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Original Article

Clinical Experience with Low-dose Modified-release Prednisone Chronotherapy in Asian Patients with Rheumatoid Arthritis in Singapore

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Objective. To examine the demographic profile and treatment patterns in patients with rheumatoid arthritis (RA) prescribed low-dose modified-release prednisone (LODOTRA®) on a named patient basis in Singapore and to evaluate safety and clinical outcome of the treatment. **Methods.** Medical records of adult patients with RA who had inadequate responses to prior RA treatment and were prescribed low-dose modified-release prednisone between January and December 2012 at a specialist clinic were reviewed retrospectively. Demographics, treatment information, relevant laboratory evaluations, and disease condition, prior to and after the start of treatment, were collected. **Results.** Thirty-eight patients were enrolled. The mean age was 52.8 years and median disease duration was 1.3 years (0.04 to 8.2 years). Patients received a mean daily dose of 5.0±1.0 mg of modified-release prednisone for a median period of 4.4 months (0.2 to 11.8 months). Before treatment, the majority of patients received disease-modifying anti-rheumatic drugs (78.9%), glucocorticoids (71.0%), and non-steroidal anti-inflammatory drugs (NSAIDs) (68.4%). After the start of treatment, prescription of NSAIDs declined from 68.4% to 28.9%. Similar laboratory findings were observed before and after treatment. The median C-reactive protein level decreased substantially from 9.8 mg/L (0.2 to 77.7 mg/L) to 3.9 mg/L (0.4 to 27.6 mg/L). High proportions of patients reported improvement or recovery from morning stiffness (94.7%) or joint pain (70.0 to 100.0%) after treatment. The median number of painful joints decreased from 4 (1 to 8) to 0 (0 to 4) after treatment. **Conclusion.** Our clinical experience in Asian patients with RA suggests that low-dose modified-release prednisone chronotherapy is associated with similar treatment patterns, safety profile, and clinical outcomes as in Western populations. **(J Rheum Dis 2015;22:76-84)**

Key Words. Rheumatoid arthritis, Prednisone, Chronotherapy, Asians, Singapore

INTRODUCTION

Rheumatoid arthritis (RA) is an autoimmune condition that affects multiple joints and leads to inflammation of the joints and the surrounding tissues [1]. Globally, the prevalence of RA ranges from 0.3% to 1.0%, with a trend of increased prevalence in developed countries [2].

The symptoms of RA are variable. The onset of the disease is generally associated with minor joint pain, stiffness, and fatigue. A circadian pattern of RA symptoms, which are worse in the morning as compared to evening, is a well-known feature of RA [3,4]. The symptoms follow the circadian rhythm of the pro-inflammatory cytokines, particularly interleukin-6 (IL-6), which increases late at night and peaks in the early morning. Endogenous production of cortisol can counter the effects of increased IL-6 levels but is perturbed in patients with RA, contributing to the emergence of morning symptoms [5,6]. Morning stiffness around the joints, which can last for an hour or more before maximal improvement, is a hallmark symptom of RA and has a significant negative impact on patients. Morning stiffness and pain may result in functional impairment, adversely affecting day-to-day activities and working life [7]. In many patients, such func-

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tional impairment may force early retirement from work, resulting in a significant economic burden to society [8].

Glucocorticoids (GCs) are a mainstay of therapy for patients with RA. However, their use may be associated with increased side effects, especially at high doses. The long-term side effects of GCs range from cataracts and osteoporosis to hypothalamic-pituitary-adrenal (HPA) axis suppression [9,10]. Use of low-dose GCs may provide a more favorable benefit-risk ratio, by reducing the risk of side effects associated with high doses. However, conventional dosing regimens of low-dose GCs (e.g., morning administration of immediate-release prednisone, at <10 mg/d) are often not effective in reducing the duration and severity of morning symptoms [11,12]. In addition, there is some evidence that administration of a dose of GC at night (12:00 a.m.) in patients with RA, when cortisol production is relatively low, may result in more potent suppression of the HPA axis than a similar dose given in the morning [13]. Although nocturnal (e.g., 2:00 a.m.) administration of low-dose immediate-release prednisone showed improvement in RA symptoms [11], this timing is inconvenient and impractical for patients, and may lead to poor adherence to medication; it may also alter circadian rhythms. To optimize GC therapy, low-dose prednisone chronotherapy using modified-release prednisone is an option. Modified-release prednisone is a formulation which allows time-targeted delivery of the GC, according to the natural circadian rhythms of endogenous cortisol and disease symptoms [14]. In this formulation, standard prednisone is enclosed within an outer coating that slowly absorbs water from the gut; the drug is released relatively rapidly from the core approximately four hours after ingestion. Hence, a tablet that is consumed at 10:00 p.m. releases the active ingredient, prednisone at approximately 2:00 a.m., coinciding with the time when levels of pro-inflammatory cytokines, particularly IL-6, are at their peak, while endogenously-produced cortisol is at its lowest concentration [15].

