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Examining the Characteristics of Colchicine-Induced Myelosuppression in Clinical Cases: A Systematic Review

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ABSTRACT. ***Objective.*** The use of colchicine has been associated with varying degrees of myelosuppression. Despite expanded use in cardiovascular and inflammatory conditions, there remains clinician concern because of potential myelosuppressive side effects. A systematic review was conducted to explore the reported myelosuppressive events of colchicine.

Methods. A systematic review was conducted using the MeSH terms ("colchicine") AND ("myelosuppression," "bone*," "marrow," "suppression," "aplasia," "leukopenia/leucopenia," "lymphopenia," "neutropenia") on September 1, 2020, and was updated on November 30, 2021. The search was conducted in PubMed, ScienceDirect, Scopus, Embase, and Cochrane Library. The search included references published from 1978 to 2020 and was limited to English-language observational studies (ie, case reports, case series, case control studies, and cohort studies) or trial data.

Results. In total, 3233 articles were screened, with 30 studies of 47 patients with myelosuppression from colchicine identified. Most patients with myelosuppression had comorbidities, including renal impairment (21/47, 44.7%). Out of 47 patients, 15 (31.9%) and 13 (27.7%) were reported to be concurrently taking cytochrome P450 3A4 (CYP3A4) inhibitors and P-glycoprotein (P-gp) efflux transporter inhibitors, respectively. Patients with renal impairment accounted for the majority of overall patients taking these CYP3A4 and P-gp inhibitors (8/15, 53.3%, and 8/13, 61.5%, respectively). Out of 21 patients with renal impairment, 13 had worsening cytopenia during colchicine use. The presentations ranged from moderate anemia (grade 2) to severe thrombocytopenia, neutropenia, and leukopenia (grade 4).

Conclusion. Colchicine has few reports of myelosuppression. The majority of patients with myelosuppression had preexisting renal impairment or concomitant CYP3A4 or P-gp inhibitor use. Caution should be taken in this subset of patients with increased monitoring.

Key Indexing Terms: anemia, cardiovascular diseases, colchicine, evidence-based medicine, gout, thrombocytopenia

Colchicine, originally derived from the ancient plant *Colchicum autumnale*, has been used for thousands of years as a prophylaxis and treatment for gout flares and, in more recent times, in inflammasome-mediated conditions, such as familial Mediterranean fever (FMF).[1] In the last decade, it has also increasingly been recognized to have a role in managing cardiovascular disease and, more recently, in reducing mortality in myocardial infarction and ischemic stroke.[2-4]

This has led to increased scrutiny of colchicine's safety and, therefore, its pharmacology. Colchicine is a substrate for cytochrome P450 3A4 (CYP3A4) isoenzyme and P-glycoprotein (P-gp) efflux transporter.[5] It has a long terminal half-life and a bioavailability of 24% to 88%.[6] It is 10% to 20% renally metabolized, with the remainder a result of hepatic metabolism.[7,8] Peak plasma concentrations can be found 1 hour after administration, and antiinflammatory effects typically occur between 24 and 48 hours after ingestion.[7] The main mechanism of action of colchicine is the inhibition of microtubule activation in rapidly dividing inflammatory cells. It plays a vital role in the treatment of crystal arthropathies through inhibition of the release of glycopeptide crystal–derived chemotactic factor from neutrophil lysosomes after phagocytosis of monosodium urate crystals.[9] However, colchicine has been shown to exist at relatively high concentrations in leukocytes, interacting with adhesion, mobilization, and degranulation of lysosomes.[10] Colchicine's inhibition of leukocyte chemotaxis has further been shown

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in concentrations as low as 1×10^{-8}/L. Recent studies have further shown an inhibition of adhesion molecules on neutrophil membranes, thereby reducing neutrophil transmigration.[8]

Cases of myelosuppression have been reported in studies, particularly with cases of colchicine toxicity from overdose and drug interactions. Other known side effects of colchicine that have been observed are gastrointestinal symptoms with nausea, vomiting, diarrhea, neuropathy, and myopathy.[11,12] An increased rate of infection is not a feature of colchicine use.[13]

This systematic review explores reported cases of myelosuppression with colchicine administration in rheumatic conditions and the circumstances in which they occur. We aim to characterize the demographic and clinical factors associated with the development of myelosuppression, particularly focusing on the preexisting comorbidities and medications that may increase its risk. As the use of colchicine has expanded to include cardiovascular and dermatological conditions, this systematic review hopes to address uncertainties around its use and potential concern over adverse myelosuppressive events. This review aims to clarify the published data to assist physicians when treating and monitoring patients with colchicine.

