathology of joint tissue, provided the patient is eligible for classification i.e. does not already meet the exclusion criteria. For instance, articular cartilage CPPD in patients with end-stage osteoarthritis cannot be used to classify the patient as CPPD disease when all symptoms are better explained by osteoarthritis (exclusion criteria)
[1]Persistent inflammatory arthritis was defined as ongoing joint swelling with pain and/or warmth in ≥1 joint(s).
[2]Typical episode was defined as an episode with acute onset or acute worsening of joint pain with swelling and/or warmth that resolves irrespective of treatment.
[3]Hereditary hemochromatosis, primary hyperparathyroidism, hypomagnesemia, Gitelman syndrome, hypophosphatasia, or familial history of CPPD disease.
[4]Synovial fluid analysis should be performed by an individual trained in the use of compensated polarized light microscopy for crystal identification.
[5]Imaging of at least one symptomatic peripheral joint by CR, US, CT, or DECT is required to be considered for classification if sufficient criteria are not met. Imaging evidence of CPPD refers to calcification of the fibrocartilage or hyaline cartilage. Do not score calcification of the synovial membrane, joint capsule, or tendon. Imaging definitions are published elsewhere [24]. Only consider involvement of peripheral joints.

Abbreviations: MTPJ metatarsophalangeal joint; CPP calcium pyrophosphate; STTJ scaphotrapeziotrapezoid joint; CMCJ carpometacarpal joint; OA, osteoarthritis; MCPJ metacarpophalangeal joint. US ultrasound; CT computed tomography; DECT dual-energy computed tomography; CR conventional radiography

Treatments:

-Overall view:

There are different therapeutic approaches in CPPD treatment. The treatment of CPPD is symptomatic. The chosen treatment pathway depends on the clinical manifestation of the disease, whether it has a an acute or a chronic course. Nevertheless, some of the therapeutic resources of treating the acute and chronic course of CPPD overlap. Both group of patients suffering from an acute or a chronic course of the disease can benefit from NSAIDs, corticosteroids and colchicine (only with a difference of lower dosage administration for chronic CPPD) [25]. Patients with chronic CPPD who are unresponsive to the NSAIDs and glucocorticoids, treatment course can be taken to the second line, using methotrexate and hydroxychloroquine. Asymptomatic patients do not require any treatment [26]. In cases of concomitance with osteoarthritis, the treatment is identical to that for OA without CPPD.

On an acute attack of CPPD, patients can additionally benefit from parenteral glucocorticoids and ACTH. For these patients , non-pharmacological methods assume greater importance**.** Rest and applying ice packs, along with joint aspiration can bring pressure relief around the affected joint. The joint aspiration not only supplies diagnostic utility and reduces the pressure on the distended joint capsules, but also can be performed alongside with administrating an intra-articular injection of long-acting glucocorticoids. [27]

Nutriment's effect on relieving the inflammatory symptoms of CPPD has yet to be investigated in future research, since there are insufficient number of research carried out. For today's state of knowledge, polyphenols, particularly epigallocatechin-3-gallate (EGCG) contained in green tea may eventually be useful due to their anti-inflammatory effects in vitro. [28]

-Curcumin's effect on specifically CPPD has not been investigated, however its safety and positive effect on improving the severity of the symptoms in patients with arthritis, including Ankylosing Spondylitis (AS), Rheumatoid Arthritis (RA), Osteoarthritis (OA), Juvenile idiopathic arthritis (JIA) and gout/hyperuricemia has been approved in several recent - randomized controlled trials. [29]

