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Original article

GOSPEL 2 – Colchicine for the treatment of gout flares in France – a GOSPEL survey subgroup analysis. Doses used in common practices regardless of renal impairment and age



Tristan Pascart^{a,b}, Sylvie Lancrenon^c, Sabine Lanz^d, Catherine Delva^c,
 Pascal Guggenbuhl^{e,f,g}, Charles Lambert^h, Jean-Pierre Aubertⁱ, Alain Saraux^j,
 Hang-Korng Ea^{k,l,m}, Frédéric Lioté^{k,l,m,*}

^a Service de rhumatologie, université catholique de Lille, hôpital Saint-Philibert, 59160 Saint-Philibert, France

^b Service de rhumatologie, université Lille 2, hôpital Roger-Salengro, 59037 Lille, France

^c Sylia-Stat, 92340 Bourg-La-Reine, France

^d Laboratoires Mayoly-Spindler, 78400 Chatou, France

^e Service de rhumatologie, CHU de Rennes, 35000 Rennes, France

^f Inserm UMR 991, 35000 Rennes, France

^g Université de Rennes 1, 35000 Rennes, France

^h Laboratoires Ipsen Pharma, 92100 Boulogne, France

ⁱ Université Paris-Diderot, Sorbonne Paris-Cité, EA recherche clinique coordonnée ville-hôpital, méthodologies et société (REMES), 75018 Paris, France

^j Service de rhumatologie, université de Bretagne Occidentale, CHU de la Cavale-Blanche, 29200 Brest, France

^k Université Paris Diderot, Sorbonne Paris Cité, 75205 Paris, France

^l Pôle appareil locomoteur, service de rhumatologie, centre Viggo-Petersen, hôpital Lariboisière, AP-HP, 2, rue Ambroise-Paré, 75010 Paris, France

^m Inserm, UMR 1132, hôpital Lariboisière, 75010 Paris, France

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ABSTRACT

Objectives: The objective of this sub-study was to assess the use of colchicine for the treatment of gout flares in real life conditions in the GOSPEL cohort following the 2006 EULAR recommendations for gout management.

Methods: This national cross-sectional epidemiologic survey included outpatients with gout suffering from acute flare followed by randomly selected primary care physicians ($n=398$) and private practice rheumatologists ($n=109$) between October 2008 and September 2009 in France. Data regarding patient characteristics and treatment prescription was collected by each physician. Glomerular filtration rate (eGFR) was estimated using the Cockcroft-Gault formula. Patients included in the survey for a gout flare filled in a specific self-questionnaire including colchicine effective intake and pain relief (numeric scale).

Results: This analysis focused on the 349 patients presenting with gout flare and treated with colchicine. Mean (\pm SD) prescribed dose of colchicine was 2.8 (\pm 0.7) mg within the first 24 hours and the cumulative dose over the first three days of treatment was 6.9 (\pm 1.8) mg. Patients with mild decline in eGFR (eDFG 60–80 mL/min) were prescribed an average initial dose of 2.8 mg (\pm 0.8) mg ($n=58$), 2.7 (\pm 0.8) mg in chronic kidney disease (CKD) stage 3 ($n=43$) and 2.5 (\pm 0.7) mg in CKD stage 4 ($n=2$). Cumulative doses of colchicine did not take into account either renal impairment or age.

Conclusions: This study draws attention to some misuse of colchicine in daily practice and the prescription of excessive doses especially in case of renal impairment. eGFR should be enforced in daily practice.

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1. Introduction

Colchicine has been the longstanding treatment of acute gout arthritis; however, its use for a long time has relied on experience-based practice rather than on evidence-based medicine until recent advances. Indeed, up to 2006 in France, textbooks and summary of product characteristics (SmPC) advocated the prescription of three milligrams on the first day of treatment of gout

* Corresponding author. Pôle appareil locomoteur, service de rhumatologie, centre Viggo-Petersen, hôpital Lariboisière, AP-HP, 2, rue Ambroise-Paré, 75010 Paris, France.