METHODS

Search strategy. This systematic review was completed in accordance with the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA), as shown in Figure 1. The review was registered prospectively with PROSPERO (CRD42020205707).

A systematic review was conducted using the MeSH terms ("colchicine") AND ("myelosuppression," "bone*," "marrow," "suppression," "aplasia," "leukopenia/leucopenia," "lymphopenia," OR "neutropenia") on September 1, 2020, and was updated on November 30, 2021. The search was conducted in PubMed, ScienceDirect, Scopus, Embase, and Cochrane Library and included references from 1978 to 2020. Demographic details and clinical findings were extracted.

Eligibility criteria. The search was limited to English-language observational studies (ie, case reports, case series, case control studies, and cohort studies) or trial data. Studies were assessed using prospective inclusion and exclusion criteria (Supplementary Table S1, available from the authors upon request).

Intentional therapeutic overdoses as a result of the treatment of disease flares that were given above the maximum recommended daily colchicine dose were included. Two reviewers completed an initial screen of 2705 titles and abstracts to remove exclusions and duplications, with a third reviewer moderating any conflicts. A second screen assessed 95 full-text articles for final inclusion. Two reviewers assessed these full-text articles, with a third reviewer moderating any conflicts.

Data extraction. A total of 30 articles for final inclusion were analyzed, and relevant information was extracted using a prospective data extraction form. Two reviewers were involved in the data extraction, with a third reviewer moderating any discrepancies. Results are presented as numbers and percentages, means and SDs, or medians and IQRs.

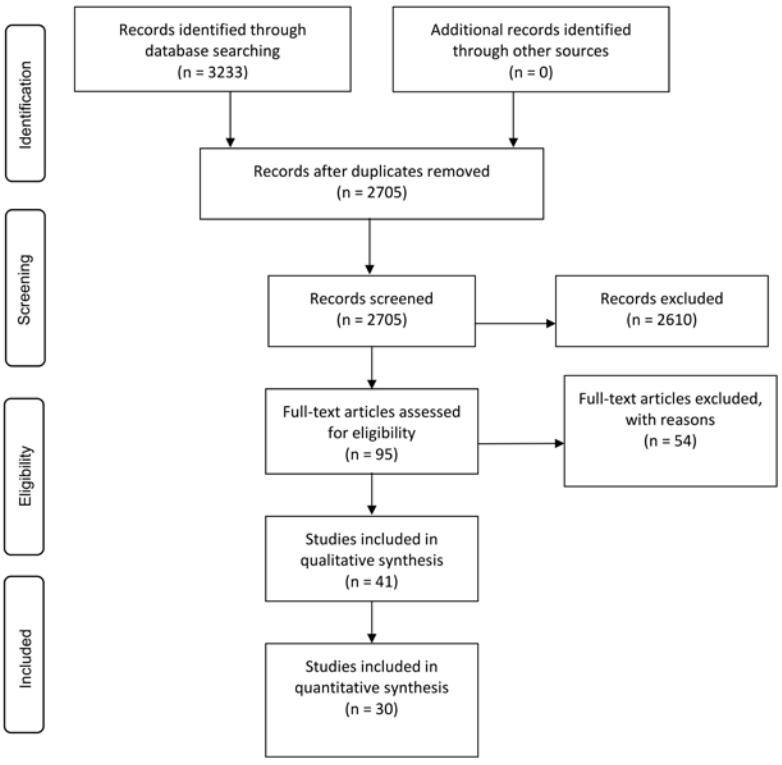


Figure 1. PRISMA flow diagram of studies assessed for colchicine use and myelosuppression. A total of 2610 articles were excluded based on title and abstract, as studies did not include cases of myelosuppression after colchicine use. In total, 54 full-text articles were excluded in the second screen, as patients were put on intravenous colchicine or patients had intentionally overdosed on colchicine. An additional 11 full-text articles were excluded, as data was in qualitative form and could not be extracted for quantitative analysis. PRISMA: Preferred Reporting Items for Systematic reviews and Meta-Analyses.

