Medication Errors with the Use of Allopurinol and Colchicine: A Retrospective Study of a National, Anonymous Internet-Accessible Error Reporting System

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ABSTRACT. ***Objectives***. To more closely assess medication errors in gout care, we examined data from a national, Internet-accessible error reporting program over a 5-year reporting period.

Methods. We examined data from the MEDMARX™ database, covering the period from January 1, 1999 through December 31, 2003. For allopurinol and colchicine, we examined error severity, source, type, contributing factors, and healthcare personnel involved in errors, and we detailed errors resulting in patient harm. Causes of error and the frequency of other error characteristics were compared for gout medications versus other musculoskeletal treatments using the chi-square statistic.

Results. Gout medication errors occurred in 39% (n = 273) of facilities participating in the MEDMARX program. Reported errors were predominantly from the inpatient hospital setting and related to the use of allopurinol (n = 524), followed by colchicine (n = 315), probenecid (n = 50), and sulfinpyrazone (n = 2). Compared to errors involving other musculoskeletal treatments, allopurinol and colchicine errors were more often ascribed to problems with physician prescribing (7% for other therapies versus 23–39% for allopurinol and colchicine, $p < 0.0001$) and less often due to problems with drug administration or nursing error (50% vs 23–27%, $p < 0.0001$).

Conclusion. Our results suggest that inappropriate prescribing practices are characteristic of errors occurring with the use of allopurinol and colchicine. Physician prescribing practices are a potential target for quality improvement interventions in gout care. (J Rheumatol 2006;33:562–6)

Key Indexing Terms:
GOUT MEDICATION ERROR ALLOPURINOL COLCHICINE QUALITY OF CARE

Gout is a chronic health condition that commonly affects older adults with comorbid illnesses[1], rendering these patients even more vulnerable to the complications of medication errors. Prior studies have shown that gout-specific medication use (i.e., allopurinol and colchicine) is often inappropriate[2-6] and, in some cases, leads to patient harm and death[3,4]. These reports underscore the need for efforts to reduce or hopefully eliminate gout medication errors and suggest that physician prescribing practices may be a central target in future quality improvement initiatives. Indeed, medication errors account for a substantial proportion of all medical errors in the USA[7].

However, before systematic efforts to improve the quality of gout care can be undertaken, more must be learned about the source and type of errors that accompany the use of gout therapies. To better characterize errors complicating gout care, we examined data from a national error reporting program and assessed the frequency and details of patient-level harm occurring as a result of reported gout medication errors.

MATERIALS AND METHODS

MEDMARX Database. Introduced by the United States Pharmacopeia (USP, Rockville, MD, USA) in 1998 as a subscription service, MEDMARX is an Internet-accessible error reporting program designed for use by hospitals and healthcare systems throughout the USA[8,9]. This database currently contains more than 850,000 medication error records with about 20,000 errors reported to the database monthly[8]. Subscribing facilities are able to collect, analyze, compare, and disseminate their medication error data as a means of improving quality of care. Healthcare personnel at participating sites (including physicians, nurses, pharmacists, and other ancillary providers) voluntarily and anonymously enter data as they become aware of a medication error. MEDMARX collects data on medication errors by guiding the user through a series of required and optional data fields. For most data fields, users are given a list of possible selections from which to choose.

Data fields include error severity, origin of error, type of error, contribut-

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ing factors, and healthcare personnel and/or products involved. For most data fields, users are allowed to select multiple responses that might apply for that particular report. Error severity is categorized using the National Coordinating Council for Medication Error Reporting and Prevention index (A through I), where ratings of E through I are indicative of patient-level harm[10]. Origin of error identifies where the medication error occurred in the medication-use process. The 5 nodes include prescribing, documenting/transcribing, dispensing, administering, and monitoring. MEDMARX users can report one or more types of errors from a list of 14 different types (i.e., wrong patient, wrong time, omission, etc.). Likewise, the contributing factors field includes an 18-item list of possible selections (i.e., poor lighting, workload increase, emergency situation, etc.).

We examined MEDMARX error data for the 5-year interval covering January 1, 1999 through December 31, 2003. Data were abstracted for errors related to the use of gout-specific products including allopurinol, colchicine, probenecid, and sulfinpyrazone. To examine whether errors occurring in the context of gout care were similar to those observed in the context of other musculoskeletal conditions, we also abstracted error data for nonsteroidal antiinflammatory drugs (NSAID; ibuprofen, celecoxib, rofecoxib, naproxen, indomethacin, valdecoxib, meloxicam, salsalate, diclofenac, etodolac, nabumetone, piroxicam, flurbiprofen, sulindac, oxaprozin, diflunisal, fenoprofen, and tolmetin), bisphosphonates (pamidronate and zoledronic acid), and disease-modifying antirheumatic drugs (DMARD; hydroxychloroquine, leflunomide, penicillamine, etanercept, aurothioglucose, auranofin, gold sodium thiomalate). We excluded errors associated with either methotrexate or sulfasalazine since these drugs are commonly used in the treatment of non-musculoskeletal conditions (i.e., malignancy or inflammatory bowel disease).