The efficacy of modified-release prednisone as a monotherapy or a combination treatment for RA has been investigated in a number of clinical trials, including the circadian administration of prednisone in rheumatoid arthritis (CAPRA)-1 [12], CAPRA-2 [16], and CAPRA-1 open-label extension [17] studies. The CAPRA-1 study compared the efficacy of modified-release prednisone vs. same-dose immediate-release prednisone therapy over a three-month period in RA patients. In this study, the modified-release prednisone group showed substantially greater reduction in the duration of morning stiffness, compared with the group that received immediate-release prednisone [12]. In an open-label extension to this study, RA patients who were originally randomized to modified-release or immediate-release treatments continued with modified-release prednisone chronotherapy for a further nine months. Both the modified-release/modified-release and immediate-release/modified-release treatment groups showed sustained improvements in morning stiffness and American College of Rheumatology (ACR20) responses at the end of the treatment period, particularly the modified-release/modified-release group, which received modified-release prednisone for the full 12 months [17]. The CAPRA-2 study compared the efficacy of modified-release prednisone to placebo therapy in RA patients who were already on disease-modifying anti-rheumatic drugs (DMARDs) and concomitant medications at stable dose. Significant reduction in morning stiffness, as well as improvement in ACR20 and ACR50 responses, was observed in the modified-release prednisone plus DMARD treatment group [16].

In these trials, favorable results were also observed for two other important patient-centered outcome measures, pain and fatigue. In the CAPRA-1 open-label extension study, patients showed clinically relevant improvements from baseline in pain intensity scores after treatment with modified-release prednisone [17]. In the CAPRA-2 study, patients who received modified-release prednisone showed reductions in morning and evening pain from baseline [16]. Improved fatigue scores were also seen in this group, indicating a reduction in fatigue levels following modified-release prednisone treatment [16].

In terms of safety, modified-release prednisone was generally well tolerated by RA patients in the above trials. The CAPRA-1 study found no clinically relevant differences in the safety profile between the modified-release prednisone and immediate-release prednisone groups, with the most frequent adverse event (AE) reported being worsening of RA. The two groups also showed similar low rates of AEs that led to premature discontinuation of treatment ($<10\%$). The rate of serious adverse events (SAEs) was very low ($<5\%$) and similar in both groups [12]. In the CAPRA-2 study, the modified-release prednisone plus DMARD and the placebo plus DMARD groups showed similar frequencies of AEs, with very few patients reporting SAEs [16].

A separate study showed that modified-release prednisone improved long-term efficacy in RA patients,

while having no adverse impact on HPA axis function [18]. In a recent observational study, RA patients who were switched from immediate-release prednisone to modified-release prednisone administered at bedtime (approximately 10:00 p.m.) showed improvements in morning stiffness duration, pain intensity, patient and physician global assessment, and disease activity score (DAS 28), over a treatment period of four months [19]. Modified-release prednisone was also reported to be well tolerated in this study.

There is little data on the use of chronotherapy involving modified-release prednisone in routine clinical practice. Also, since most published studies were conducted in Western countries, data are not currently available for the Asian populations. Our study examined the demographic profile and treatment patterns in patients with RA who were prescribed low-dose modified-release prednisone on a named patient basis in a specialist clinic in Singapore. It also evaluated the safety profile and clinical outcome of low-dose modified-release prednisone chronotherapy.