Myelosuppression was defined as any 1 of the following: leukopenia (< 3000/mm^3), neutropenia (< 1500/mm^3), thrombocytopenia (< 75,000/mm^3), and anemia (< 10 g/dL for female patients; < 13.5 g/dL for male patients).[14]

Grading for myelosuppression was based on previously published scales.[14] The probability of adverse drug reactions was based on the Naranjo Adverse Drug Reaction Probability Scale (Naranjo Scale), where each study was scaled and results were reported as follows: "certain," "probable," "possible," or "unlikely."[15]

Details from the included articles were extracted; these included demographics, comorbidities, renal function, other medications, method of diagnosis, treatment course, and outcome. Hematological outcomes measured were hemoglobin (Hb), white cell count, platelets, and neutrophil counts. These are presented in Table 1 and Table 2.

RESULTS

The initial search results yielded 2705 references. In total, 2610 articles were excluded and 95 were included after the first review of titles and abstracts. After full-text review, 54 references were excluded, leaving 41 articles. A further 11 articles were excluded as a result of qualitative data not being reported adequately or studies that involved intravenous colchicine use. In total, 30 articles comprising 47 patients who had myelosuppression from colchicine were included.[16-45]

Clinical characteristics. Out of the 47 patients reported, 25 (53.2%) were female and 22 (46.8%) were male. These patients had a mean age of 48 (SD 27) years.

Of the 47 patients that had an indication for colchicine listed, 17 used colchicine for gout (36.2%), 16 used it for FMF (34%), 4 used it for arthralgias (8.5%), and 2 used it for Behçet disease (4.3%). The remainder of indications for colchicine can be seen in Table 1.

Table 1. Patient demographics from 30 studies of patients with myelosuppression from colchicine.

	N = 47
Age, yrs, mean (SD)	48 (27)
Sex	
Female	25 (53.2)
Male	22 (46.8)
Ethnicity	
White	8 (17)
Jewish Moroccan or Syrian	1 (2.1)
Turkish	1 (2.1)
Korean	2 (4.3)
Black	1 (2.1)
Italian	1 (2.1)
Not reported	33 (70.2)
Indication for colchicine	
Gout	17 (36.2)
Familial Mediterranean fever	16 (34)
Arthralgias	4 (8.5)
Behçet disease	2 (4.3)
Renal amyloidosis	1 (2.1)
Primary biliary cirrhosis	1 (2.1)
Postpericardiotomy syndrome	1 (2.1)
Pericarditis	1 (2.1)
Active hepatitis	1 (2.1)
Pseudogout	1 (2.1)
Chronic pain	2 (4.3)

Data are in n (%) unless otherwise indicated.

The Charlson Comorbidity Index (CCI) mean score was 3.2 (SD 2.4) across all reported cases and 4.3 (SD 2.2) in those with renal impairment (Table 2). Across the data, the most commonly reported comorbidities included hematological disease, cardiovascular disease, and renal disease.

A total of 21 patients were reported to have chronic renal impairment or acute kidney injury from colchicine drug interactions. Out of 21 patients, 13 (61.9%) were reported to have worsening of their chronic renal impairment during colchicine use.

Other recorded side effects noted were diarrhea (42.6%), abdominal pain (19.1%), vomiting (12.8%), fever (17%), pneumonia (4.3%), erythematous skin eruptions (4.3%), and mental confusion (4.3%; Table 2). Among the patients with renal impairment, other side effects noted were diarrhea (57.1%), abdominal pain (23.8%), vomiting (23.8%), fever (23.8%), pneumonia (9.5%), erythematous skin eruption (4.8%), and mental confusion (9.5%).

Concurrent medications. Out of 47 patients regularly prescribed colchicine, 15 (31.9%) and 13 (27.7%) patients were reported to be concurrently taking CYP3A4 inhibitors and P-gp inhibitors, respectively (Table 2). Out of 21 people who had renal impairment, 8 took both CYP3A4 and P-gp inhibitors. These patients with renal impairment accounted for the majority of overall patients taking these CYP3A4 and P-gp inhibitors (53.3% and 61.5%, respectively).