E-mail address: frederic.liote@lrp.aphp.fr (F. Lioté).

flare, two milligrams on the next two days and one milligram on subsequent days. With the acute gout flare receiving colchicine evaluation (AGREE) trial, Terkeltaub et al. provided strong data regarding the use of low dose (1.8 mg at day 1) of colchicine for acute gout flares at onset [1]. The first randomized controlled trial on colchicine in acute gout [2] essentially revealed correct efficacy of the drug with a poor tolerance profile at high doses (mean dose of colchicine 6.7 mg at day 1). Although its level of evidence has recently been discussed [3], the AGREE trial provided evidence that low dose colchicine permitted equal efficacy with better tolerance than such high doses.

These data further supported the previous 2006 recommendations of the European League Against Rheumatism (EULAR) [4] that advocated limiting colchicine doses to 1.5 mg daily. Further to this study, international recommendations such as the 2012 American College of Rheumatology (ACR) guidelines [5] and the upcoming 2014 EULAR recommendations, more firmly advise prescribing initial low doses of colchicine for gout flares, stressing the risk high doses may entail. In France a pharmacovigilance survey led to a reduction in colchicine dosage to 3 mg at the maximum daily dose after 2009.

However, several studies draw attention to the major discrepancy existing between what is being recommended and the treatments patients are administered in real life conditions [6–9]. Furthermore, data regarding colchicine doses after the first 24 hours of treatment remain insubstantial, and colchicine doses to be used after the first day of treatment in daily practice so far remain unknown.

Colchicine's side effects, especially pancytopenia, rhabdomyolysis or neuromyopathy [10], can prove to be severe and even fatal [11–13]. Drug-drug interactions [14] and comorbidities, especially renal impairment [15], can dramatically modify colchicine pharmacokinetics and accelerate such side effects. Previous studies have shown the relatively restricted knowledge of physicians regarding gout, its comorbidities and treatment, including colchicine [8,9]. No study has so far investigated whether physicians tend to tailor their use of colchicine to meet their patients' profile, especially in cases of renal impairment.

The objective of this study was to provide an assessment of the use of colchicine in France for the treatment of gout flares in real life conditions after the 2006 EULAR recommendations and prior to the publication of the AGREE trial and French National updates.

2. Methods

2.1. Survey design

This survey is part of the GOSPEL survey, completed in 2009, whose design and patient characteristics have been published elsewhere [16]. This national cross-sectional epidemiologic survey included outpatients at least 18 years of age diagnosed by their own physician as being afflicted by gout. Selected physicians participating in the study were primary care physicians (PCPs) and private practice rheumatologists whose demographic distribution and geographic characteristics were representative of the physician population taking care of gouty patients throughout continental France. In short, physicians were invited to include their next two outpatients with gout to take part in the study. Each patient was assessed twice, during the baseline visit on the day they were included in the study, and three to six months later either during a second visit or during a phone call (as determined by each physician). Patients' characteristics, gout history and treatments prescribed were recorded by physicians at the end of the baseline visit. Patients were given two self-questionnaires; the first included a part dedicated to patients suffering from gout flare with data

regarding daily assessment of pain to be returned within 15 days after the baseline visit.

The research project was approved by the French Data Protection Authority (Commission nationale informatique et libertés [CNIL]), and the financial arrangements for remunerating investigators were approved by the French Board of Physicians (Conseil national de l'ordre des médecins).

2.2. Renal function

The assessment of chronic kidney disease (CKD) [17,18] was limited to significant alteration of estimated glomerular filtration rate (eGFR). Stage 2 CKD was not determined given that there was no research for proteinuria, renal imaging, or kidney histology findings. Creatinine clearance estimated by the Cockcroft and Gault formula gave an estimation of the GFR (eGFR). Mild decline in eGFR was defined as a decreased eGFR between 60 and 80 mL/min, stage 3 CKD was defined as a moderate alteration in eGFR between 30 and 60 mL/min, stage 4 CKD expressed a severe decrease in eGFR between 15 and 30 mL/min, and stage 5 CKD relates to kidney failure with eGFR below 15 mL/min [17].