MATERIALS AND METHODS

This was a single-center retrospective chart review study of patients with RA who were prescribed low-dose modified-release prednisone on a named patient basis between January and December 2012 at a specialist clinic in Singapore. Eligible patients were at least 18 years of age at the time of diagnosis, were deemed by their treating physician to have inadequate responses to prior RA treatment, and had a baseline visit and at least one follow-up visit after the start of low-dose modified-release prednisone chronotherapy.

The protocol and data collection form was approved by the Parkway Independent Ethics Committee (PIEC) (approval no. PIEC/2012/042). Given the retrospective nature of this study, a waiver of informed consent was granted. Hence, no informed consent was obtained from the patients. No study-related activities were initiated before the ethical clearance. The study was conducted according to the principles of the Declaration of Helsinki, International Conference on Harmonisation-Good Clinical Practice guidelines and Singapore regulatory guidelines. Patient confidentiality was maintained throughout the study.

Relevant data were extracted from the medical records up to 31 December 2012. Patient demographics and information on modified-release prednisone treatment were collected. Information on RA medications, laboratory evaluations, and disease condition, prior to and after the start of low-dose modified-release prednisone chronotherapy, were collected. RA medications documented included DMARDs, GCs, non-steroidal anti-inflammatory drugs (NSAIDs), and biologics. Laboratory evaluations collected included fasting glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), total cholesterol, total triglycerides, and C-reactive protein (CRP). Assessment of the course of morning stiffness or joint pain at the follow-up visit was based on physician's clinical judgment and patients' report of their conditions. A patient's condition was categorized as 'recovered' if the patient did not experience the condition at the follow-up visit but experienced it at baseline, as 'improved' if the patient felt better, as 'no change' if the condition did not change, as 'worsened' if the patient felt worse, and as 'newly-reported joint pain' or 'newly-reported morning stiffness' if a new condition was reported at the follow-up visit but was absent at baseline.

Study outcomes evaluated included treatment patterns, clinically significant laboratory findings, and CRP level prior to and after the start of low-dose modified-release prednisone chronotherapy. In addition, the course of morning stiffness and joint pain after the start of treatment and the total number of painful joints before and after the start of treatment were also evaluated. Safety of the treatment was assessed on the basis of clinically significant laboratory findings, defined as fasting glucose >120 mg/dL, ALT >102 U/L, AST >81 U/L, and 20% increase from baseline for total cholesterol and triglyceride. Effect of the treatment on clinical outcomes was assessed based on improvements in CRP level and morning stiffness or joint pain, as well as reduction in the number of painful joints after treatment. Painful joints after treatment were defined as joints that remained painful, or have worsened or newly-reported pain after treatment.

Descriptive statistics were used to summarize demographics, RA medications, laboratory findings, and disease information. All statistical analyses were performed using IBM SPSS Statistics ver. 20.0 (IBM Co., Armonk, NY, USA).

RESULTS

Patient characteristics

A total of 38 patients were enrolled. Patient demographics and baseline clinical characteristics are summarized in Table 1. The mean age was 52.8 ± 12.8 years, with

Table 1. Demographics and baseline clinical characteristics (n=38)

Characteristic	
Age (yr)	52.8±12.8
Female	35 (92.1)
Race	
Chinese	22 (57.9)
Indian	13 (34.2)
Malay	3 (7.9)
Disease duration since diagnosis (yr)	1.3 (0.04~8.2)
Morning stiffness	19 (50.0)
Joint pain	38 (100.0)
Total number of painful joints	4 (1~8)
Shoulder pain	15 (39.5)*
Left	8 (21.1)
Right	12 (31.6)
Elbow pain	11 (28.9)*
Left	6 (15.8)
Right	9 (23.7)
Wrist pain	12 (31.6)*
Left	7 (18.4)
Right	7 (18.4)
Finger pain	24 (63.2)*
Left	16 (42.1)
Right	19 (50.0)
Knee pain	27 (71.1)*
Left	20 (52.6)
Right	20 (52.6)
Ankle pain	15 (39.5)*
Left	10 (26.3)
Right	8 (21.1)
Other sites	12 (31.6)

Values are presented as mean±standard deviation, number (%), or median (range). *Patients can have pain on the left side only, right side only or on both right and left sides.

