American Pain Society
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ADVOCACY
PUBLISHED BY ELSEVIER

The Journal of Pain, Vol 12, No 1 (January), 2011: pp 29-40
Available online at www.sciencedirect.com

Analgesic Prescribing Errors and Associated Medication Characteristics

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Abstract: Medication errors involving analgesics, including mistakes in prescribing, are a major contributor to suboptimal therapeutic outcomes and preventable adverse patient events. A systematic evaluation of 2,044 prevented (near-miss) analgesic prescribing errors detected in a teaching hospital was performed to better understand these errors and contributing error-prone analgesic medication characteristics. The overall detected error rate was 2.87 errors per 1,000 analgesic orders, with the error rate more than twice as high in pediatric patients than in adults. Error rates varied widely between drugs, dosage forms, and routes of administration, but there was general consistency of error rates within drug groups with similar characteristics. Commonly prescribed medications were associated with the most errors, but less frequently prescribed agents had higher error rates. A number of factors were found to contribute to errors, and the following characteristics contributed to 40% of errors: availability in dose forms for multiple routes of administration; modified dosage forms; atypical dosage regimens; sound-alike drug names; and analgesics used on an ongoing scheduled basis.

***Perspective:** Identifiable analgesic product characteristics and uses are associated with higher risk for errors. The findings of this study can guide patient and caregiver education, and can be incorporated into medication safety strategies to reduce patient risk from analgesic errors.*

***Key words:** Analgesics, prescribing, errors, adverse events, pharmacists.*

Analgesic medications account for a major proportion of adverse drug events (ADE) in both adult and pediatric hospitalized patients.[4,9,11,28] The high frequency of ADE reported with analgesics reflects the common use of these agents, variable patient response, and the seriousness of adverse events. Previous studies[4,9,11,23] have reported that a significant proportion of analgesic-related ADE are preventable. Medication mismanagement, including overt errors, suboptimal therapeutic use, and inadequate monitoring all contribute to these preventable events.[2,4,5,8,9,11,12,20,23,24,28,29] Errors with analgesic drugs occur in all steps of the medication-use process, with prescribing mistakes a major cause of actual and potential adverse drug events due to these agents.[2,4,6,9,11,12,16,23,24,28] Certain characteristics of medications and their use appear to be problem prone, and analgesic medications as a class possess many of these characteristics.[6,23] Improved understanding of analgesic errors, contributing factors, and problem-prone analgesic medication characteristics should provide information useful in risk-reduction strategies.

Error reporting and analysis has been used to drive safety initiatives in the healthcare setting. Analysis of errors that have occurred but are detected and prevented (near-miss errors) are routinely used in high reliability organizations to monitor and improve processes.[26,27] We examined a large data base of pharmacist-detected and prevented, near-miss prescribing errors to quantify and define analgesic medication-prescribing errors and to identify characteristics and uses associated with increased risk for errors.

Methods

The study was conducted in a 631-bed tertiary care teaching hospital located in Northeastern New York State, and was approved by the institutional review board. At the study hospital, medications are prescribed by handwriting on a standard unformatted blank

Received January 15, 2010; Revised March 19, 2010; Accepted April 21, 2010.

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1526-5900/$36.00

doi:10.1016/j.jpain.2010.04.007

hospital order sheet, or completing standard preprinted order sets and protocols (computer prescriber order entry [CPOE] is not yet available). Medication-prescribing error data was systematically collected over a 5-year period from January 1, 2003 to December 31, 2007, using a previously described error-monitoring process.[15,16] All confirmed analgesic prescribing errors involving inpatients (most written by house staff) detected and corrected by pharmacists during the study period were included. Prescribing errors were defined as wrong drug, wrong dose, wrong frequency, wrong route, wrong dosage form, wrong administration directions, presence of contraindication to prescribed drug, unnecessary/inappropriate duplicative therapy, important drug-drug interaction, wrong patient, and history of significant hypersensitivity-type reaction to the prescribed analgesic. In order to clearly understand errors, additional information was obtained through direct conversation with involved prescribers and pharmacists, and/or review of all available patient medical or pharmacy records. When an order contained more than 1 error, each error was counted as an individual error in the database.