Myelosuppression. The median average time to myelosuppression from initiating colchicine dosage in addition to a different drug or as a result of a cumulative dose was 7.0 (IQR 4.8-10.5) days (Table 2).

Treatment and outcomes. Presentations ranged in severity. In mild cases, discontinuation of colchicine was sufficient for recovery of cell counts (17/47, 36.2%).

In 10 out of 47 cases (21.3%), administration of granulocyte colony-stimulating factor (G-CSF) was required for profound neutropenia. Of those 10 cases treated with G-CSF, 5 recovered (50%) and 5 died (50%). Indications for colchicine treatment and management outcomes are indicated in Table 1 and Table 2, respectively.

In total, out of 47 patients, 24 recovered and 18 were deceased; however, within the group with renal impairment, 12 out of 21 (57.1%) patients were deceased, whereas 6 out of 21 (28.6%) recovered. Recovery rates in patients with preexisting renal impairment were lower than those without preexisting renal impairment (Table 2).

Treatment outcomes for patients with renal impairment. Patients with renal impairment were classified as those with stated preexisting renal impairment—defined as kidney damage for ≥ 3 months, as defined by structural or functional abnormalities of the kidney, with or without decreased glomerular filtration rate (GFR) or GFR < 60 mL/min/1.73m^2 for ≥ 3 months[46]—or acute kidney injury (AKI) within each study (n = 21).

Across the studies, many studies reported colchicine doses taken prior to myelosuppression because of acute flares that were

Table 2. Patient clinical presentation and investigation results from 30 studies of patients with myelosuppression from colchicine.

	All Patients, n = 47	Patients With Renal Impairment[a], n = 21
Naranjo Adverse Drug Reaction Probability Scale[b]	Possible or probable	Possible or probable
Charlson Comorbidity Index, mean (SD)	3.2 (2.4)	4.3 (2.2)
Investigations, mean (SD), grade		
Nadir Hb, g/dL	10.1 (2.8), grade 1	9.7 (3.2), grade 2
Nadir platelets, $\times 10^9$/L	153.1 (137.8), none	69.0 (38.0), grade 4
Nadir neutrophil count, $\times 10^9$/L	1.2 (1.6), grade 2	0.7 (0.6), grade 3
Nadir WCC, $\times 10^9$/L	8.7 (31.2), none	2.0 (1.8), grade 2
Concurrent medications	CYP3A4	CYP3A4
CYP3A4 inhibitors		
Yes	15 (31.9)	8 (38.1)
No	32 (68.1)	13 (61.9)
P-gp inhibitors		
Yes	13 (27.7)	8 (38.1)
No	34 (72.3)	13 (61.9)
Lead time to myelosuppression, days, median (IQR)	7.0 (4.8-10.5)	7.0 (4.0-10.0)
Regular daily colchicine dose[c], mg, mean (SD)	0.8 (0.8)	0.8 (0.8)
Cumulative colchicine dose taken prior to myelosuppression[d], mg, mean (SD)	3.0 (2.9)	2.5 (2.4)
Duration of myelosuppression, days, median (IQR)	7.0 (4.0-10.8)	7.0 (4.0-9.0)
Hypocellularity on bone marrow aspirate	14 (29.8)	10 (21.3)
Additional side effects		
Diarrhea	20 (42.6)	12 (57.1)
Abdominal pain	9 (19.1)	5 (23.8)
Vomiting	6 (12.8)	5 (23.8)
Fever	8 (17)	5 (23.8)
Pneumonia	2 (4.3)	2 (9.5)
Erythematous skin eruptions	2 (4.3)	1 (4.8)
Mental confusion	2 (4.3)	2 (9.5)
Treatment		
Supportive care	5 (10.6)	3 (14.3)
Ceasing colchicine	17 (36.2)	8 (38.1)
G-CSF	10 (21.3)	6 (28.6)
Gastric lavage and activated charcoal	8 (17)	0 (0)
Not reported	7 (14.9)	4 (19)
End outcomes		
Recovery	24 (51)	6 (28.6)
Death	18 (38)	12 (57.1)
Not reported	5 (11)	3 (14.3)