a female preponderance of 92.1%. More than half of the study population was Chinese, 34.2% were Indians, and 7.9% were Malays. The median disease duration was 1.3 years (0.04 to 8.2 years). Half of the patients experienced morning stiffness and patients had a median of 4 (1 to 8) painful joints at baseline, with knee (71.1%) and finger (63.2%) being the most commonly affected joints. Patients received a mean daily dose of 5.0±1.0 mg of modified-release prednisone. The median duration of treatment was 4.4 months (0.2 to 11.8 months), with the majority of patients (89.5%) receiving treatment between more than one month to about one year.

Medications for rheumatoid arthritis at baseline

RA medications prescribed for maintenance treatment at baseline are summarized in Table 2. The majority of the patients received DMARDs (78.9%), GCs (71.0%), and NSAIDs (68.4%) prior to the start of low-dose modified-release prednisone chronotherapy. Hydroxychloroquine and methotrexate were the most commonly prescribed DMARDs, used by 55.3% and 52.6% of the patients, respectively. Celecoxib (42.1%) and etoricoxib (31.6%) were the most frequently prescribed NSAIDs. RA medications prescribed for flare at baseline are summarized in Table 3. A total of 25 patients received RA medications for flare. Betamethasone and triamcinolone were the most frequently prescribed, used by 65.8% and 31.6% of the patients, respectively.

Concomitant medications for rheumatoid arthritis after the start of low-dose modified-release prednisone chronotherapy

Concomitant RA medications prescribed for maintenance treatment after the start of low-dose modified-release prednisone chronotherapy are summarized in Table 2. DMARDs remained the most commonly prescribed concomitant RA medications, used by 73.7% of patients. Hydroxychloroquine and methotrexate remained the most frequently prescribed DMARDs, used by 52.6% and 57.9% of the patients, respectively. Prescription of NSAIDs declined substantially from 68.4% to 28.9% after the start of treatment (Figure 1). The number of patients who received biologics after the start of treatment (n=11) remained largely the same as before treatment (n=9).

RA medications prescribed for flare after the start of low-dose modified-release prednisone chronotherapy are summarized in Table 3. The number of patients who received RA medications for flare after the start of treatment (n=28) remained largely the same as at baseline (n=25). Both betamethasone and triamcinolone remained the most frequently prescribed RA medications for flare, used by 65.8% and 23.7% of the patients, respectively.

Effect of low-dose modified-release prednisone chronotherapy on laboratory test results

Clinically significant laboratory findings before and after the start of low-dose modified-release prednisone chronotherapy are summarized in Table 4. Among patients with available results, few had clinically significant find-

Table 2. Maintenance medications prescribed

Maintenance medications for RA (dosage)	At baseline		After start of treatment	
	Number (%)	Median (range)	Number (%)	Median (range)
DMARDs	30 (78.9)		28 (73.7)	
Hydroxychloroquine (mg/d)	21 (55.3)	266.7 (200.0～400.0)	20 (52.6)	200.0 (200.0～300.0)
Methotrexate (mg/wk)	20 (52.6)	8.8 (5.0～12.5)	22 (57.9)	10.0 (5.0～15.0)
Leflunomide (mg/wk)	7 (18.4)	100.0 (100.0～100.0)	3 (7.9)	100.0 (100.0～100.0)
Sulfasalazine (mg/d)	5 (13.2)	1,000.0 (1,000.0～1,000.0)	3 (7.9)	1,000.0 (1,000.0～1,000.0)
Minocycline (mg/d)	3 (7.9)	100.0 (100.0～100.0)	3 (7.9)	100.0 (100.0～100.0)
NSAIDs	26 (68.4)		11 (28.9)	
Celecoxib (mg/d)	16 (42.1)	350.0 (200.0～400.0)	6 (15.8)	350.0 (200.0～400.0)
Etoricoxib (mg/d)	12 (31.6)	102.5 (90.0～120.0)	7 (18.4)	120.0 (90.0～120.0)
Glucocorticoid-prednisone (mg/d)	27 (71.0)	8.3 (5.0～16.3)	4 (10.5)	10.0 (5.0～11.7)
Biologics	9 (23.7)		11 (28.9)	
Etanercept (mg/mo)	8 (21.1)	25.0 (12.5～100.0)	11 (28.9)	25.0 (8.3～100.0)
Adalimumab (mg/mo)	1 (2.6)	40.0 (40.0～40.0)	1 (2.6)	20.0 (20.0～20.0)
Golimumab (mg/mo)	1 (2.6)	25.0 (25.0～25.0)	1 (2.6)	50.0 (50.0～50.0)