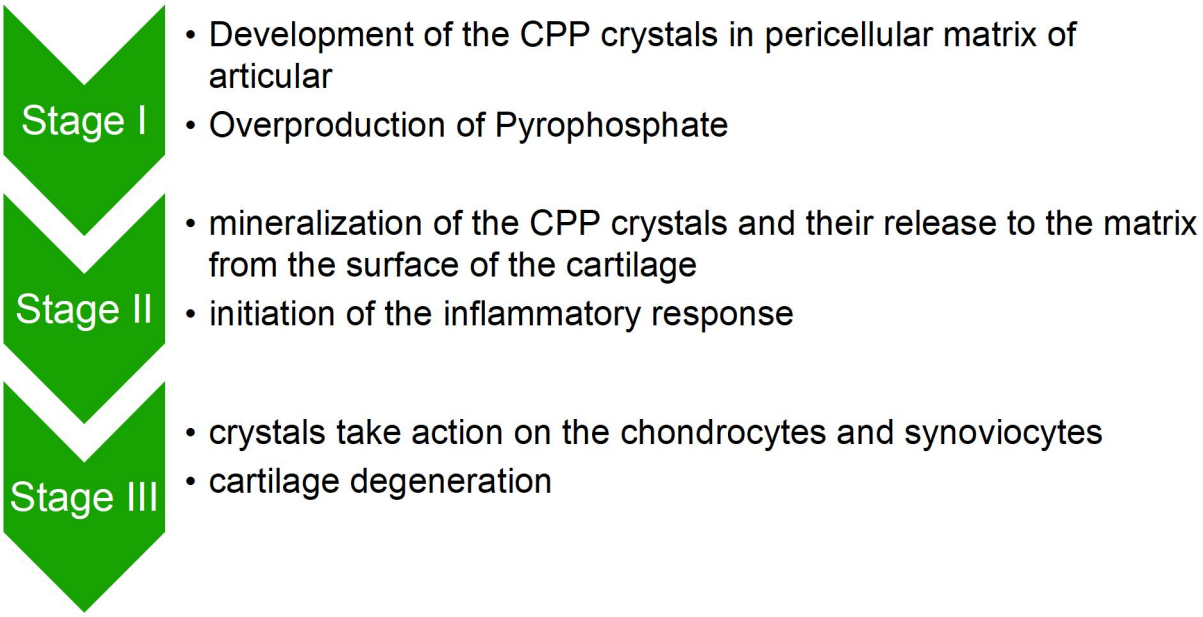
-Radiosynovectomy [30] is another therapeutic option, which can safely be repeatedly performed in patients suffering from acute or chronic Crystalopathy-related inflammatory joint effusion. This method as presented the best outcomes for hemophilia patients [31]. Among CPPD patients, those who have at least once been unresponsive to the standard administration of intraarticular long-acting steroids[32]. The procedure consists in the intraarticular administration of a radioisotope in the form of a radiocolloid into the affected joint's cavity under ultrasound guidance. The Beta-emission of the radioisotope leads to fibrosis and extinguishing the inflammatory process. The effectiveness of the procedure can later be monitored through US examination or MRI, findings such as thickened synovium, lack of evidence on increased vascularity, interarticular adipose tissue edema and strands of fibrosis in the joint cavity are signs of improvement.

-Surgical approach:

Theoretically surgical removal of the calcium pyrophosphate crystals is viable and effective, though there are very few case reports and research done in this regard. The available case reports which have hitherto been published are in concern of endoscopic surgery for CPPD in the cervical ligamentum flavum which is a very rare clinical condition. they show a satisfying clinical and radiologic outcome, proving the successful removal of the CPP. [33][34] [35]

Pharmacological treatment approach:

For a better understanding of the pharmacological approach to CPPD treatment, we will be explaining each of the pharmacological strategies based on the pathophysiological phases of the disease.



It is worth mentioning that currently the usage of anty-crystal agents such as Probenecid, even though not very popular yet, seems to be promising and should be a target of further research and studies. Probenecid is an anion transport inhibitor which impedes the export of excess extracellular inorganic pyrophosphate (ePPi) to the matrix where crystals form. [36]

<table>
<tr><td colspan="3">CPPD</td></tr>
<tr><td>ACUTE</td><td colspan="2">CHRONIC</td></tr>
<tr><td rowspan="2">-INTRA-ARTICULAR/ p.o CORTICOSTEROIDS.
-NSAIDs
-COLCHICINE p.o (0.5 mg up to maximum 3–4 times daily))
- 1L-1Beta inhibitor</td><td>INFALAMMATORY</td><td>NON-INFLAMMATORY</td></tr>
<tr><td>-NSAIDs
-SYSTEMIC CORTICOSTEROIDS
-COLCHICINE (0.5–1.0 mg daily)
-METHOTREXATE</td><td>(treatment similar to osteoarthritis *)
-INTRA-ARTICULAR CORTICOSTROIDS</td></tr>
</table>