Analgesic medications were classified into groups based on drug class and dosage forms: acetaminophen, oral nonsteroidal anti-inflammatory agents (NSAIDs), combination products, immediate release (IR) oral opioids (all opiates/opioids were classified as opioids for simplicity), long acting/controlled release (LA) oral opioids, transdermal fentanyl, injectable opioids, tramadol, patient-controlled analgesics (PCA), adjunctive agents (represented by gabapentin and pregabalin) when used for pain symptoms, triptan antimigraine agents (sumatriptan at the study hospital), and agents with local analgesic/anesthetic properties used by any route (capsaicin, local anesthetic products and phenazopyridine). Each error was evaluated for the role of global contributing causes: Failure to modify therapy based on patient-specific information; inadequate drug-therapy knowledge; confusion or inappropriate use of a dosage form; improper route, improper dose for route of administration, use of multiple routes of administration concurrently; mistakes in dose calculations and decimal-point placement; a mental slip or failure to execute plan when prescribing; and failure due to use of prescribing nomenclature. A single primary global contributor was assigned for each error. Based on previous observations and literature,[1-15] each error was evaluated for contribution of the following error-prone medication characteristics: Atypical dosing regimen; drug used on an ongoing (not as needed) basis; availability of both parenteral and oral dosage forms; available in modified dosage forms; and sound-alike medication names.

Only errors with the potential to be carried out, and if carried out, had a reasonable potential for adverse patient effects (reduced effectiveness or increased risk for side effects) were included. Assessments of potential adverse outcomes of each error was classified as either serious/severe or significant based on available patient and pharmacologic information regarding risk for adverse events as previously described and validated (Appendix A).[15,16] Error classification and severity rating were determined by consensus among the authors. The number of orders for each analgesic was determined from the hospital's pharmacy computer database. Due to the nature of the data, lack of clinical meaning of small but statistically significant error differences between analgesic drugs, a descriptive data evaluation was utilized. The significance of analgesic error rates between adults and children was determined using chi-square analysis.

Results

A total of 714,290 orders for the included analgesics were reviewed by pharmacists during the study period, with a total of 2,044 (.29%) confirmed prescribing errors detected. A total of 243 cases occurred in pediatric patients accounting for .59% of the 40,996 pediatric analgesic orders. Twenty-two percent of errors (449 errors) were rated as potentially serious or severe, with 63 (14%) of these serious errors occurring in pediatric patients (Table 1).

Types of Analgesic-Prescribing Errors

Examples of analgesic error types are listed in Table 2. The proportion of error types varied between adults and pediatrics, and by analgesic group. Dosing errors (duplicate therapies, over- and under-dosing) accounted for 53.5% of the adult errors but almost three-quarters of pediatric errors. Prescribing to patients with known allergies/cross-allergy risk accounted for 21% of adult errors but only .4% of pediatric errors. Comparing drug groups, overdoses were predominant with triptans (80.6%), local/topical agents (91%), fentanyl patches (58%), and tramadol (62.5%). Allergic-type reaction risk (eg, strong history of hypersensitivity to the prescribed analgesic) was a common error with NSAIDs (39.7%), injectable opioids (35.4%), and IR oral opioids (24.2%). Potentially serious errors were most commonly due to prescribing an analgesic to patients with history of serious hypersensitivity reaction to the specific agent or an agent with high risk for cross-reaction, and overdoses (Fig 1).

Analgesics Involved in Errors and Relative Error Rates

The number of orders written, number of detected errors, and error rates for each analgesic drug group are listed in Table 1. (The number of orders written, number of detected errors, and error rates for each individual analgesic are listed in Appendix B).

Frequency of Errors

Commonly used agents accounted for the majority of errors, while the highest error rates were found with the less commonly prescribed agents (Fig 2). The analgesics involved in errors varied between the adult and pediatric populations. Of the analgesic drug groups overall, the LA opioids (402 errors, 19.7% of total errors), combination drugs (270 errors, 13.2%), injectable opioids (268

Table 1. Analgesic Order Numbers, Prescribing Errors, and Error Rates per 1000 Orders (Rates for Individual Agents Available Upon Request to Author)