Data are in n (%) unless otherwise indicated.[a] Patients recorded impaired renal function based on individual study. [b] Likelihood of causality, by the Naranjo Adverse Drug Reaction Probability Scale: probable or definite (≥ 5), possible (1-4), or unlikely (≤ 0).[56] [c] Maximum dose of colchicine is < 3 mg/day in adults.[5] [d] Acute colchicine dose taken during a flare immediately before myelosuppression. Some doses were above the daily recommended colchicine dosage. CYP3A4: cytochrome P450 3A4; G-CSF: granulocyte colony-stimulating factor; Hb: hemoglobin; P-gp: P-glycoprotein; WCC: white cell count.

nearly 3 times greater than their normal daily colchicine dose. The mean cumulative colchicine dose taken prior to myelosuppression was 3.0 (SD 2.9) mg, whereas the group with renal impairment had a cumulative mean dose of 2.5 (SD 2.4) mg. However, the mean daily colchicine dose across all participants was 0.8 (SD 0.8) mg, and that of the group with renal impairment was 0.8 (SD 0.8) mg.

Hematological cell counts. Across the patients, the mean nadir Hb count was 10.1 (SD 2.8) (grade 1), indicating mild anemia. Thrombocytopenia was unremarkable across the studies as a whole; however, patients who had worsening of their preexisting renal conditions or developed AKI as a result of colchicine toxicity had severe thrombocytopenia, as indicated by a mean nadir platelet count of 69.0 (SD 38.0) × 10^9/L (grade 4). The

mean nadir white cell count was 2.0 (SD 1.8) × 10^9/L (grade 2 leukopenia), only in those with renal failure. Across the studies included, the mean nadir neutrophil count was 1.2 (SD 1.6) × 10^9/L (grade 2 neutropenia), whereas the group with renal impairment had worse neutropenia, as seen by a mean nadir neutrophil count of 0.7 (SD 0.6) × 10^9/L (grade 3). Overall, the median duration of myelosuppression was 7.0 (IQR 4.0-10.8) days.

None of the 30 reported studies had severe myelosuppression across all cell lines (defined as Hb < 6.5 g/dL, platelets < 25 × 10^9/L, neutrophils < 0.5 × 10^9/L, and leukocytes < 1 × 10^9/L).[14]

A large portion of myelosuppression cases (15/47, 31.9%) were in patients who concomitantly took CYP3A4 inhibitors, such as clarithromycin and cyclosporine (Table 3). A significant number of these patients (13/47, 27.7%) also took P-gp inhibitors, such as erythromycin and amiodarone (Table 3).

Naranjo Scale. According to the Naranjo Scale, across the studies, colchicine causality was deemed "possible" or "probable." There remains uncertainty as to whether colchicine was the main causative agent of myelosuppression (Figure 2).

An overall representation of colchicine dose taken with or without CYP3A4 inhibitors by patients is represented in Figure 2.

DISCUSSION

To our knowledge, this is the first systematic review to examine published cases of myelosuppression in colchicine use in the context of rheumatic conditions. We identified 30 reports of 47 patients with myelosuppression. Across the 47 studies, there were 15 patients taking CYP3A4 inhibitors and 13 patients taking P-gp inhibitors, suggesting that drug interactions contributed to myelosuppression. Within the group of 21 people with renal impairment, 8 were taking CYP3A4 inhibitors and 8 were taking P-gp inhibitors. Among the 30 reports, the CCI mean value was 3.2 (SD 2.4; Table 2). Notably, 4 patients had febrile neutropenia, although 2 of these patients had chronic renal impairment, whereas 1 patient developed septic neutropenia as a result of coadministration with anakinra.

Although excluded from the study, a study by Sag et al[47] contained pediatric cases that presented a contrast with adult cases, where a decrease in colchicine doses resolved leukopenia. Although information on concurrent medications among these patients was not reported, this provides a comparison to adult cases, where myelosuppression was dependent on comorbidities and use of other medication.

Table 3. CYP3A4 and P-gp inhibitor interacting medications with colchicine in examined cases.