Analysis. The chi-square statistic and Fisher's exact test, when appropriate, were used to compare error characteristics (harm rate, error source, etc.) of gout-specific medications with medicines used for other musculoskeletal disorders. We limited our comparisons involving gout treatments to allopurinol and colchicine since there were only a limited number of errors reported for probenecid (n = 50) and sulfinpyrazone (n = 2). All analyses were performed using SAS v8.2 (Cary, NC, USA).

RESULTS

During the 5-year retrospective period, there were a total of 582,397 medication errors from 701 unique healthcare facilities across the USA recorded in MEDMARX. Of these errors 891 (0.15%) were related to the use of gout-specific medicines, occurring in 874 individual patients. More than one-half of these errors (57%) involved inpatients and 13% involved outpatients (source of care was not coded in 30%). Gout medication errors were observed in more than one-third (n = 273, 39%) of participating facilities. Of all the reported errors related to gout-specific medications, the most frequently reported error was with allopurinol (n = 524 reports) followed by colchicine (n = 315), probenecid (n = 50), and sulfinpyrazone (n = 2). During the same 5-year period, there were 2246 medication errors (n = 2098 or 93% from NSAID) reported with medicines used for other musculoskeletal conditions (NSAID, DMARD, and bisphosphonates).

Characteristics of errors occurring with allopurinol, colchicine, and other musculoskeletal medicines are summarized in Table 1. Medication errors involving allopurinol and colchicine were significantly more likely than other medication errors to be attributable to problems associated with prescribing and were less frequently due to problems with drug administration. Compared to errors occurring with other treatments, physicians were more commonly implicated in gout medication errors (7% vs 23–39%, $p < 0.0001$), while nursing staff were less often responsible for these errors (50% vs 23–27%, $p < 0.0001$). Consistent with the origin of errors, prescribing error was identified more commonly as the specific type of error with both colchicine (19%) and allopurinol (17%) compared to with other musculoskeletal medicines (7%, $p < 0.0001$ for difference). We observed no difference in the frequency of different contributing factors with the use of gout medications compared to errors occurring with other medications.

Of the total errors attributed to physicians, detailed reports were available for 91 (83%) of the allopurinol and 107 (88%) of the colchicine errors. For allopurinol, the most commonly identified physician errors included incomplete or illegible orders (48%), followed by excessive dosing (25%). Of 23 patients given excessive allopurinol doses, 17 were noted to have impaired renal function. For colchicine, the most common physician errors included excessive dosing (56%), followed by incomplete or illegible orders (31%). Of 60 patients receiving excessive colchicine doses, 34 had documentation of renal impairment, and 3 patients without documented renal dysfunction were prescribed excessive intravenous doses.

Errors resulting in patient harm were slightly less common with gout-specific medications (0.6% of allopurinol-related errors and 1.6% of colchicine errors) than with other musculoskeletal medications (2.1%). There were 3 errors with allopurinol and 5 errors with colchicine resulting in patient harm. These errors are detailed in Table 2. Of the 5 reported errors leading to harm with the use of colchicine, 2 were related to the mistaken use of clonidine (an antihypertensive agent) instead of colchicine, and 2 were secondary to excessive drug dosing.

DISCUSSION

Despite their availability as gout treatments for more than 40 years, errors with allopurinol and colchicine remain widespread, affecting more than one-third of facilities participating in a national medication error reporting program. In contrast to errors occurring with other musculoskeletal disease treatments, gout medication errors (occurring predominantly in the inpatient hospital setting) are more often ascribed to physicians and errant prescribing practices and less often related to drug administration or nursing personnel.

To our knowledge, this study represents the first comprehensive effort to detail the origins and types of error occurring with the use of gout treatments. Although other investigators have shown that inappropriate prescribing practices are commonplace in gout, previous studies have not provided a detailed understanding of medication errors (i.e., personnel involved, contributing factors, harm rates, and error type and origin). Detailed insight into these errors is a necessary prerequisite before any effective remedial action can be taken. Our results extend prior observations suggesting that physi-

Table 1. Characteristics of errors occurring with the use of allopurinol, colchicine, and other musculoskeletal medications: results from MEDMARX database (January 1, 1999 to December 31, 2003). Values are number (%).