DMARDs: disease modifying anti-rheumatic drug, d: day, mo: month, NSAIDs: non-steroidal anti-inflammatory drugs, RA: rheumatoid arthritis, wk: week.

Table 3. Flare medications prescribed

Flare medications for RA	At baseline	After start of treatment
Yes	25 (65.8)	28 (73.7)
NSAIDs		
Ketorolac	7 (18.4)	5 (13.2)
Diclofenac	5 (13.2)	2 (5.3)
Naproxen and esomeprazole	1 (2.6)	0
Glucocorticoids		
Betamethasone	25 (65.8)	25 (65.8)
Triamcinolone	12 (31.6)	9 (23.7)
Dexamethasone	0	1 (2.6)
No	13 (34.2)	10 (26.3)

Values are presented as number (%). NSAIDs: non-steroidal anti-inflammatory drugs, RA: rheumatoid arthritis.

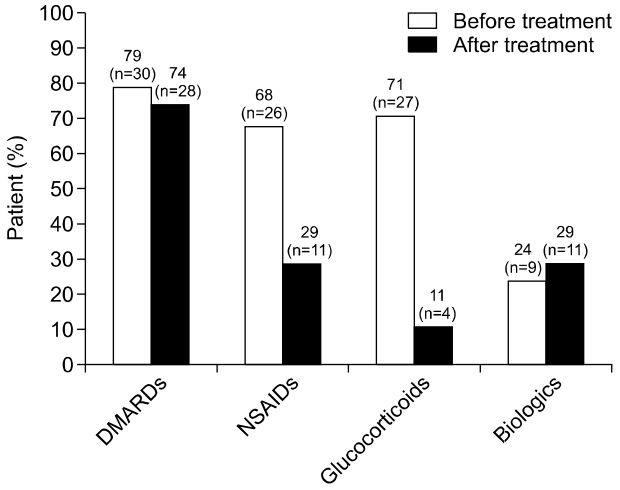

Figure 1. Prescription of maintenance medication among patients with rheumatoid arthritis before and after the start of low-dose modified-release prednisone chronotherapy. DMARDs: disease modifying anti-rheumatic drugs, NSAIDs: non-steroidal anti-inflammatory drugs.

ings after the start of treatment, similar to baseline. Before the start of the treatment, four patients had fasting hyperglycemia, and one had elevated ALT. During treatment with low-dose modified-release prednisone, four patients experienced fasting hyperglycemia and two patients each had 20% increase in triglycerides and total cholesterol levels from baseline.

Effect of low-dose modified-release prednisone chronotherapy on clinical outcomes

Among patients with available results, median CRP level decreased substantially from 9.8 mg/L (0.2 to 77.7 mg/L) at baseline (n=9) to 3.9 mg/L (0.4 to 27.6 mg/L) after the start of low-dose modified-release prednisone chronotherapy (n=8). Among patients who experienced morning stiffness at baseline (n=19), nearly all (94.7%) were considered to have recovered or improved after the start of treatment (Figure 2). High proportions of patients reported improvements or recovery from joint pain after treatment, ranging from 70.0% (n=14) among those who experienced knee pain at baseline to 100.0%

Table 4. Laboratory test findings before and after the start of low-dose modified-release prednisone chronotherapy