(ANAKINARA) -REST AND ICE PACK APPLICATION	-1L-1Beta inhibitor -PHYSIOTHERAPY -JOINT REPLACEMENT	

Acute treatment:

-NSAIDs / Colchicine :

NSAIDs and Colchicine which are both reached out in first line of treatment with the aim of rapid pain relief, have different mechanism of action but bringing a similar result [38] Colchicine inhibits the microtubules and disrupts the impairing of the immune cell, chemotaxis and as a result disturbs the inflammation driven by the NLRP3 inflammasome [39]. It hasn't been yet well studied in treating CPPD patients, the thus far research has shown that colchicine shows equivalent efficacy in comparison to prednisone, only with a higher safety profile in elderly patients [37].

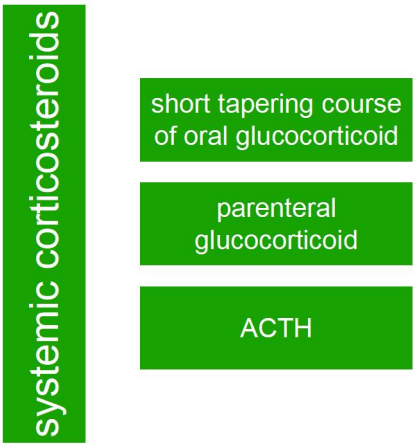
NSAIDs on the other hand inhibit the cyclo-oxygenase enzyme and therefore the conversion of arachidonic acid into prostaglandins and prostacyclins. It is necessary to add up gastroprotection alongside to NSAIDs.

-**hyaluronan injections**: are contraindicated in CPPD, due to their associations with inducing acute crystal arthritis.

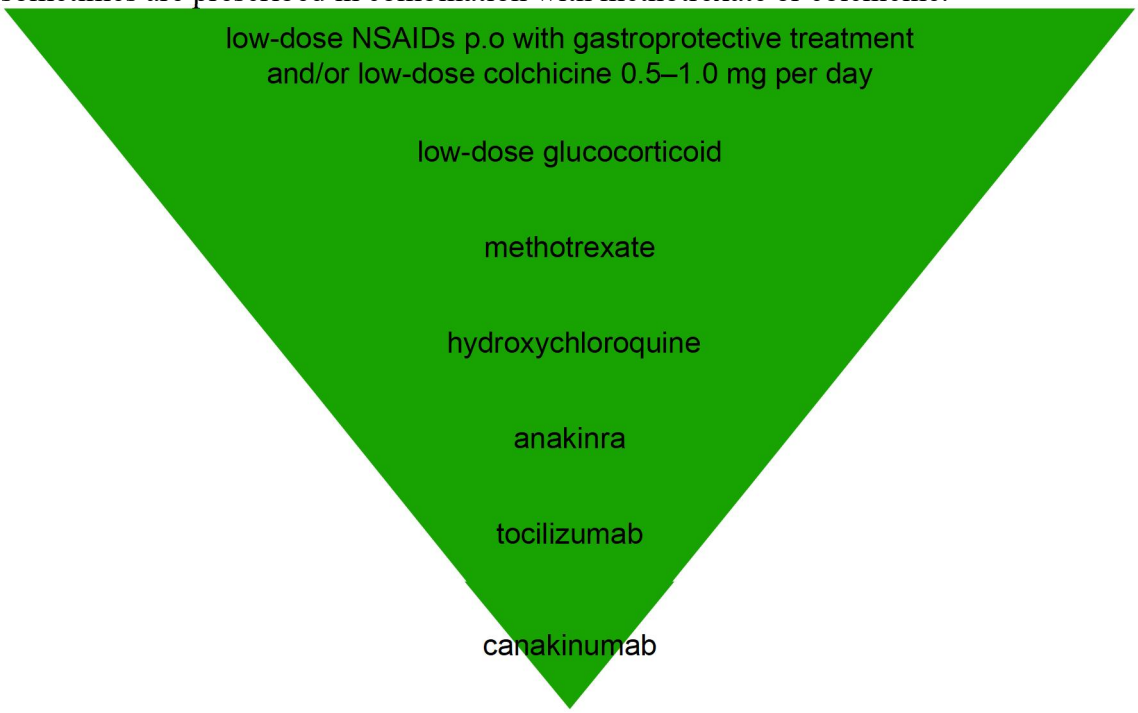
-Corticosteroids and ACTH:

Due to wide range of NSAIDs side effects and contraindications and also in patients who didn't get a satisfying therapeutic result from intra-articular glucocorticoids injections, systemic glucocorticoids become an essential option. Earlier research has shown that corticosteroids can also successively bring rapid relief from the symptoms [40]. Despite their efficacy, because of the wide spectrum of the side effect, they are not preferred, and their usage is limited.

ACTH is another alternative in case of contraindications to NSAIDs. Its high effectiveness (response rate 77.9% to 100%) and low risk of a few side effects, which were all mild symptoms in case of occurring, makes it an eligible candidate for the first-line therapy in patients with acute crystal-induced arthritis [41][42]. ACTH seems to not only stimulate the endogenic steroid release from the adrenal glands, but also stimulates melanocortin receptors on macrophages and with through this mechanism downregulates the inflammation.



Chronic treatment:
The treatment strategies which overlap between the acute and chronic course of the CPPD have already been discussed earlier in this paper. In this section we will discuss the therapeutic options specific for the chronic CPPD. In the diagram below, we listed the treatment options, including the off-label biological medications in descending order of frequency. As visible in the diagram, the treatment options are heterogeneous, and each of the lower-placed medications can be added to the previously used one if the therapeutic results were not satisfactory. As an example, anakinra and tocilizumab are second or third line and sometimes are prescribed in combination with methotrexate or colchicine.



-Methotrexate
Having an anti-inflammatory and immunosuppressive profile of efficacy, Methotrexate [43] is a valuable therapeutic option especially for patients who suffer from polyarticular CPPD with recurrent acute attacks and resistant to the classic NSAIDs and corticosteroids' treatment.

The carried-on research through years had shown contraventions on MTX efficacy. One of the experiments which did not approve the efficacy of MTX was a double-blind, crossover randomized controlled trial [44] executed in 2014. The authors brought in 2 different population of patients into one group in this experiment and tested the Methotrexate's therapeutic benefits on them. Some of the patients included presented recurrent (more than three in a 6-month period) episodes of acute arthritis separated by asymptomatic periods, and the others suffering from persistent, polyarthritis-like inflammatory disease, all from the older population of the patients (75+ year olds). These 2 groups of patients show 2 different profiles of CPPD, therefore comparing the effect of methotrexate on them might not be reliable. Additionally due to the impropriety of their evaluation technique in selecting the patients into the study and the low statistical power of the whole study, the results of this study should not be taken as a definitive result of MTX's impracticality. Other studies affirmed therapeutic effectiveness of Methotrexate, but at the same time encouraged researchers to put it under more studies and experiments. Summing up, low-dose MTX (5-20 mg/week) significantly

reduced the amount of pain, swelling of joints and the serum levels of inflammatory biomarkers. [45]

Noted side effects registered in these studies were hematologic abnormalities due to morrow-suppressive effect of Methotrexate, elevated liver enzymes, nausea, transient lymphopenia and pancytopenia.

Hydroxychloroquine

Hydroxychloroquine initially known as an antimalarial medication, is also widely used for its immunomodulatory and anti-inflammatory properties in rheumatic and autoimmune diseases. Hydroxychloroquine has a different mechanism of action in comparison to the other conventional medications used in rheumatic arthropathies, for this reason, it is considered to be a great complement for the other compounds in combination pharmacotherapy of CPPD. It increases the pH level of the intracellular, since the acidic environment is necessary for digesting the antigenic protein and for the resulted peptides to assemble with the alpha and beta chains of the MHC II proteins, it results in diminishing the formation of peptide-MHC protein complex which is required for CD4+ T cells' stimulation and this eventually leads to the down-regulation of the immune response[46].