Analgesic Group and Analgesic Drug	Adult Orders	Adult Errors	Adult Errors per 1,000 Orders	Adult Serious Errors	Adult Serious Errors per 1,000 Orders	Ped Orders	Ped Errors	Ped Errors per 1,000 Orders	Ped Serious Errors	Ped Serious Errors per 1,000	Total Orders	Total Errors	Total Errors per 1,000 Orders	Total Serious Errors	Serious Errors per 1,000 Orders
Acetaminophen	95,793	51	.53	14	.15	16,507	56	3.39	10	.61	112,300	107	.95	24	.21
NSAIDs	61,739	199	3.22	92	1.49	2,038	30	14.72	5	2.45	63,777	229	3.59	97	1.52
Combination oral analgesics	199,016	222	1.12	48	.24	7272	48	6.60	8	1.10	206,288	270	1.31	56	.27
Tramadol	3,754	48	12.79	2	.53	33	0	0	0	0	3,787	48	12.67	2	.53
Immediate release (IR) oral opioids	17,715	144	8.13	41	2.31	569	17	29.88	5	8.79	18,284	161	8.81	46	2.52
Long acting (LA) oral opioids	8,413	384	45.64	71	8.44	114	18	157.89	4	35.09	8,527	402	47.14	75	8.80
Transdermal Fentanyl	4,083	52	12.74	10	2.45	192	4	20.83	0	0	4,275	56	13.10	10	2.34
Injectable opioids	235,411	216	.92	53	.23	12,944	52	4.02	28	2.16	248,355	268	1.08	81	.33
Injectable NSAID-Ketorolac	25,783	207	8.03	46	1.78	728	11	15.11	0	0	26,511	218	8.22	46	1.74
Patient controlled analgesia (PCA)	11,804	9	.76	5	.42	346	1	2.89	1	2.89	12,150	10	.82	6	.49
Adjunctives Gabapentin/ pregabalin	6,373	97	15.22	1	.16	171	2	11.70	2	11.70	6,544	99	15.13	3	.46
Triptans- Sumatriptan	1,344	97	72.17	2	1.49	71	1	14.08	0	0	1,415	98	69.26	2	1.41
Local Anesthetics / Topical	2,055	75	36.50	1	.49	11	3	272.73	0	0	2,066	78	37.75	1	.48
Total- all drugs	673,383	1,801	2.68	386	.57	40,996	243	5.93	63	1.54	714,279	2,044	2.87	449	.63

Table 2. Examples of Analgesic Medication Prescribing Errors

Error Type	*Example*
Overdose / duplicative therapy	Ibuprofen and celecoxib prescribed concurrently
	Morphine 5 mg intravenously in 5-kg child
	Fentanyl transdermal 50 mcg/hr for acute pain in opiate naïve patient
Allergy	Ibuprofen ordered for patient with well-documented history of aspirin and NSAID allergy
	Morphine ordered in patient with recent and well-documented history of anaphylactoid reaction to morphine
Underdose	Fentanyl 10 mcg intravenously ordered for a 27-year-old 80-kg patient
	Gabapentin 300 mg orally every 8 hours as needed for neuropathic pain
Dosage form	Oxycodone SR 10 mg orally every 4 hours as needed
	Morphine sulfate IR 60 mg orally every 12 hours
Wrong route	Ketorolac 30 mg ordered to be given subcutaneously
	Oxycodone SR ordered per tube
	Sumatriptan 6 mg ordered to be given by intramuscular injection
Wrong drug	Oxycodone LA ordered, morphine LA intended
	Morphine 10 mg orally ordered, methadone intended
Contraindication	Ibuprofen ordered for patient with active upper gastrointestinal bleed
	Ketorolac in patient admitted with acute coronary syndrome

errors, 13.1%), and oral NSAIDs (229 errors, 11.2%) were involved in the most errors. In pediatrics, the injectable opioids (52 errors, 19.8% of total pediatric errors), combination analgesics (48 errors, 18.3%), and NSAIDs (30 errors, 11.4%) were most common. Overall, potentially serious errors most commonly involved oral NSAIDs (97 serious errors, 21.6% of serious errors), injectable opioids (81 serious errors, 18% of serious errors), and oral LA opioids (79 serious errors, 17.6% of serious errors). Pediatric serious errors most commonly involved injectable opioids (28 serious errors, 44.4% of pediatric serious errors) and acetaminophen (10 serious errors, 15.9% of serious pediatric errors). (Table 1, Fig 3).