Potency	CYP3A4 Inhibitors Used With Colchicine	P-gp Inhibitors Used With Colchicine
Strong	· Clarithromycin	· Unknown
Moderate	· Diltiazem · Erythromycin	· Unknown
Unspecified potency	· Cyclosporine · Levothyroxine · Amiodarone · Metformin · Omeprazole	· Clarithromycin · Cyclosporine · Erythromycin · Amiodarone

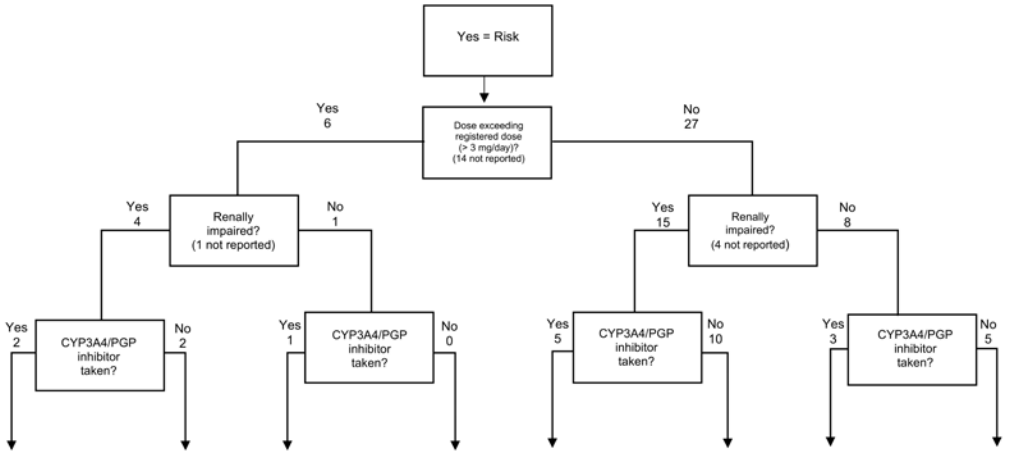
CYP3A4: cytochrome P450 3A4; P-gp: P-glycoprotein.

Among the studies, none of the cases reported severe myelosuppression across all hematological cell lines. Further, patients with the most severe myelosuppression were observed to have taken a higher than recommended colchicine daily dose because of acute flares; in addition, these patients had preexisting renal impairment or were taking CYP3A4 or P-gp inhibitors concomitantly with their dosage of colchicine during the time of myelosuppression (Figure 2). Colchicine has a widely acceptable safety profile within the rest of the patient population. However, there is a need for further monitoring in patients with multimorbidities and those with renal impairment. Many cases represented in the peer-reviewed literature based on the Naranjo Scale indicated an uncertainty as to whether colchicine was the main causal agent of myelosuppression.

Because of the increasing use of colchicine in recent years, it is important to clarify as much as possible the safety of this drug. Colchicine is increasingly being used in cardiovascular conditions and in patients with other comorbidities who also take other medications that may cause drug interactions. Numerous studies involving the use of colchicine in cardiovascular conditions have described its safety and efficacy. As discussed in a study by Andreis et al,[48] hematological adverse events did not increase as a result of using colchicine, and its use was concluded to be safe.

In this study, despite worsening of some cell line counts across the studies, these cases of myelosuppression were particularly concentrated in those with preexisting renal conditions or in those taking other medications as a result of comorbidities, specifically colchicine interactions with CYP3A4 inhibitors, such as clarithromycin and cyclosporine.[49] CYP3A4 metabolism and P-gp inhibitor transport have known interactions with colchicine's oral bioavailability, metabolism, and excretion.[49-51] The use of colchicine with strong CYP3A4 inhibitors, such as clarithromycin, and P-gp inhibitors, such as cyclosporine, should be closely monitored, particularly when patients have comorbidities such as renal or hepatic impairment (Table 3). However, within the general population, only minimal effects of cell counts can be attributed to the use of colchicine alone.

Because of quantitative limitations in this study, the frequency of myelosuppression caused by colchicine use could not be examined. However, the Colchicine Cardiovascular Outcomes Trial from Tardif et al[3] examining the safety of low-dose colchicine in myocardial infarction showed no serious adverse events of anemia, leukopenia, or thrombocytopenia in the colchicine group compared to the placebo group. Further, in the Low-Dose Colchicine trial, Nidorf et al[52] reported that neutropenia and other disturbances to the hematological lines were uncommon in the colchicine group. The frequency of myelosuppressive events in these 2 studies was not significantly increased in the colchicine use group compared to the placebo group, further suggesting that myelosuppressive events are uncommon and