2.3. Colchicine doses

For every single patient presenting with gout flare, each physician wrote down the prescribed dose of colchicine corresponding to each day of treatment of gout flare. Cumulative doses of colchicine prescribed for the first three days of treatment were obtained by adding up each daily dose. Dose adjusted to age was assessed by comparing daily and cumulative doses between age groups (under 55 years of age, between 55 and 65 years of age, between 65 and 75 years of age, and above 75 years of age). Dose adaptation to CKD was assessed by comparing daily and cumulative doses of colchicine prescriptions. The doses prescribed on the first day of treatment were compared to the doses authorized in France at the time of the GOSPEL study and subsequently, according to dose limitations in 2011 up to a maximum of 3 mg on day 1 and considering that prescription above 2 mg for patients older than 75 years or with CKD 3 were inappropriate.

2.4. Treatment efficacy

Treatment efficacy was assessed by using patient daily self-reported pain on a pain severity numeric scale ranging from 0 (absence of pain) to 6 (very severe pain, impairing daily activities and sleep) using a last observation carried forward (LOCF) analysis. Pain relief was considered attained when the level of pain was declared as 0 or 1 (mild pain that can be ignored).

2.5. Statistical analysis

Statistical analysis was descriptive and performed using SAS version 8.2 (SAS Institute, Cary, NC, USA). Qualitative variables were reported as numbers and percentages (%) of each response modality. Quantitative variables were reported as numbers, mean \pm SD.

3. Results

3.1. Treatment of flare and patients' characteristics

A total of 349 patients presenting with gout flare at the time of the visit and treated by colchicine were included in this sub-study, among which 313 were treated by PCPs and 36 by private practice rheumatologists (Fig. 1). Global characteristics of the whole GOSPEL cohort were reported elsewhere [16]. Patients were on average 63.1 (\pm 11.4) years old and 86.5% were male. Among the 349 patients, 23.3% were under 55 years of age, 33.1% between 55 and 65 years,

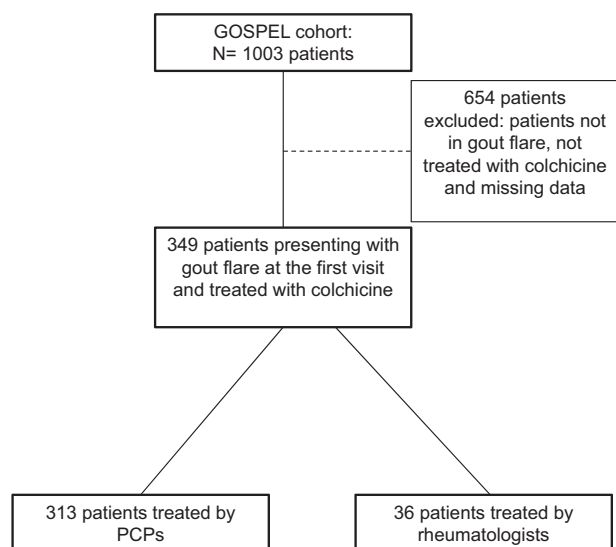


Fig. 1. Flow chart of patients who met inclusion criteria for the sub-study population. PCPs: primary care physicians.

26.5% between 65 and 75 years, and 17.2% at least 75 years. Renal function was only assessed in 264 (75.6%) of these patients, among whom 158 (59.8%) had normal renal function, 59 (22.3%) mild decline in eGFR, 45 (17%) CKD 3, and two patients CKD 4 (Table 1). Among this population, 17.6% of patients presented with tophaceous gout and 69.5% of patients suffered from at least three flares each year.

Gout flare was treated with colchicine as monotherapy by 79.7% of physicians whereas the others prescribed a combination therapy, colchicine with NSAIDs (19.2% of PCPs and 30.6% of rheumatologists). One single physician prescribed an association of colchicine and corticosteroids. Colchicine was prescribed as a single compound (Colchicine®) in 23.2% of cases, or associated with tiemonium methylsulfate and opium (Colchimax®) for 76.8% of patients (78.0% of patients treated by PCPs and 66.7% of patients by rheumatologists).

Table 1

Patients' characteristics of the GOSPEL cohort, of patients seen for gout flare and treated by colchicine in the GOSPEL cohort and patients respectively treated by primary care physicians and rheumatologists for this gout flare.