Rates of Error

The overall error rate was 2.87 errors per 1,000 orders, with a serious prescribing error rate of .63 per 1,000 orders. Error rates were significantly higher in pediatric than adult patients for both total (chi-squared = 144.2, $P < .001$) and serious (chi-squared = 57.1, $P < .001$) errors. The overall pediatric prescribing error rate was 5.93 per 1,000 orders, and serious errors occurred in 1.54 per 1,000 orders (Table 1). Rates of error varied widely between individual drugs, and between drug groups. However, there was general consistency in magnitude of error rate for commonly prescribed drugs within each group (eg, different drugs but with similar characteristics). Of note was the greater error rate with codeine and propoxyphene, either alone or in combination with acetaminophen, compared to other agents in those groups. The high error rates with both agents was due to dosing errors and contraindications for use. Wide variability in error rates between dosage forms of the same medication (ie, IR versus LA oral morphine) was found, while similar dosage forms of different analgesics (ie, LA oxycodone and LA morphine) generally had a similar magnitude of error rate.

The highest individual analgesic error rates occurred with some infrequently prescribed agents—buprenorphine, aspirin-butalbital, and benzocaine. Of the commonly prescribed individual analgesics (>2,000 orders), the highest error rates were found to occur with LA oral oxycodone (47.5 errors per 1,000 orders) and an LA oral morphine (45.28 errors per 1,000 orders). Of the very commonly prescribed analgesics (>10,000 orders), ketorolac injection (8.22 errors per 1,000 orders) had the highest error rate. For pediatric patients, the highest error rates of analgesics prescribed more than once occurred with oral LA oxycodone (7 of the 12 orders had an error).

Comparing drug group error rates, triptans (69.26 errors per 1,000 orders), LA opioids (47.14 errors per 1,000 orders), and local topical anesthetics (37.75 errors per 1,000 orders) had the highest error rates overall. In pediatrics, some very uncommonly prescribed classes had very high errors rates—local/topical anesthetics (273 errors per 1,000 orders), LA oral opioids (157.89

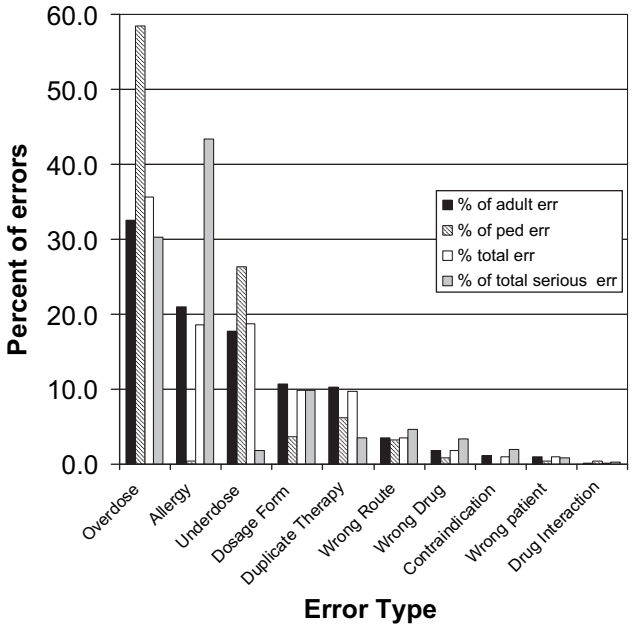

Figure 1. Type of analgesic prescribing error as a percent of total errors.

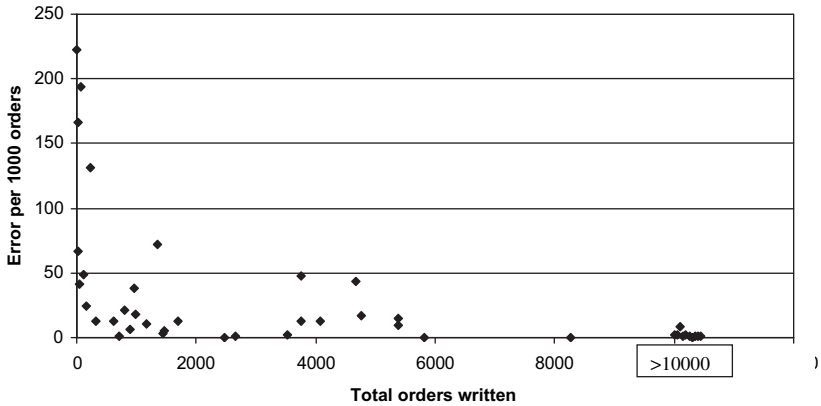

Figure 2. Analgesic prescribing error rate versus number of orders written for each analgesic agent.