	Allopurinol (n = 524)*	Colchicine (n = 315)*	Other MSK Medicines† (n = 2246)	p Allopurinol vs Other	p Colchicine vs Other
Error resulting in patient harm	3 (0.6)	5 (1.6)	48 (2.1)	0.02	0.52
Origin of error	N = 437	N = 289	N = 2246		
Prescribing	99 (23)	112 (39)	208 (9)	< 0.0001	< 0.0001
Transcribing/documenting	119 (27)	72 (25)	537 (24)	0.14	0.71
Dispensing	150 (34)	57 (20)	627 (28)	0.007	0.003
Administering	75 (17)	46 (16)	860 (38)	< 0.0001	< 0.0001
Monitoring	0 (0)	2 (0.7)	14 (1)	0.15	0.70
Type of error‡	N = 381	N = 226	N = 2160		
Omission error	92 (24)	63 (28)	616 (29)	0.06	0.74
Improper dose/quantity	75 (20)	39 (17)	355 (16)	0.12	0.75
Prescribing error	73 (19)	39 (17)	148 (7)	< 0.0001	< 0.0001
Unauthorized drug	39 (10)	30 (13)	330 (15)	0.01	0.42
Extra dose	27 (7)	7 (3)	239 (11)	0.02	0.0002
Wrong time	23 (6)	14 (6)	226 (11)	0.007	0.04
Wrong patient	21 (6)	12 (5)	243 (11)	0.0007	0.006
Staff responsible for error‡	N = 478	N = 312	N = 2245		
Physician	109 (23)	121 (39)	162 (7)	< 0.0001	< 0.0001
Nurse	130 (27)	73 (23)	1132 (50)	< 0.0001	< 0.0001
Pharmacist	88 (18)	56 (18)	304 (14)	0.006	0.04
Pharmacy Technician	97 (20)	21 (7)	378 (17)	0.07	< 0.0001
Unit secretary/clerk	28 (6)	23 (7)	92 (4)	0.09	0.009
Factors contributing to error‡	N = 263	N = 169	N = 2151		
None, not determined, or not provided	160 (61)	106 (69)	1395 (65)	0.20	0.58
Distractions	51 (19)	25 (16)	434 (20)	0.76	0.09
Workload increase	21 (8)	7 (5)	171 (8)	0.98	0.07
Inexperienced staff	21 (8)	7 (5)	144 (7)	0.43	0.20

* Denotes total number of errors for allopurinol and colchicine, respectively (there were no missing values for error severity); due to missing values, the numbers of observations for error node, error type, staff responsible, and contributing factors are less than the total number of reported errors (number available for each category shown). † Includes NSAID (ibuprofen, celecoxib, rofecoxib, naproxen, indomethacin, valdecoxib, meloxicam, salsalate, diclofenac, etodolac, nabumetone, piroxicam, flurbiprofen, sulindac, oxaprozin, diflunisal, fenoprofen, and tolmetin), bisphosphonates (pamidronate and zoledronic acid), and DMARD (hydroxychloroquine, leflunomide, penicillamine, etanercept, aurothioglucose, auranofin, gold sodium thiomalate). ‡ Characteristics with frequency less than 5 not shown.

Table 2. Allopurinol and colchicine errors resulting in patient harm from the MEDMARX database (January 1, 1999 to December 31, 2003).

Medicine	Harm Severity*†	Description
Allopurinol	F	Allopurinol and azathioprine ordered concurrently; patient developed pancytopenia and neutropenic fever
	F	Patient given unauthorized drugs including allopurinol; precise nature of resulting harm not detailed
	F	Allopurinol given to wrong patient; precise nature of resulting harm not detailed
Colchicine	F	Order for colchicine 0.6 mg every 8 h incorrectly entered as clonidine 0.6 mg po every 8 h; patient developed hypotension requiring fluid resuscitation and dopamine infusion
	E	Patient incorrectly given clonidine 0.6 mg instead of ordered colchicine; patient monitored closely and remained normotensive
	E	Patient given intravenous colchicine that deviated from facility protocol; precise nature of resulting harm not detailed
	E	Colchicine given to wrong patient; patient monitored closely; outcome not detailed
	F	Patient given unordered colchicine for 10 days; patient transferred to higher level of care with hospitalization prolonged by 6–10 days

* National Coordinating Council for Medication Error Reporting and Prevention. NCC MERP taxonomy of medication errors. www.nccmerp.org/pdf/taxo2001-07-31.pdf (accessed December 18, 2005). † A: Circumstances or events that have the capacity to cause error; B: An error occurred, but the error did not reach the patient; C: An error occurred that reached the patient but did not cause patient harm; D: An error occurred that reached the patient and required monitoring to confirm that it resulted in no harm to the patient and/or required intervention to preclude harm; E: An error occurred that may have contributed to or resulted in temporary harm to the patient and required intervention; F: An error occurred that may have contributed to or resulted in temporary harm to the patient and required initial or prolonged hospitalization; G: An error occurred that may have contributed to or resulted in permanent patient harm; H: An error occurred that required intervention necessary to sustain life; I: An error occurred that may have contributed to or resulted in the patient's death.

