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Effectiveness and safety of canakinumab in cryopyrin-associated periodic syndrome: a retrospective study in China

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Abstract

Objective Cryopyrin-associated periodic syndrome (CAPS) is characterized by excessive IL-1β release resulting in systemic and organ inflammation. As an anti-IL-1 agent, canakinumab has been approved with all CAPS phenotypes in USA and European countries. However, the use of canakinumab in CAPS in Chinese patients was rarely reported. In this study, we aimed to assess the effectiveness and safety of canakinumab in Chinese patients with CAPS.

Methods Patients with CAPS treated with canakinumab were included. Clinical data were collected retrospectively from medical records. Treatment response was evaluated by CAPS disease activity score, C-reactive protein (CRP), and/or serum amyloid A (SAA) levels. Data was analyzed at canakinumab initiation, at months 1, 3, 6, 9, and 12, or the last follow-up.

Results A total of 10 CAPS patients were included. 40% of patients were males, the median age at disease onset was 2.5 (2.5, 6) days and the median duration of follow-up while on canakinumab was 22.5 (8.5, 27.5) months. 80% (8/10) of CAPS patients presented with moderate-severe disease activity before the canakinumab treatment. 30% (3/10) of patients required canakinumab dose increase to control disease activity. After treatments, 60% (6/10) of CAPS patients achieved complete remission without relapse and the rest showed minimal disease activity. Clinical symptoms such as fever and rash were improved significantly in most patients (80%). Although abnormal imaging in brain MRI remained in over half of those patients, neurological manifestations were all relieved. 60% (6/10) of patients received prednisone before starting canakinumab therapy and five of them discontinued prednisone later. The most common adverse event was infection (40%). No serious adverse events occurred during the treatment of canakinumab.

Conclusions Canakinumab may be effective and tolerable for Chinese CAPS patients, helping to reduce the dosage of corticosteroids. However, additional trials on large samples are required to further evaluate its efficacy and safety in China.

Keywords Canakinumab, Cryopyrin-associated periodic syndrome, Interleukin-1, Auto-inflammatory diseases, NLRP3

Introduction

Cryopyrin-associated periodic syndrome (CAPS) is a rare autosomal dominant auto-inflammatory disease caused by gain-of-function mutations in nucleotide-binding oligomerization domain (NOD)-like receptor family, pyrin domain- containing 3 (NLRP3) gene, resulting in constitutive activation of the inflammasome and

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increased IL-1β secretion. The prevalence of CAPS in France was reported approximately 1/360 000 [1]. So far, neither large samples study of CAPS nor treatment strategies in CAPS have been stated in China. CAPS includes a group of 3 overlapping disorders, ranging in severity: familial cold auto-inflammatory syndrome (FCAS; mild phenotype); Muckle-Wells syndrome (MWS; moderate phenotype), and chronic infantile neurological cutaneous articular syndrome (CINCA; severe phenotype). CAPS usually manifests with fever, urticarial rash, conjunctivitis, arthritis and elevated acute-phase reactants [2]. Patients also develop central nervous system disease as well as impairment of hearing and vision, primarily occurring in the moderate to severe CAPS phenotypes.

Most CAPS disease-associated mutations are located in exon 3, which codes for the central triple-ATPase domain called NACHT, responsible for nucleotide oligomerization, and there are a few mutations in C terminal exons that code for the Leucine-rich repeat (LRR) domain [3]. NLRP3 nucleates an intracellular multi-molecular complex called the NLRP3 inflammasome and this complex enables the activation of proinflammatory protease caspase-1. Caspase-1 can cleave pro-interleukin (IL)-1β and pro-IL-18 in their biologically active forms (IL-1β, IL-18) [4]. The gain-of-function mutations in NLPR3 lead to overproduction of IL-1β and subsequent systemic inflammation.

Canakinumab is a fully human monoclonal antibody that selectively binds to IL-1β and prevents IL-1β-induced inflammatory mediator production. Canakinumab has been approved in Europe and the United States for all CAPS children to control disease activity and decrease organ damage [5]. However, we found limited information about canakinumab therapy in Chinese CAPS patients. In this study, we described the cohort of Chinese patients with CAPS receiving canakinumab to evaluate its efficacy and potential adverse effects.