Patient characteristics	GOSPEL cohort (n = 1003)	Patients in gout flare treated by colchicine (n = 349)	Patients treated by PCPs (n = 313)	Patients treated by rheumatologists (n = 36)
Male	87.8% (879)	86.5% (302)	87.2% (273)	80.6% (29)
Family history of gout	19.2% (191)	17.6% (61)	17.4% (54)	19.4% (7)
Obesity (BMI ≥ 30 kg/m ²)	28.7% (286)	29.6% (103)	30.7% (96)	20.0% (7)
Hypertension	54.5% (543)	49.7% (173)	50.2% (157)	45.7% (16)
Coronary artery disease	8.8% (87)	5.5% (19)	5.1% (16)	9.1% (3)
Diabetes mellitus	14.9% (148)	14.3% (49)	15.2% (47)	6.1% (2)
Dyslipidemia	47.2% (468)	48.7% (169)	50.2% (157)	35.3% (12)
Cerebrovascular accident	3.1% (31)	2.9% (10)	2.9% (9)	3.0% (1)
Age (years)				
<55	24.2% (241)	23.3% (80)	24.3% (75)	14.3% (5)
[55–65[33.0% (328)	33.1% (114)	33.7% (104)	28.6% (10)
[65–75[26.1% (259)	26.5% (91)	25.6% (79)	34.3% (12)
≥75	16.7% (166)	17.2% (59)	16.5% (51)	22.9% (8)
Creatinine clearance: CKD % (n)				
< 15 mL/min: stage 5 CKD	0.1% (1)	0% (0)	0% (0)	0% (0)
[15–30[mL/min: stage 4 CKD	1.3% (9)	0.8% (2)	0.4% (1)	5.0% (1)
[30–60[mL/min: stage 3 CKD	18.2% (127)	17.0% (45)	16.4% (40)	25.0% (5)
[60–80[mL/min: mild RI	23.4% (163)	22.3% (59)	20.9% (51)	40.0% (8)
≥80 mL/min: no CKD	57.0% (397)	59.8% (158)	62.3% (152)	30.0% (6)

BMI: Body Mass Index; CKD: chronic kidney disease; PCP: primary care physician; RI: mild renal impairment; creatinine clearance calculated with the Cockcroft and Gault formula.

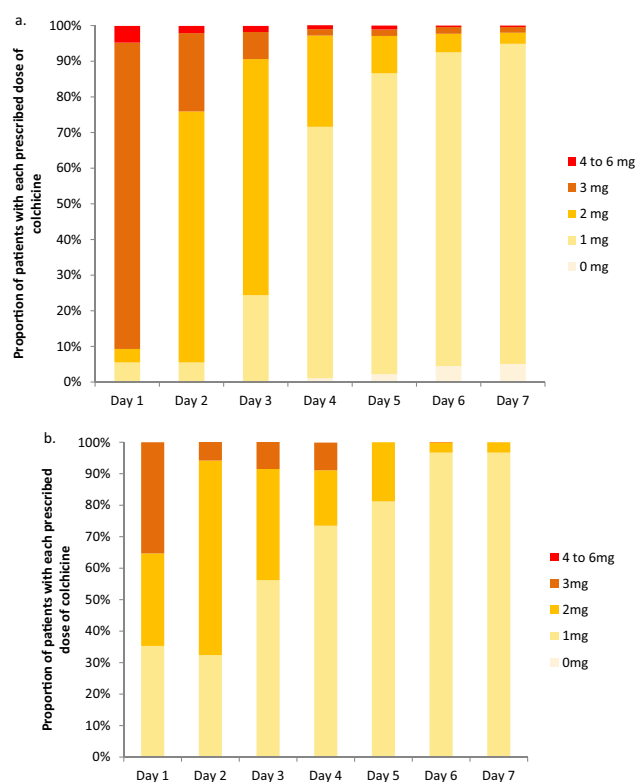


Fig. 2. Proportion of patients being prescribed each daily doses of colchicine on the first seven days of treatment for the treatment of gout flares: a: by primary care physicians (n = 313); b: by rheumatologists (n = 36).