cian-based interventions are needed in future gout quality improvement efforts. In a large study of elderly patients presenting to an urban academic emergency department, gout was among the leading indications for the receipt of an inappropriate medication[2]. In a separate audit from a large teaching hospital[5], researchers found that more than 80% of all discharge prescriptions for allopurinol deviated from published dosing guidelines[3]. In another study, 22% of hospital patients receiving a new prescription for allopurinol required a pharmacy-based intervention because of either excessive dosing or lack of an approved drug indication[6]. It has been observed that more than one-half of patients who develop allopurinol-related hypersensitivity have been prescribed the agent for the treatment of asymptomatic hyperuricemia[3], a practice without current evidence-based support. In 1988, Wallace and Singer systematically detailed the published experience with severe toxicity resulting from the use of intravenous colchicine[4]. In each case, toxicity resulted from inappropriate drug use, most commonly excessive dosing.

Although allopurinol and colchicine errors led to patient-level harm infrequently in our study, the harm rate (errors leading to harm/total errors) for colchicine (1.6%) was similar to that observed with other musculoskeletal treatments (2.1%) and slightly higher than the 1% rate previously reported with all medications[11]. Despite the existence of dosing guidelines[4], excessive dosing of colchicine persists. In our review of colchicine errors leading to patient harm, 2 of these errors were related to the use of inappropriately high doses of colchicine. This is consistent with our prior observation of excessive and harmful colchicine dosing from another national medication error reporting program (Medication Error Reporting database)[12]. In addition to inappropriate dosing in the MEDMARX database, another repeated error resulting in patient harm was the mistaken administration of clonidine (an antihypertensive agent) in the place of prescribed colchicine, perhaps related to the similarities in the agents' names.

Our results also have implications for future initiatives aimed at reducing or eliminating gout medication errors. Although nonspecific errors in drug administration are common to many medications, our findings suggest that quality improvement initiatives in gout should focus on physician education and optimizing prescribing behaviors. Physician-based interventions that have been used to effectively optimize prescribing behavior with other treatments include computer-based physician order entry, electronic decision support, medication forms, and standardized protocols for drug prescribing and administration[13-15].

Despite the strengths of our methodological approach and the large national sample of medication errors available in this novel dataset, there are limitations to this study. Because the volume of specific medication use is not known for health care facilities participating in MEDMARX, it is not possible to calculate the incidence of specific medication errors. We were not able to comprehensively examine errors with other gout treatments, likely because of the relatively low prescription volume for agents such as probenecid and sulfinpyrazone. Additionally, errors reported to MEDMARX have not been verified for accuracy or completeness. However, the use of standardized definitions and strict reporting protocols serve to increase the internal validity of these reports. As with other spontaneous reporting programs[16], we anticipate that gout medication errors in MEDMARX are subject to substantial underreporting. Despite these limitations, spontaneous reporting programs remain a highly cost-effective means for examining medication error[16] and have provided a framework for other successful error prevention programs[17].

Because MEDMARX error reports most commonly come from the inpatient hospital setting, they may not be generalizable to outpatient management, the context for most gout care. Although gout care occurs mostly in the outpatient setting, the quality of inpatient gout management is still an important issue. It has been estimated that gout affects about 1% to 4% of all hospitalized patients[18]. Compared to ambulatory patients, hospital inpatients are more ill and have greater comorbidity and are therefore at heightened risk for adverse drug complications. In order to place gout treatment errors in an appropriate context, we limited our comparisons to errors occurring with agents used to treat other musculoskeletal conditions (i.e., NSAID, DMARD, and bisphosphonates). It is possible that differences observed with gout medication errors may reflect unique attributes not of allopurinol or colchicine errors but rather those occurring with other treatments. However, this appears unlikely since a previous review of MEDMARX errors occurring over a 3-year period revealed error characteristics for all medications that were similar to our observations with NSAID, DMARD, and bisphosphonates[9].

In a recent survey of general practitioners, an overwhelming majority claimed to be confident in the diagnosis and management of gout[19]. Despite the level of confidence that physicians self-report with gout care, our results suggest that improvements in physician practice and prescribing behaviors should be part of a comprehensive effort aimed at improving quality and reducing medication errors for inpatient gout management. MEDMARX data analysis has been the basis for past preventive efforts aimed at reducing medication errors with other non-gout treatments. Based on these results, similar provider-based interventions (including education and performance feedback) could be employed to reduce gout medication errors in this highly vulnerable population.

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