Methods

Patient cohort and study approval

A retrospective analysis was performed in 10 patients who suffered from CAPS receiving treatment with canakinumab from March 2021 to February 2024 in Shenzhen Children's Hospital. The diagnosis of CAPS in this study was based on the 2021 EULAR/ACR criteria [5]. Data of age, gender, treatments, disease course, adverse effects, clinical manifestations, and laboratory findings were extracted from the medical electronic database at canakinumab initiation, at 1, 3, 6, 9, and 12 months, or the last follow-up. Laboratory tests included peripheral white blood count (WBC), liver and kidney function tests, serum CRP and SAA levels. Other therapies were all stopped (apart from corticosteroids) before initiation of canakinumab. The study was approved by the ethics committee of Shenzhen Children's Hospital. The legal guardians of all patients had signed the informed consent for the study and treatment with canakinumab.

Disease activity score and response to canakinumab

Effectiveness assessments included patient-reported auto-inflammatory diseases activity index (AIDAI), global assessment scales for physicians and patients/parents (PGA, PPGA), and inflammatory markers. Inflammatory markers included SAA and CRP. The AIDAI score captured disease activity over time including patient-reported frequency and severity of inflammatory clinical symptoms [6, 7]. Patients were asked to complete a 1-month prospective diary before their scheduled clinical appointment. Physicians and patients/parents performed a global assessment with the following symptoms: rash, arthralgia, myalgia, headache or migraine, conjunctivitis, fatigue or malaise, and other symptoms related or unrelated to CAPS. Global assessment was performed with the use of a 5-point scale for disease activity: absent, minimal, mild, moderate, or severe [8].

Complete remission was defined as absence of clinical symptoms (AIDAI score <9), PGA and PPGA of 0/10, and normal inflammatory markers (CRP ≤ 0.5 mg/L and/or SAA ≤ 10 mg/L). Minimal disease activity was defined as AIDAI score ≥ 9, PGA and PPGA $\leq 2/10$, and inflammatory markers $\leq 3\times$upper limit of normal (ULN). Moderate-severe disease activity was defined as AIDAI score ≥ 9, PGA and PPGA $>2/10$, and inflammatory markers $>3\times$ULN [6]. Disease flare was defined as PGA $>2/10$, or CRP level of >30mg/L.

Statistical analysis

Statistical analysis was performed using GraphPad Prism software (version 8.0.1, GraphPad Inc.). Continuous variables were expressed as medians with interquartile ranges (IQR, Q3-Q1), and categorical variables were presented as percentages. The comparative analysis utilized parametrical and non-parametrical tests as appropriate. A value of $p<0.05$ was considered statistically significant.

Results

Patient demographics and baseline characteristics

Ten patients from nine families were enrolled (6 with CINCA, 3 with MWS, and 1 with FCAS), including 4 male and 6 female patients (Table 1). The median age at onset was 2.5 (2.5,6) days and the median age at diagnosis was 9.5 (3.5, 98) months. Patients 1 and 4 were sisters from one family (Table 2). Their father presented with CINCA and developed renal amyloidosis.

Table 1 Demographics and clinical characteristics of patients

Characteristics, median (IQR, Q1,Q3), unless specified	Total ($n=10$)
Male, n (%)	4 (40)
Disease onset age (days)	2.5 (2.5, 6)
Age at diagnosis (months)	9.5 (3.5, 98)
Symptoms, n (%)	
Fever	10 (100)
Facial features	1 (10)
Erythema/urticarial rash	10 (100)
Neurologic involvement	5 (50)
Seizure	0
Number of patients in whom CSF analysis was performed	6 (60)
Sterile meningitis	5 (50)
Abnormalities in brain imaging	3 (30)
Hearing impairment	4 (40)
Ophthalmologic involvement	4 (40)
Optic neuritis	2 (20)
Papilledema	2 (20)
Conjunctivitis	3 (30)
Keratitis	0
Iritis	0
Musculoskeletal involvement	5 (50)
Arthralgia	2 (20)
Myalgia	1 (10)
Arthritis	2 (20)
Short Stature (< -2SD)	4 (40)
CAPS phenotype, n (%)	
FCAS	1(10)
MWS	3 (30)
CINCA	6 (60)
Age at initiation of canakinumab treatment (months)	25.5 (14.75, 127.5)
Duration of treatment (months)	22.5 (8.5, 27.5)
Number of patients taking steroid	
Before starting canakinumab treatment, n (%)	6 (60)
After starting canakinumab treatment, n (%)	1 (10)
Treatments before canakinumab	
Tocilizumab	3 (30)
TNF inhibitor	1 (10)
MTX	3 (30)
Dosing of canakinumab at start of treatment (mg/kg)	4 (4, 7)
Maximum dosing of canakinumab during the treatment course (mg/kg)	5 (4, 8)
Dosing of canakinumab at last follow up (mg/kg)	5 (4, 8)