3.2. Colchicine prescription

3.2.1. Initial dosing of colchicine within the first 24 hours

As shown in Fig. 2, initial dose was 1 mg for 8.6% of physicians within the first 24 hours of treatment, 2 mg for 6.5%, and 3 mg was the most common initial dose for 80.6%. Higher doses were uncommon: 4 mg were only prescribed by 2.5% of physicians and 1.8% prescribed a higher loading dose of 5 mg or 6 mg (for six

patients). Average dose usually prescribed by physicians on the first day of treatment was 2.8 (± 0.7) mg. PCPs and rheumatologists showed different prescription patterns, 2.9 (± 0.6) mg and 2.0 (± 0.9) mg, respectively. All prescriptions above 3 mg were made by PCPs. In addition, one-third of rheumatologists (35.3%) did not use loading doses (compared to 5.5% of PCPs) and limited their first daily prescription to 1 mg of colchicine (Fig. 2).

3.2.2. Cumulative doses of colchicine over the first three days of treatment of gout flare

The average cumulative dose of colchicine prescribed over the first three days of treatment was 6.9 (± 1.8) mg, and ranged from 3 to 18 mg. Patients were prescribed a cumulative dose of 7 mg in 56% of the cases, 6 mg in 16%, 8 mg in 13%, and 9 mg in 5% of patients. The mean cumulative dose prescribed by rheumatologists was 5.3 (± 1.6) mg, and 7.0 (± 1.7) mg by PCPs.

3.2.3. Prescription of colchicine over the first week of treatment

Daily prescriptions of colchicine over the first week of treatment are outlined in Fig. 2 for patients treated by both PCPs and rheumatologists. At day 4, 28.2% of physicians prescribed at least 2 mg daily, 13.9% and 5.0% of them still prescribed 2 mg and above at day 5 and day 7, respectively. When comparing both groups of physicians, prescribed doses of colchicine were lower in patients treated by rheumatologists and no daily prescription exceeded 3 mg per day, as opposed to patients treated by PCPs who received prolonged doses above 3 mg per day throughout the week.

3.3. Adjustment of doses to age and renal impairment

3.3.1. Age

The colchicine dose prescribed by physicians within the first 24 hours was 2.9 (± 0.9) mg when patients were under 75 years of age and 2.6 (± 0.7) mg when patients were older. A proportion of 75.5% of patients with an age above 75 years was prescribed at least 3 mg on the first day. Cumulative doses on the first three days of treatment were also equivalent at all ages (Fig. 3a).

3.3.2. Renal impairment

In case of mild decline in eGFR, patients were prescribed an average initial daily dose of 2.8 mg (± 0.8) mg, 2.7 (± 0.8) mg in CKD stage 3 and 2.5 (± 0.7) mg in CKD stage 4. Patients without renal impairment were prescribed an average dose of 2.9 (± 0.6) mg of colchicine on the first day of treatment. Prescribed cumulative doses of colchicine on the first three days of treatment related to renal impairment are reported in Fig. 4. Among the 17.8% patients suffering from stage 3 CKD or worse, 75.6% were prescribed at least 3 mg of colchicine within the first 24 hours. However, 86.0% of patients suffering from stage 3 CKD received a loading dose of colchicine compared to 95.1% in the group of patients with normal renal function. Nevertheless, cumulative doses over the first three days of treatment were similar with 6.5 (± 1.8) mg and 7.0 (± 1.5) mg colchicine, respectively (Fig. 3b).

3.3.3. Combination of age and renal impairment

When combining age and renal function, over the first three days of treatment, patients under 65 years of age and with eGFR above 60 mL/min were prescribed an average cumulative dose of colchicine of 7.0 (± 1.6) mg ($n = 132$). Patients older than or equal to 65 years of age were prescribed an average dose of 6.6 (± 1.7) mg of colchicine when eGFR was below ($n = 42$) and 6.9 (± 1.4) mg when eGFR was above ($n = 68$) 60 mL/min. On the first day of treatment, patients at least 65 years old and with CKD3 were prescribed 4 mg in one case and 3 mg in 76.2% ($n = 32$) of cases. Fig. 4 illustrates the proportion of patients being prescribed doses on the first day of