Different studies through years have shown both clinical improvement and well tolerance in patients taking hydroxychloroquine[47]. It is proved to be a well-tolerated element in combined treatment of arthritis, increasing the effectiveness of other therapeutic components, such as methotrexate [48]. In this study, the patients who responded well to hydroxychloroquine were administrated a dosage of 100 to 400 mg/day for 6 months. The higher the dose of hydroxychloroquine was, the larger the number of patients responded to the treatment. In other words, 60% of the patients taking 100mg/day of hydroxychloroquine responded with lower objective symptoms such as swelling and tenderness of the affected joints after the first month, while 100% of the patients responded to the treatment after 6 months of 400mg/day administration of the medication.[49]

Biologics in CPPD treatment:

Thanks to experiments carried out in previous years, it is known that the CPP crystals not only induce IL-1β expression by macrophages and monocytes, but also strongly induce IL-6 expression [50][51]. Knowledge of this fact opened new pathways in treating CPPD and rationalized the usage of IL-1β and IL-6 blockade. In this section, the biological treatment which makes this blockade possible, is reviewed.

-Anakinra:

It's the recombinant form of human interleukin-1 (IL-1) receptor antagonist widely used in rheumatoid arthritis, gout and CPPD. Arthropathies related with crystal deposition involve production and activation of IL-1β. Anakinra competitively inhibits the inflammatory effect of interleukin-1β. Several studies have shown that not only it has a fruitful effect on extinguishing the local inflammation, but also it is highly safe and well tolerated brings rapid improvement of symptoms [52][53] The main side effect due to the method of administration of anakinra which is daily (due to anakinra's short half-life) injection, is skin reactions at the injection site [54]. The safety profile of Anakinra in monotherapy for patients with end-stage renal disease on Haemodialysis has been studied in a recent case study from 2024[55]. This case report has presented the case of two patients both with refractory CPPD and end-stage renal disease. Both patients were struggling with deterioration of renal function and CPPD relapse while taking the conventional treatment (Colchicine and corticosteroids). On the course of this study both corticosteroids and colchicine were completely withdrawn and

anakinra was administrated for a period of 6 months, both patients sustained remission on anakinra treatment, and no side effects were reported by the patients.

-Tocilizumab

A monoclonal antibody which competitively inhibits the binding between IL-6 and its receptor, which consequently disturbs signal transduction to inflammatory mediators and prevents the summoning of B and T cells. Following this mechanism of action, patients with CPPD and RA can benefit from a significant improvement [56]

In cases which anakinra wasn't effective, Tocilizumab turned out to be successful in controlling and improving the symptoms [57]. In this pilot study with 11 patients who were recruited to the study with confirmed primitive CPPD – radiographic findings had proved chondrocalcinosis in multiple joints, one patient with approved diagnosis of synovial fluid by polarised light microscopy, seven patients with an idiopathic CPPD, one patient with ANKH mutation and three patients with CPPD due to Gitelman's disease. Age median of studied patients was 64, all had a history of failure, intolerance, contraindications or unsatisfying results of improving the symptoms and treating CPPD using NSAIDs, colchicine and anakinra, left with a daily dose of prednisone. This research included both weekly subcutaneous and monthly intravenous infusions of tocilizumab. The follow up revealed decrease in disease activity which helped them taper their treatment or eventually stop taking prednisone.

-Canakinumab:

Very few research so far has targeted the usage of Canakinumab and its possible benefits on specifically CPPD, in one of the reviewed papers which had studied the use of canakinumab in gout's treatment, revealed clinical improvement in one of the patients who was mainly being treated due to gouty arthritis, but additionally had synovial fluid examination was positive for CPPD crystals [58].