CSF cerebrospinal fluid, *CAPS* Cryopyrin-associated periodic syndrome, *FCAS* familial cold autoinflammatory syndrome, *MWS* Muckle-Wells syndrome, *CINCA* chronic infantile neurological cutaneous articular syndrome, *TNF* tumor necrosis factor, *MTX* methotrexate

All patients exhibited systemic inflammation, fever, and urticaria-like rash (Figs. 1, 2A, and 4). Patient 7 had special facial features with frontal bossing and a large cephalic perimeter. Among the 10 patients, 50% (5/10) had neurological involvement, presenting with sterile meningitis (elevated white cells but cultures were negative in cerebrospinal fluid) (50%), hydrocephalus (20%), headache (20%), ventriculomegaly (30%) and abnormalities in thalamus (10%) (Fig. 1F, G). 50% (5/10) had musculoskeletal involvement, and 20% (2/10) were severe (Fig. 1D, I). 40% (4/10) had ocular disease, presenting with optic neuritis (20%) (Fig. 1H) and papilledema (20%). 40% (4/10) had auditory disease, suffering from mild hearing loss (decreased auditory threshold). 40% (4/10) patients showed developmental delay, all presenting with low body weight or short stature, but without intellectual disability (Table 3).

Before canakinumab treatment, most patients (60%, 6/10) received oral corticosteroids, tocilizumab and methotrexate were given to 30% (3/10) of patients, 10% received TNF inhibitor (Table 1).

Efficacy of canakinumab in CAPS

The median duration of follow-up while on canakinumab treatment was 22.5 (8.5,27.5) months. The median initial dosage of canakinumab was 4 (4,7) mg/kg and the median dosage of canakinumab used at the last follow-up time for maintenance was 5 (4,8) mg/kg (Table 2, Fig. 2C). 30% (3/10) of patients required canakinumab dose increase during the period of canakinumab treatment and all of them were patients with CINCA. Patient 5 occurred intermittent fever and elevated levels of CRP when disease flare. The dosage of canakinumab was gradually increased (finally 8mg/kg given at 4-week intervals), he still suffered occasional fever until now. Patient 7 had severe joint abnormalities before treatment and occurred occasional fever after 3 doses of canakinumab in 4mg/kg, then we increased canakinumab dosage to 6mg/kg at the fourth time. Patient 8 used lower dosage of canakinumab firstly because he was the youngest one. No additional infection was observed, and he still suffered slightly elevated levels of CRP at 1 month follow up, then we adjusted the dosage of canakinumab to 4mg/kg. Patients with CINCA required higher dosage of canakinumab (7 (4.5,8) mg/kg) than those with other phenotypes (4 (4,5) mg/kg) for maintain minimal disease activity or remission. The median interval of canakinumab usage was every 8 (5,8) weeks.

Before canakinumab treatment, all patients in our cohort presented with moderate-to-severe disease activity (Fig. 2B). Overall, complete remission was observed in 60% (6/10) of CAPS patients at the last follow-up (Table 2, Fig. 2B), all of them had no disease flare, patient 10 even extended the interval of canakinumab to maintain remission. Clinical symptoms such as fever and rash (80%) were improved significantly in most patients (Figs. 1, and 2A). Patient 6 and 10 with optic neuritis