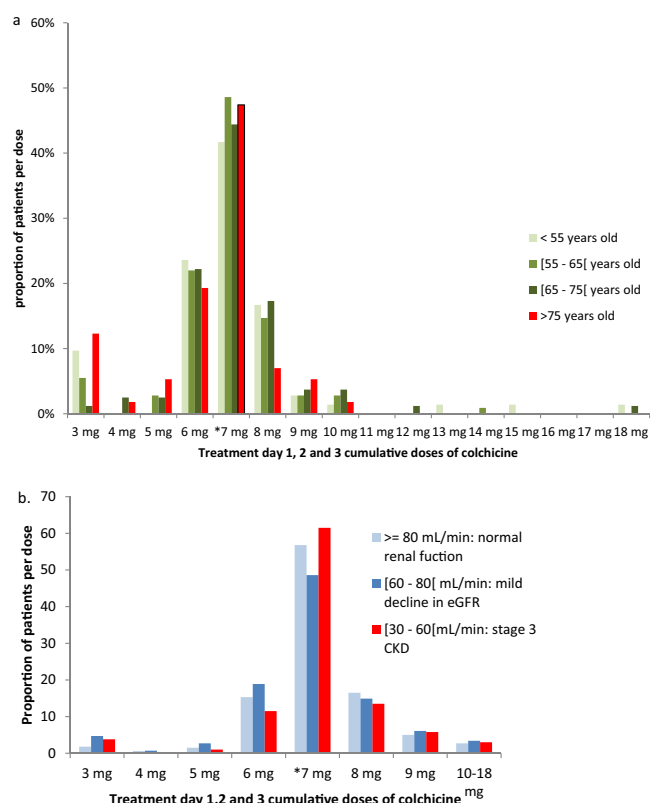


Fig. 3. Cumulative doses of colchicine prescribed on the first three days of treatment of the gout flare according to patients' (a) age and (b) renal impairment. CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate. *Traditional pattern of 3 mg on the first day and 2 mg the next two days used in 2009 in France.

treatment above the dose limitations enforced in 2011. A proportion of 18.6% of prescriptions were inappropriate when taking into account both age and renal impairment.

3.4. Treatment efficacy

On average, treatment with colchicine was administered 40 (± 55) hours after the onset of flare. Patients treated by PCPs commenced their treatment faster (37 [± 40] hours, median 24 hours) compared to those treated by rheumatologists (73 [± 126] hours, median 48 hours).

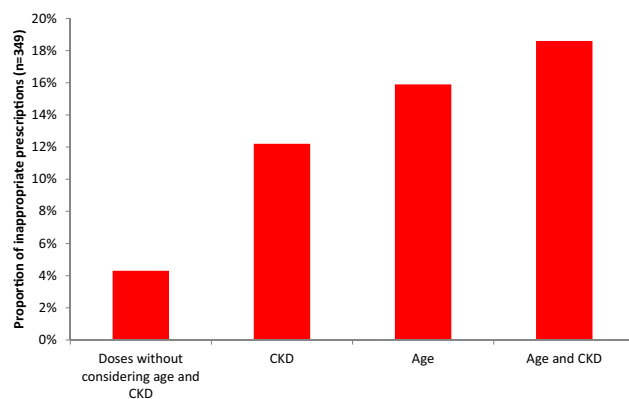


Fig. 4. Proportion of patients receiving doses of colchicine in the first 24 hours of treatment above the doses limitation in 2011 in France without consideration for (i) age (>75 years) or (ii) renal impairment (CKD), taking into account only one or both of them. CKD: chronic renal disease, namely CKD < 60 mL/min.

Before treatment initiation, average pain was 4.9 (± 0.9) cm on the numeric pain scale. Average pain on day 2 was 3.6 (± 1.3) cm, 2.7 (± 1.4) cm on day 3, 1.4 (± 1.2) cm on day 5, and 0.8 (± 1.0) cm on day 7. Pain relief was achieved for 4.5% of patients on day 2, 20.4% on day 3, 56.6% on day 5 and 79.0% on day 7. At the end of the first week 42.4% of patients treated by rheumatologists complained of chronic pain compared to 18.5% for those treated by PCPs.