Conclusion:

As the third most common arthropathy, CPPD needs to be taken into consideration when it comes to differential diagnosis of joint inflammation, particularly in elderly patients. Diagnosis of the disease includes a comprehensive approach, including the clinical symptoms, detailed medical history- different metabolic deficits, burdened family history and associated comorbidities can be decisive in constructing the proper diagnosis, imaging techniques and ultimately the golden standard for facilitating diagnosis: synovial fluid analysis under PLM.

The treatment is chosen based on the phenotype and course of the disease. Both pharmacological and non-pharmacological treatments can be fruitful. Further research on biological medications can bring new insights to treating CPPD.

Authors' Contribution

Authors' Contributions Statement:

Conceptualization: Krystyna Zabojska, Aleksandra Cygnarowicz, Aneta Klaudia Wojtas, Urszula Korotko, Aneta Mandziuk, Kinga Witowska, Mariola Turemka, Mikolaj Biskupski, Negar Hosseinnejad, Karolina Sacher

Data Curation: Krystyna Zabojska, Aleksandra Cygnarowicz, Aneta Klaudia Wojtas, Urszula Korotko, Aneta Mandziuk, Kinga Witowska, Mariola Turemka, Mikolaj Biskupski, Negar Hosseinnejad, Karolina Sacher

FormalAnalysis: Krystyna Zabojska, Aleksandra Cygnarowicz, Aneta Klaudia Wojtas, Urszula Korotko, Aneta Mandziuk, Kinga Witowska, Mariola Turemka, Mikolaj Biskupski, Negar Hosseinnejad, Karolina Sacher

Investigation: Krystyna Zabojska, Aleksandra Cygnarowicz, Aneta Klaudia Wojtas, Urszula Korotko, Aneta Mandziuk, Kinga Witowska, Mariola Turemka, Mikolaj Biskupski, Negar Hosseinnejad, Karolina Sacher

Methodology: Krystyna Zabojska, Aleksandra Cygnarowicz, Aneta Klaudia Wojtas, Urszula Korotko, Aneta Mandziuk, Kinga Witowska, Mariola Turemka, Mikolaj Biskupski

Project Administration: Krystyna Zabojska, Aleksandra Cygnarowicz, Aneta Klaudia Wojtas, Urszula Korotko, Aneta Mandziuk, Kinga Witowska, Mariola Turemka, Mikolaj Biskupski, Negar Hosseinnejad,

Resources: Krystyna Zabojska, Aleksandra Cygnarowicz, Aneta Klaudia Wojtas, Urszula Korotko, Aneta Mandziuk, Kinga Witowska, Mariola Turemka, Mikolaj Biskupski, Karolina Sacher

Software: Krystyna Zabojska, Aleksandra Cygnarowicz, Aneta Klaudia Wojtas, Urszula Korotko, Aneta Mandziuk, Kinga Witowska, Mikolaj Biskupski, Negar Hosseinnejad, Karolina Sacher

Supervision: Krystyna Zabojska, Aleksandra Cygnarowicz, Aneta Klaudia Wojtas, Urszula Korotko, Aneta Mandziuk, Mariola Turemka, Mikolaj Biskupski, Negar Hosseinnejad, Karolina Sacher

Validation: Krystyna Zabojska, Aleksandra Cygnarowicz, Aneta Klaudia Wojtas, Urszula Korotko, Kinga Witowska, Mariola Turemka, Negar Hosseinnejad, Karolina Sacher

Visualization: Krystyna Zabojska, Aleksandra Cygnarowicz, Aneta Klaudia Wojtas, Aneta Mandziuk, Kinga Witowska, Mariola Turemka, Mikolaj Biskupski, Negar Hosseinnejad, Karolina Sacher

Writing–Original Draft: Krystyna Zabojska, Aleksandra Cygnarowicz, Urszula Korotko, Aneta Mandziuk, Mariola Turemka, Mikolaj Biskupski, Negar Hosseinnejad, Karolina Sacher

Writing– Review & Editing: Krystyna Zabojska, Aneta Klaudia Wojtas, Urszula Korotko, Aneta Mandziuk, Kinga Witowska, Mariola Turemka, Mikolaj Biskupski, Negar Hosseinnejad, Karolina Sacher

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