Table 2 Treatment with canakinumab in CAPS patients

Patients	Phenotype	NLRP3 gene mutation	Concomitant treatments	Canakinumab dosing	Canakinumab duration (months)	Canakinumab at last follow-up	Disease activity at last follow-up	Concomitant treatments at last follow-up	Remaining symptoms	Remaining abnormal laboratory findings	Infectious adverse events	Other non-infections Adverse events			
												skin and subcutaneous tissue disorders	gastrointestinal disorders	blood and lymphatic system disorders	liver enzyme elevations
1	FCAS	T348M	No	4 mg/kg q8w	3	ongoing	Remission	No	No	No	No	No	No	No	No
2	MWS	Y443H	prednison (0.47 mg/kg.d)	9 mg/kg q4w→8 mg/kg q4w	12	ongoing	Minimal	No	Occasional rash	No	No	dry skin	diarrhea	No	No
3	MWS	D305N	No	4 mg/kg q8w	27	ongoing	Minimal	No	No	CRP↑ESR↑	No	No	No	No	No
4	MWS	T348M	No	4 mg/kg q8w	3	ongoing	Remission	No	No	No	No	No	No	No	No
5	CINCA	L266P	prednison (1.18 mg/kg.d)	2 mg/kg q4w→8 mg/kg q4w	38	ongoing	Minimal	prednison (0.14 mg/kg.d)	Occasional rash and fever	CRP↑	viral upper respir-tory tract infectiom	No	diarrhea	No	No
6	CINCA	I336V	prednison (0.42 mg/kg.d)	8 mg/kg q4w	11	ongoing	Minimal	No	Occasional fever	No	No	No	No	No	No
7	CINCA	K570N	prednison (0.48 mg/kg.d)	4 mg/kg q8w→6 mg/kg q8w	27	ongoing	Remission	No	No	No	gastro-enteritis, bronchitis	rash	No	thrombo-penia	No
8	CINCA	C631F	prednison (0.51 mg/kg.d)	8 mg/kg q8w	18	ongoing	Remission	No	No	No	viral upper respir-tory tract infectiom	No	No	No	No
9	CINCA	I482F	prednison (0.71 mg/kg.d)	2 mg/kg q8w→4 mg/kg q8w	29	ongoing	Remission	No	No	No	bronchitis	rash	No	No	No
10	CINCA	V404L	No	4 mg/kg q4w→4 mg/kg q8w	29	ongoing	Remission	No	No	No	No	No	No	No	No

FCAS familial cold autoinflammatory syndrome, *MWS* Muckle-Wells syndrome, *CINCA* chronic infantile neurological cutaneous articular syndrome, *CRP* C-reactive protein, *ESR* erythrocyte sedimentation rate