Laboratory finding	Before treatment	After start of treatment
Fasting glucose level (mg/dL)	92.5 (70.0～216.0)	99.0 (67.0～156.0)
Abnormal*	4	4
Normal	24	12
Unknown	10	22
Triglyceride level (mg/dL)	100.0 (24.0～314.0)	88.0 (34.2～225.0)
Abnormal*	Not determined	2
Normal	Not determined	7
Unknown	11	29
Total cholesterol level (mg/dL)	196.0 (126.0～303.0)	218.0 (108.5～314.0)
Abnormal*	Not determined	2
Normal	Not determined	7
Unknown	11	29
ALT (U/L)	16.0 (8.0～123.0)	19 (9.0～87.0)
Abnormal*	1	0
Normal	27	16
Unknown	10	29
AST (U/L)	24.5 (14.0～66.0)	22.0 (14.0～75.0)
Abnormal*	0	0
Normal	28	16
Unknown	10	29

Values are presented as median (range) or number only. ALT: alanine aminotransferase, AST: aspartate aminotransferase. *Abnormal laboratory findings: fasting glucose ＞120 mg/dL, 20% increase from baseline for triglycerides and total cholesterol, ALT＞102 U/L, AST＞81 U/L.

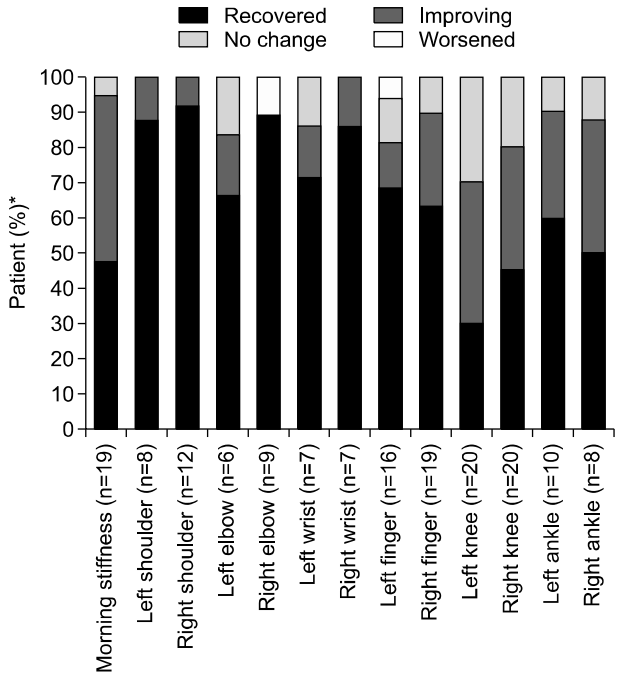

Figure 2. Course of disease condition after the start of low-dose modified-release prednisone chronotherapy compared to baseline. *Among patients with morning stiffness or pain at baseline.

(n=12) among those who experienced shoulder pain. There were only two reports of worsened condition from baseline after the start of treatment: one was worsening pain on the right elbow while the other was on the left finger. There were no newly reported cases of morning stiffness or joint pain after treatment. The median number of painful joints decreased from 4 (1 to 8) at baseline to 0 (0 to 4) after treatment.

DISCUSSION

Currently, little published data is available on the use of low-dose modified-release prednisone chronotherapy in RA patients in routine clinical practice settings. Data on its use among Asian populations is also very limited. Our study provides a unique opportunity to examine the demographic profile and treatment patterns in patients with RA who were prescribed low-dose modified-release prednisone and to evaluate safety and clinical outcome of the treatment in a routine specialist clinical practice setting in Singapore.

Our study shows female predominance (92.1%) in the study population and disease onset at around 52 years of

age. Similar findings were observed in other studies. In a recent study of RA patients in Italy, 74% of the study population were female and age of onset was 52 years [19]. In the CAPRA-1 study, 86% of the RA patients were female and age of onset was 45 years [12].

Our study shows that among RA medications used for maintenance treatment, DMARDs (78.9%), GCs (71.0%), and NSAIDs (68.4%) were commonly prescribed to patients before the start of low-dose prednisone chronotherapy. After the start of therapy, DMARDs remained the most commonly prescribed concomitant RA medication (73.7%), while the use of NSAIDs decreased substantially to 28.9%. These findings suggest a high level of compliance with international treatment guidelines for the management of RA, which recommend the use of DMARDs to prevent long-term damaging effects of RA, and addition of GCs and NSAIDs to alleviate RA symptoms [20-22]. The reduced usage of NSAIDs after the start of low-dose modified-release prednisone suggests that, for the majority of patients, their condition could be adequately controlled with DMARDs and modified-release prednisone, reducing the need for additional RA medications such as NSAIDs for alleviation of their symptoms. This is encouraging as patients could consequently reduce their exposure to unwanted side effects of these medications. Interestingly, the observed reduction in prescription of concomitant RA medications, particularly NSAIDs, appears consistent with the findings of a recent German study involving RA patients who switched from conventional low-dose GCs to modified-release prednisone. Based on longitudinal analysis of pain-relieving medication prescriptions for these patients, it was estimated that concomitantly prescribed analgesics and NSAIDS were significantly reduced after initiation of modified-release prednisone treatment [23].