3.5. Tolerance

Amongst side effects reported by patients, dyspepsia affected 49.7% of patients (severe in four cases), 40.4% patients complained of nausea (severe in four patients), 10.0% of patients reported vomiting (severe in one); 10.5% of patients had constipation, and abdominal discomfort was reported by 69.5% (severe in 10 patients), stomach ache affected 38.0%, pyrosis was reported by 26.2% (severe in two patients). Diarrhea affected 76.1% of patients (slightly for 98, mild for 129, and severe for 31). At the final visit, treatment was reported to have been discontinued due to such side effects in only five cases, and dose was decreased in one (68 missing patients).

4. Discussion

This survey provides an overview of the use of colchicine for the treatment of acute gout flares. The prominent results relate to the high doses of colchicine usually prescribed by French physicians in 2009, in particular to elderly patients and those with renal impairment.

This survey was carried out three years after the 2006 EULAR recommendations for the management of gout [4], and one year before publication of the AGREE trial [1]. The way treatment was prescribed at the time of the study was consistent with European and French regulatory agencies that still recommended loading doses of 3 mg a day and authorized up to 4 mg of colchicine daily intake. Therefore, only 1.8% of patients received colchicine dosage above the maximum dose authorized in France at that time, and 4.3% taking current 2015 national recommendations into account. The maximal daily dose was finally limited to 3 mg in France in September 2011 (following a dear doctor letter from the French pharmacovigilance Authorities) as well as recommendations to limit doses in cases of age above 75 years and CKD 3.

With respect to the new 2012 ACR and the 2014 EULAR recommendations recently presented [19], only 14% received less than 2 mg colchicine on day 1, as evidenced by the AGREE trial and the new FDA recommendations. Colchicine's efficacy in controlling gout flare is known to be significant if the first intake takes place in the first 36 hours (if possible within the first 12 hours from onset). This could account for the difference in initial doses prescribed by PCPs since rheumatologists, as subspecialists, tend to see their patients after the onset of flare. However, given the median of 48 hours delay for rheumatologists, one could have expected a greater proportion of patients not treated by a loading dose above 1 mg. The late initiation of colchicine could explain why flares affecting patients treated by rheumatologists were less successfully treated within the first week of treatment than those treated by PCPs. Another plausible explanation for the better outcome of treatment of patients followed-up by GPs is that patients treated by rheumatologists were in average older and with more severe renal impairment.

No strong data has been provided so far regarding the doses of colchicine that should be used after the first day of treatment, although recent guidelines tend to argue for their reduction [5]. Doses recommended at the time by the French regulatory agency by means of the SmPC for the treatment of gout flares was 2 mg

of colchicine daily on the second and third day of treatment and 1 mg subsequently. One cannot help but feel concerned about the immoderate 6 mg doses being prescribed daily and the high doses being sustained thereafter as observed in our cohort. Such a treatment could end up being hazardous for patients. However, by chance no serious intoxication was reported in this cohort given the high doses patients had been prescribed.

This survey also points out the fact that, in France, colchicine is rarely used solely by itself. It was almost systematically associated with anticholinergic and opioid compounds (in France with tiemonium methylsulfate and opium). Tiemonium methylsulfate is associated with colchicine to prevent gastrointestinal (GI) side effects and, therefore, to improve treatment maintenance. The use of such compounds in patients at risk of developing serious side effects remains a moot point, with a risk of overlooking diarrhea as the first sign of colchicine toxicity [20] although this data is still debatable as intoxication in such a situation might not be as severe. Many patients in our study had CKD and were therefore at risk of developing more severe colchicine intoxication. The overuse of anti-cholinergic drugs in our cohort could also have led to severe adverse effects in patients where treatment was maintained and GI symptoms were not taken into account.

The analysis of both daily and cumulative doses clearly reveals the differences between traditionally prescribed doses of colchicine for gout flares and the low doses that proved sufficient in the AGREE trial a year later [1], although these results have recently been debated in a Cochrane review [3]. However, these low doses (1.5 mg on day 1) had already been advocated by the EULAR three years earlier and had clearly not been implemented, especially in general practice [4]. This raises the issue of how international guidelines [5,21] are being disseminated throughout the world and the effective change they can bring in daily care.