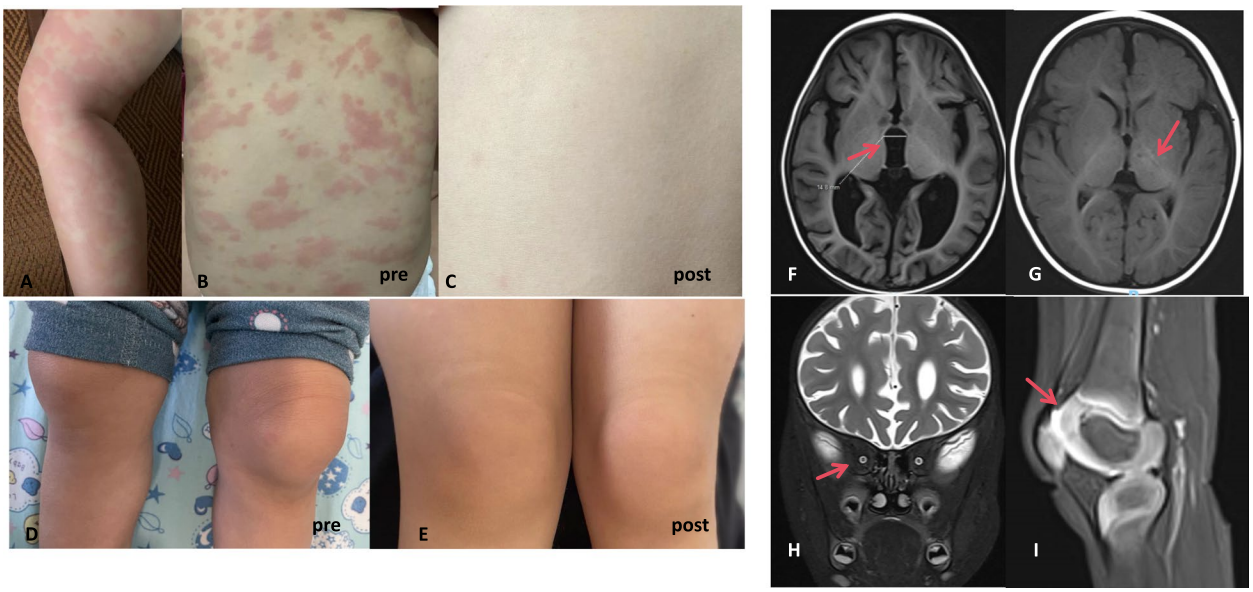

Fig. 1 Phenotype of CAPS patients. **A**, **B** urticaria-like rash before canakinumab treatment; **C** rash after canakinumab treatment. **D** swelling of bilateral knee joint before canakinumab treatment; **E** knee joint swelling relieved after canakinumab treatment. **F**, **G** (before canakinumab treatment): ventriculomegaly and abnormalities in thalamus in brain magnetic resonance imaging; **H** optic neuritis in eye magnetic resonance imaging; **I** synovial enhancement and fluid in keen joint in magnetic resonance imaging

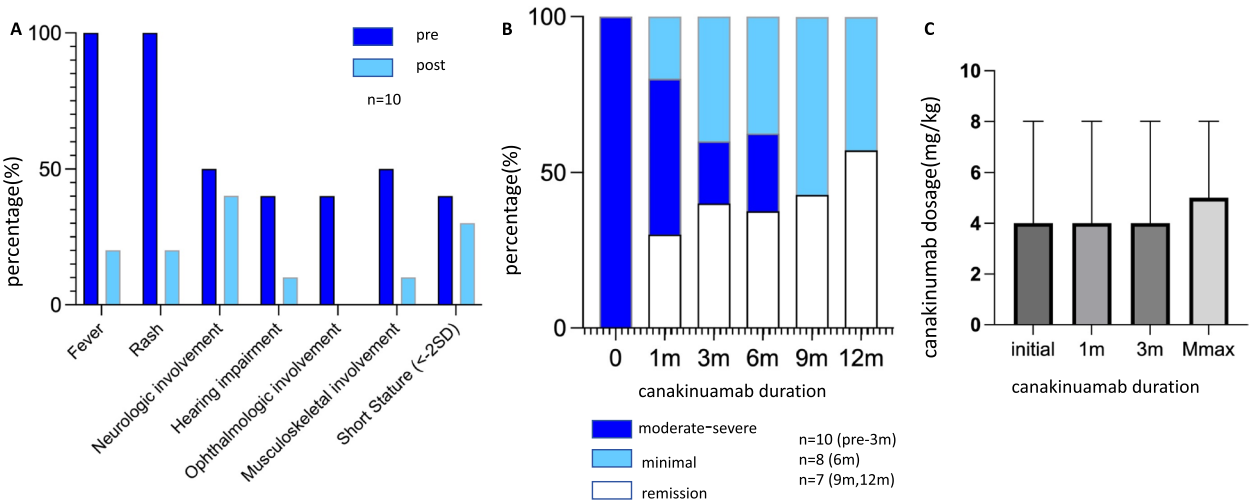

Fig. 2 Treatment outcomes in CAPS patients during canakinumab therapy. **A** response after canakinumab treatment in each manifestations; **B** response after canakinumab treatment; **C** canakinumab dosage during period of treatment pre: before canakinumab treatment; post: after canakinumab treatment; 1,3,6,9,12m: 1 month and 3,6,9,12 months after canakinumab therapy; Mmax: at the last follow up time; the boxes and whiskers indicate median and 25th-75th percentile

recovered after four dosages of canakinumab therapy. 2 patients with papilledema also recovered after three dosages of canakinumab therapy. Musculoskeletal disease was alleviated in the majority of patients, leaving patient 7 with synovial enhancement in magnetic resonance imaging (MRI) (Fig. 1I). Except for patient 10 showing mild hearing loss, hearing loss returned in other patients were recovered. Headaches and other manifestations related to central nervous system were relieved in patients with neurological involvement during canakinumab treatment. Ventriculomegaly and hydrocephalus in brain MRI existed as previously without aggravation.