Our study showed that low-dose modified-release prednisone chronotherapy was associated with a generally good safety profile in patients who received modified-release prednisone and other concomitant RA medications at the investigator's discretion in a clinical practice setting. Similar laboratory findings were observed before and after the start of low-dose prednisone chronotherapy. During treatment with modified-release prednisone, only a few patients had clinically significant laboratory findings; four had fasting hyperglycemia, two had increased triglycerides, and two had increased total cholesterol. This finding is in line with results from large clinical trials conducted in Western populations, in which the safety profile of low-dose modified-release prednisone chronotherapy was found to be similar to that of control treatments involving either the active ingredient (immediate-release prednisone) [12] or placebo [16]. In addition, modified-release prednisone has been shown to improve long-term outcomes in RA patients, without adversely affecting HPA axis function [18].

In terms of clinical outcomes, our results showed that treatment with modified-release prednisone along with concomitant RA medications was associated with decreased CRP levels as well as improvement or recovery in morning stiffness or joint pain. The median CRP level was reduced by 60% after the start of low-dose modified-release prednisone chronotherapy. About 95% of the patients who experienced morning stiffness at baseline reported improvement or recovery after the start of treatment. High proportions of patients (70 to 100%) reported improvements or recovery from pain at specific joints after treatment. The total number of painful joints reduced substantially after the start of treatment. These findings are broadly similar to those previously reported in clinical trials of low-dose modified-release prednisone chronotherapy in RA patients [12,16,17]. In these studies, patients receiving low-dose modified-release prednisone chronotherapy, with or without other concomitant RA medication, showed considerable improvement in morning stiffness, as well as in other RA severity measures.

Our findings need to be interpreted within the limitations of the study design and sample size. Firstly, this is a small study conducted in only one clinic in one Asian country. It may not be representative of RA patient populations in other clinics in Singapore or other Asian countries. Nonetheless, our results are generally consistent with other studies. Future studies involving additional Asian countries will provide more information on the use of modified-release prednisone in other populations of Asian patients with RA. Next, the short duration of modified-release prednisone treatment in this study does not allow long-term safety information in the study population to be collected. Future studies with longer study duration among Asian patients with RA will provide information about the long-term safety of modified-release prednisone in this patient population. Due to the retrospective nature of this study, the number of patients with available data for laboratory tests was relatively small and AEs could not be recorded. Hence, we were unable to fully assess the safety and tolerability

of modified-release prednisone in the entire study population. Future studies should include relevant laboratory test results and AE recording for the entire study population, in order to provide more comprehensive data on the safety and tolerability of modified-release prednisone in routine clinical practice. Further, the assessment of the disease condition was based on physician's judgment and patient's recall. Therefore, there is potential for bias in the results. Evaluation of these outcomes using objective measurement tools, such as the DAS28 may provide more reliable results. Finally, improvement in clinical outcomes observed in this study could not be solely attributed to treatment with modified-release prednisone as patients also received concomitant RA medications. Nonetheless, our study provides a unique opportunity to examine the safety of modified-release prednisone in RA patients receiving different concomitant RA medications in routine clinical practice. This is generally not possible in a clinical trial setting, where safety is usually evaluated in patients receiving only one or two specific concomitant medications.

CONCLUSION

Our observational study contributes to our understanding of RA patients and RA treatment patterns in Singapore. Our clinical experience suggests that low-dose modified-release prednisone chronotherapy in Asian patients with RA is associated with a generally good safety profile and improvement in clinical outcomes, similar to the Western populations.

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CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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