Severity of hematological cell lines								
Thrombocytopenia	Grade 4 (2)	Grade 2 (1), NR (1)	NR (1)	-	Grade 1 (2), NR (3)	Grade 4 (1), Grade 3 (3), Grade 1 (2), None (2), NR (2)	Grade 1 (1), NR (2)	Grade 3 (1), Grade 4 (2), None (1), NR (1)
Neutropenia	Grade 3 (1), NR (1)	Grade 4 (1), NR (1)	Grade 4 (1)	-	Grade 1 (1), NR (4)	Grade 4 (1), Grade 3 (1), NR (6)	NR (3)	Grade 4 (1), NR (4)
Leukopenia	Grade 1 (1), Grade 2 (1)	Grade 4 (1), None (1)	Grade 4 (1)	-	Grade 4 (1), Grade 3 (1), Grade 2 (1), Grade 1 (1), NR (1)	Grade 4 (4), Grade 3 (3), None (2), NR (1)	Grade 2 (2), None (1)	Grade 4 (1), Grade 3 (1), Grade 2 (1), None (2)
Anemia	Grade 2 (1), NR (1)	Grade 4 (1), NR (1)	Grade 2 (1)	-	Grade 3 (1), Grade 2 (2), None (1), NR (1)	Grade 2 (1), Grade 1 (1), None (1), NR (6)	None (1), NR (2)	None (1), Grade 1 (2), NR (2)
Naranjo Adverse Drug Reaction				-				
Definite/probable	2	1	1	-	3	8	1	3*
Possible	0	1	0	-	2	2	2	2
Doubtful	0	0	0	-	0	0	0	0

Figure 2. Cases that took/did not take doses exceeding recommended colchicine dose, with concurrent renal impairment and use of CYP3A4 inhibitor/P-gp inhibitor and corresponding Naranjo Adverse Drug Reaction Probability scores. * Patient was on concurrent azathioprine. CYP3A4: cytochrome P450 3A4; NR: not reported; P-gp: P-glycoprotein.

potentially a result of complicating factors, such as coadministration of interacting medications.

Over the past decade, there has been increasing awareness of safety concerns around the use of some antiinflammatory medication to treat gout flares. This includes side effects from glucocorticoid toxicity and the use of nonsteroidal antiinflammatory drugs, such as exacerbation of hypertension and increased cardiovascular events.[53] As a result, there has been an increased appreciation of the effectiveness of colchicine in the prophylaxis of gout flares preceding the initiation of urate-lowering therapy.[54] As the value of colchicine in acute gout flares is increasingly recognized, there have also been exciting developments of its therapeutic use being explored in cardiovascular and dermatological conditions. With these new developments, there may be concerns among unfamiliar prescribers over the myelosuppressive side effects of colchicine. Results from this review provide reassurance around the lack of myelosuppressive adverse events seen in this case series and other recent, large, randomized controlled trials.

There are limitations to this work. The main limitation is the lack of quantitative data in the studies. This made quantitative data analysis challenging and, as a result, a large portion of these studies were excluded. In addition, most included studies were case reports; therefore, we were unable to examine the rate of myelosuppression with colchicine use.

Collating and assessing the collective experience of adverse event reports is generally considered an effective method for signal detection of rare events. However, broader pharmacoepidemiological studies using data linkage to match full blood count results with prescribing and clinical context may reveal more about the durability of such a signal, particularly as colchicine becomes more widely used in nonrheumatological indications.

In conclusion, traditionally, colchicine continues to be used as the mainstay prophylactic treatment in gout and FMF, among other rheumatic conditions. In recent times, therapeutic uses of colchicine have expanded significantly among nonrheumatological conditions.[55] However, there remains some concern in some clinicians' minds regarding myelosuppression with colchicine use. Our systematic review found that bone marrow suppression generally occurred only in those with preexisting renal conditions, in patients with comorbidities where CYP3A4 and P-gp inhibitors were used in addition to colchicine, and in 1 case of anakinra interaction with colchicine. The doses taken immediately prior to myelosuppression were also higher than the usual prescribed daily doses. We were able to conclude that adverse drug reactions are likely multifactorial.

Colchicine's expanding use and indications, both in rheumatology and nonrheumatological conditions, makes it a unique and important drug for the present and future. This review hopes to overcome any uncertainties over the use of colchicine and enable clinicians to use it with confidence.

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