The median scores of AIDAI before treatment were 55.5 (25.75,62) and the median scores of PGA and PPGA

Table 3 Outcome in CAPS patients treated with canakinumab

Patients	Phenotype	age at diagnosis (months)	the start age of treatment (months)	initial manifestations before treatment	manifestations after treatment
1	FCAS	125	125	Febrile attacks, urticaria-like rash, slightly papilledema, WBC/CRP↑	No
2	MWS	22	32	Febrile attacks, urticaria-like rash, arthralgia, WBC/CRP/SAA↑	Occasional rash
3	MWS	125	135	Febrile attacks, urticaria-like rash, arthralgia and joint swelling, CRP/SAA↑	occasionally arthralgia, intermittent CRP↑ESR↑
4	MWS	155	155	Febrile attacks, urticaria-like rash, intermittent arthralgia, slightly decreased auditory threshold, WBC/CRP/SAA↑	No
5	CINCA	4	14	Febrile attacks, urticaria-like rash, occassional right limb pain, decreased auditory threshold, sterile meningitis, WBC/CRP/SAA↑	Occasional rash and intermittent fever,WBC/CRP↑frequently
6	CINCA	5	26	Febrile attacks, urticaria-like rash, optic neuritis, sterile meningitis and hydrocephalus, WBC/CRP/SAA↑	Occasional fever, hydrocephalus
7	CINCA	13	25	Febrile attacks, urticaria-like rash, arthralgia and joint swelling, sterile meningitis and hydrocephalus, WBC/CRP/SAA↑	synovial enhancement, hydrocephalus
8	CINCA	6	6	Febrile attacks, urticaria-like rash, decreased auditory threshold, sterile meningitis and abnormalities in thalamus, WBC/CRP↑	Abnormalities in thalamus
9	CINCA	5	15	Febrile attacks, urticaria-like rash, sterile meningitis, papilledema, WBC/CRP↑	No
10	CINCA	2	18	Febrile attacks, urticaria-like rash, optic neuritis, decreased auditory threshold, WBC/SAA↑	slightly decreased auditory threshold

FCAS familial cold autoinflammatory syndrome, *MWS* Muckle-Wells syndrome, *CINCA* chronic infantile neurological cutaneous articular syndrome, *WBC* white blood cell, *CRP* C-reactive protein, *SAA* serum amyloid A

were 6 (4,7.5). The scores of AIDAI, PGA, and PPGA decreased greatly in all patients after canakinumab treatment (Fig. 3A, B). The levels of inflammatory markers including CRP, erythrocyte sedimentation rate (ESR), and SAA were decreased significantly after canakinumab treatment, while patients 5 and 3 still experienced elevated levels of CRP 1–2 weeks before next dosage of canakinumab treatment (Table 2, Fig. 4).

Six patients used corticosteroids as concomitant treatments with canakinumab, and the median dosage of corticosteroids was 0.45 (0,0.56) mg/kg/d. After 3 months of treatment of canakinumab, the median dosage of corticosteroids decreased to 0 (0,0.11) mg/kg/d ($p<0.05$). At the last follow-up time, only patient 5 required intermittent minimal corticosteroids (2.5mg) because of occasional fever and elevated level of CRP, others used canakinumab as monotherapy without relapse. (Fig. 3C).

Safety of canakinumab in CAPS

Canakinumab was tolerable in most patients. No patients discontinued canakinumab treatment due to adverse events. The most common adverse event was respiratory infection (40%, 4/10). Immune thrombopenia occurred in patient 4 induced by once respiratory infection, which returned to normal after the usage of immunoglobulin (Table 2). No other bloodwork abnormalities were observed. Notably, 3 patients experienced occasional white fibrous papular rash at the first two dosages of canakinumab, which disappeared in the later treatment. Severe adverse events, notably serious infection was not observed. In addition, adverse events were not increased related to canakinumab dose increase.