The use of colchicine with patients with renal impairment is not well established [5]. However, it is a well-known fact that they are responsible for major pharmacokinetics modifications and can trigger severe side effects at usual doses [15,22]. The striking evidence provided by this GOSPEL 2 sub-study is the gap between inappropriate colchicine dosage and renal impairment. In addition, colchicine was prescribed in two cases of CKD stage 4, not taking into account French recommendations. The GOSPEL 1 survey had already demonstrated that a low total of 5.2% of gouty patients had only been identified by their physicians as being affected by CKD, whereas after creatinine clearance calculation (Cockcroft–Gault formula), it appeared that 42% percent of patients were suffering from a mild decline in eGFR to moderate/severe CKD. This reinforces the presumption that physicians do not use equations for the estimation of GFR which are easily available nowadays [23]. Ethnicity was unavailable in the GOSPEL collected data, thus renal function could not be assessed using the MDRD formula, which would probably have revealed more severe CKD than those estimated by the Cockcroft–Gault Formula. The CKD-EPI equation offering the most accurate assessment of CKD [24] could not be used for the same reason. Moreover, nearly one-quarter of patients did not have their renal function monitored. Indeed, current results corroborate the fact that our results related to colchicine over-prescription with respect to renal impairment are probably under-estimated.

Our study advocates the need to generalize the prescription for laboratory testing of eGFR rather than doing so exclusively from serum creatinine levels; hopefully nowadays many laboratories systematically provide one to three mentioned eGFRs. This is essential to provide an accurate estimation of renal function, identify patients with CKD, and adapt colchicine prescription accordingly. However, progress seems to have been made as rheumatologists already reduced their prescription of colchicine. This is further reassuring as they tend to take care of patients with more severe renal impairment.

Recently, the French regulatory agencies recommended reducing doses of colchicine with patients over 75 years of age, which is apparently not always respected in daily practice. Oral corticosteroids are an alternative to colchicine in that the CKD setting still seemed underused at the time of the GOSPEL study.

A limitation to our study is that data are only related to prescription habits of a single country. Comparative data between neighbouring countries [25,26] revealed disparities in pharmacologic prescriptions. Our results might therefore have been quite different had the study been performed in another country. However, several studies tackled the issue of the limited knowledge of physicians regarding gout and its management [6–9], suggesting probably similar results of the same study performed elsewhere. It should be recalled that NSAIDs are preferred for the treatment of acute gout in many North European countries compared to South European countries.

Drug-drug interaction is a key issue when using colchicine with patients presenting such comorbidities. Indeed, statins can trigger muscle impairment during colchicine treatment [27,28]. Macrolides and pristinamycin should also be strictly avoided as indicated by Terkeltaub's study [14] and this key point has been recalled by the French pharmacovigilance authorities in a dear doctor letter. This specific issue was not addressed in the GOSPEL study.

The pattern of colchicine prescription by French physicians in 2009 underlines the decisive advances brought about by the AGREE trial [1] and consecutive international guidelines. Our study further emphasizes how potentially damaging the side effects of colchicine can be, all the more so since they are being underestimated by physicians. Our investigation also draws attention to the effectiveness of prescribing lower doses of this drug as advocated by Terkeltaub et al. [1], as well as ACR and EULAR recommendations [4,5]. Subscribing to this approach could lead to a profitable decrease in colchicine over-prescription. However, the discrepancy between everyday practice and the 2006 EULAR recommendations, together with the further necessity for French regulatory agencies to warn physicians to be consistent in their prescriptions of colchicine (2011 and 2013), demonstrate that little has changed in the way treatments are still being handled. Such a study underlines the guidance needed regarding colchicine prescription that was updated in recent international guidelines. Implementation of such major recommendations and quality indicators are key issues in daily practice. However, general practitioners can hardly be expected to keep up to date with international guidelines published in specialized journals. National regulatory agencies are essential to communicate such guidelines. In 2009 in France, no caution was suggested in case of renal impairment or age above 75 years. In 2014 in the SmPC, a 3 mg dose on the first day is still allowed and guidance in case of renal impairment and an elderly patient remains vague. Although this survey brings to light that colchicine use in clinical practice is far removed from international guidelines and published data, practitioners rarely cross the threshold of doses authorized by their regulatory agency. We highlight that encouraging national regulatory agencies to update their guidelines is essential to promoting better use of colchicine, especially in elderly and CKD patients.

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Disclosure of interest

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C. Lambert: employee of Ipsen Pharma.

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