Discussion

In European and American countries, consensus or recommendations for CAPS diagnosis, management, and monitoring have been stated [5, 6], while the study of large cases in CAPS or effectiveness and safety of canakinumab in CAPS remains unknown in China. Herein, we firstly described the use of canakinumab in Chinese patients with CAPS. Disease activity was improved greatly in all patients and most of them achieved

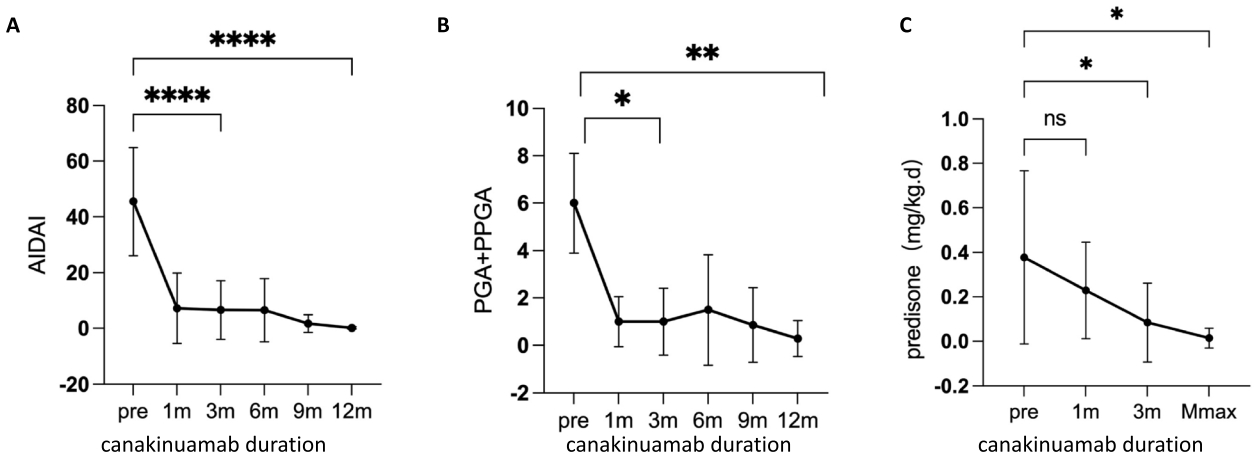

Fig. 3 Disease activities and doses of prednisone in CAPS patients during canakinumab therapy. pre: before canakinumab treatment; 1,3,6,9,12 m: 1 month and 3,6,9,12 months after canakinumab therapy; Mmax: at the last follow up time; AIDAI: patient-reported auto-inflammatory diseases activity index; PGA + PPGA:global assessment scales for physicians and patients/parents ns: no significant; * $p < 0.05$; the boxes and whiskers indicate mean with SD

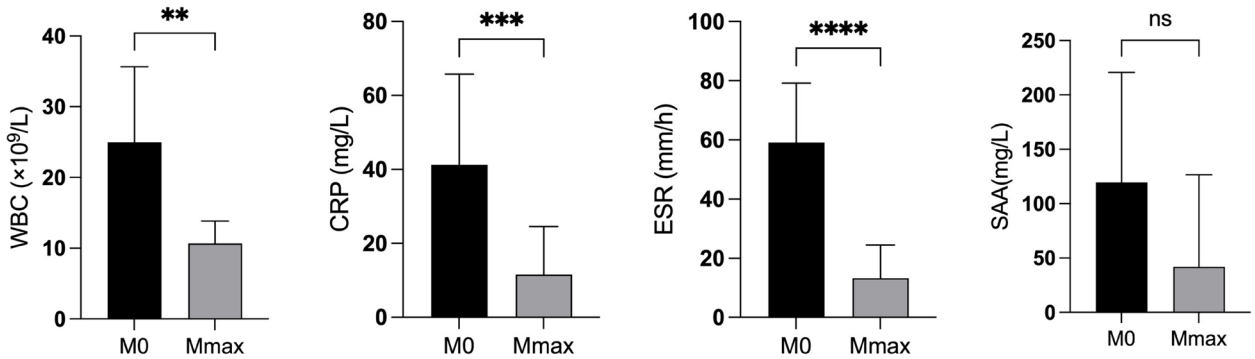

Fig. 4 Laboratory characteristics in CAPS patients before and after canakinumab therapy. M0: before canakinumab treatment; Mmax: at the last follow-up time after canakinumab therapy. WBC: white blood cell; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; SAA: serum amyloid A. ns: no significant; ** $p < 0.01$; *** $p < 0.001$; **** $p < 0.0001$; the boxes and whiskers indicate mean with SD

sustained disease remission after canakinumab therapy. Miyamoto T et al. described that canakinumab was effective in controlling symptomatic disease activities and CRP levels, and the efficacy was sustained for more than 10 years [9]. Walker UA also showed that more than 90% of patients experienced mild or no disease activity after receiving canakinumab and the response was sustained for up to 6 years [10]. Consistent with the reported results, our findings have also demonstrated that canakinumab may be effective for the treatment of CAPS, while the long-term effectiveness need more follow-up time to evaluate.

Moreover, previous reports showed that anti-IL-1 therapy improved stature, musculoskeletal disease, and the progression of other organ damage, such as deafness, visual impairment, and neurological disease [9, 11, 12]. In our study, canakinumab appeared to improve inflammation, rash, musculoskeletal disease and vision. Although abnormal changes in brain MRI remained unchanged in most patients, their neurological symptoms were relieved. The follow-up in our study was not long term, making it difficult to analyze changes in organ damage; therefore, the follow-up period should be extended.

In addition, 30% of patients in our group experienced canakinumab dose increase and all of them are presented with CINCA. The median dosage of canakinumab at the last follow-up time in our group in patients with CINCA was 7mg/kg, which is much higher than in patients with other phenotypes of CAPS (4mg/kg). Consistent with our results, Kuemmerle-Deschner JB et al. described that 72% of patients in CAPS achieved complete response after dose increase, and children or severe CAPS phenotype required higher

dose of canakinumab [13]. Moreover, dose increase was not associated with an increased rate of adverse events. Therefore, a higher dosage of canakinumab may be required and tolerated in some CAPS patients, especially those of young age with severe phenotypes.

The most common adverse event in our group was infection, especially respiratory infection. The safety profile was consistent with that reported in previous [14], even with relevant higher dosage of canakinumab. No deaths and serious adverse events were reported during the study. No patients discontinued canakinumab treatment due to adverse events. The use of canakinumab may be well tolerated in most patients.

This study had limitations on its small sample size in a single center and it was retrospective. Another limitation was that we lacked long-term canakinumab treatment response data, as the longest follow-up period was 38 months. Longer follow-up and future prospective clinical trials are required to further evaluate the long-term efficacy and safety of canakinumab in Chinese patients with CAPS.

Conclusions

Treatment with canakinumab in Chinese CAPS patients may be effective and safe, helping to control disease activity and reduce the use of corticosteroids. These data provide the basis for randomized control trials to evaluate the efficacy and safety of canakinumab in Chinese CAPS patients.

Abbreviations

CAPS	Cryopyrin-associated periodic syndrome
ESR	Erythrocyte sedimentation rate
CRP	Creactive protein
SAA	Serum amyloid A
FCAS	Familial cold auto-inflammatory syndrome
MWS	Muckle-Wells syndrome
CINCA	Chronic infantile neurological cutaneous articular syndrome
AIDAI	Patient-reported auto-inflammatory diseases activity index
PGA/PPGA	Global assessment scales for physicians and patients/parents
MRI	Magnetic resonance imaging
IL	Interleukin

Authors' contributions

XZ collected and analyzed data, and drafted the manuscript, JF collected and analyzed data. TH designed the study, critically reviewed and revised the manuscript. YH, YX, RW, YL and ZY contributed to collect data. JY supervised data collection, and critically reviewed and revised the manuscript for important intellectual content. All authors contributed to the article and approved the submitted version.

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Availability of data and materials

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding authors.

Declarations

Ethics approval and consent to participate

The studies involving human participants were reviewed and approved by the Ethics Committee of Shenzhen Children's Hospital. Written informed consent to participate in this study was provided by the participants' legal guardian.

Consent for publication

We assure that the data presented here was not published elsewhere and the article has not been submitted to any other journal. We give our consent for the publication of the manuscript "Effectiveness and safety of canakinumab in cryopyrin-associated periodic syndrome: a retrospective study in China".

Competing interests

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest. Patients accessed canakinumab on their own expenses and without any company participation.

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