errors per 1,000 orders); however, high error rates were also found with the more commonly prescribed IR oral opioids (29.88 errors per 1,000 orders), injectable NSAIDs (15.11 errors per 1,000 orders), and oral NSAIDs (14.72 errors per 1,000 orders). (Table 1, Fig 4)

Analgesic Characteristics and Global Contributing Factors Associated With Errors

Global medication-use system factors contributing to errors also varied between adults and pediatric patients and among analgesic classes. The most common primary global contributor overall, and in adults, was failure to modify therapy based on specific patient characteristics (34.8% of total errors) and lack of drug-therapy knowledge or information (28.4% of errors). In pediatric patients, calculation/decimal-placement errors (46.9% of pediatric errors) were most common. Serious errors were most commonly due to failure to modify therapy based on patient information (48.1% of serious errors overall and 18.9% of serious pediatric errors) and calculation/decimal-point placement (19.6% of serious errors overall and 46.9% of serious pediatric errors). (Fig 5).

The contribution of preidentified specific error-prone characteristics to mistakes overall and to specific analgesic drugs and groups is listed in Table 3. The error-prone characteristics of availability of multiple-dosage forms (10.2% of errors), modified-release dosage forms (9.9% of errors), atypical dosage regimens (7.6% of errors), sound-alike drug and dosage form names (7% of errors), and agents administered on an ongoing (around the clock) basis (6.7% of errors) together contributed to 40.6% of detected errors and accounted for a large proportion of errors for analgesics groups possessing the characteristic.

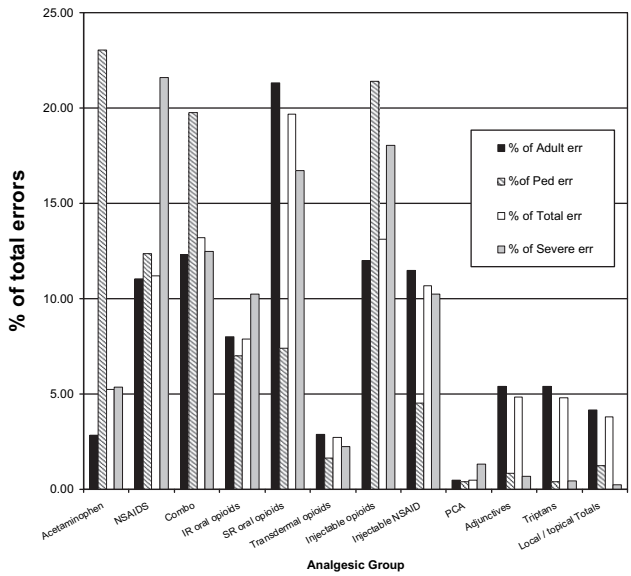

Figure 3. Percent of errors involving each analgesic group.

Discussion

Analgesic medications are commonly involved in errors and subsequent harm in hospitalized patients.[4,9,11,12,23,28] Understanding the causes of errors is a necessary part of designing and testing risk-reduction strategies. This study used a near-miss error-reporting system to provide a level of detail about analgesic prescribing errors not previously available. Consistent with earlier studies, we found failure to consider patient-specific information and inadequate prescriber drug-therapy knowledge to be the primary global proximal causes of error,[2-4] and higher error rates in pediatric patients.[9,12] This study provides substantial quantitative information regarding the contribution of problem-prone medication characteristics and uses to errors.

Problem-Prone Medication Characteristics

Most experienced caregivers are aware of error-prone medications and medication uses. Variable error risk between medications has previously been reported,[15,16,23] strongly suggesting certain drug characteristics and uses contribute to errors. Awareness of error-prone medications often leads to implementation of error-reduction initiatives by individual caregivers or more broadly within the system as a whole. Thus, identifying such characteristics is often a first step to improving

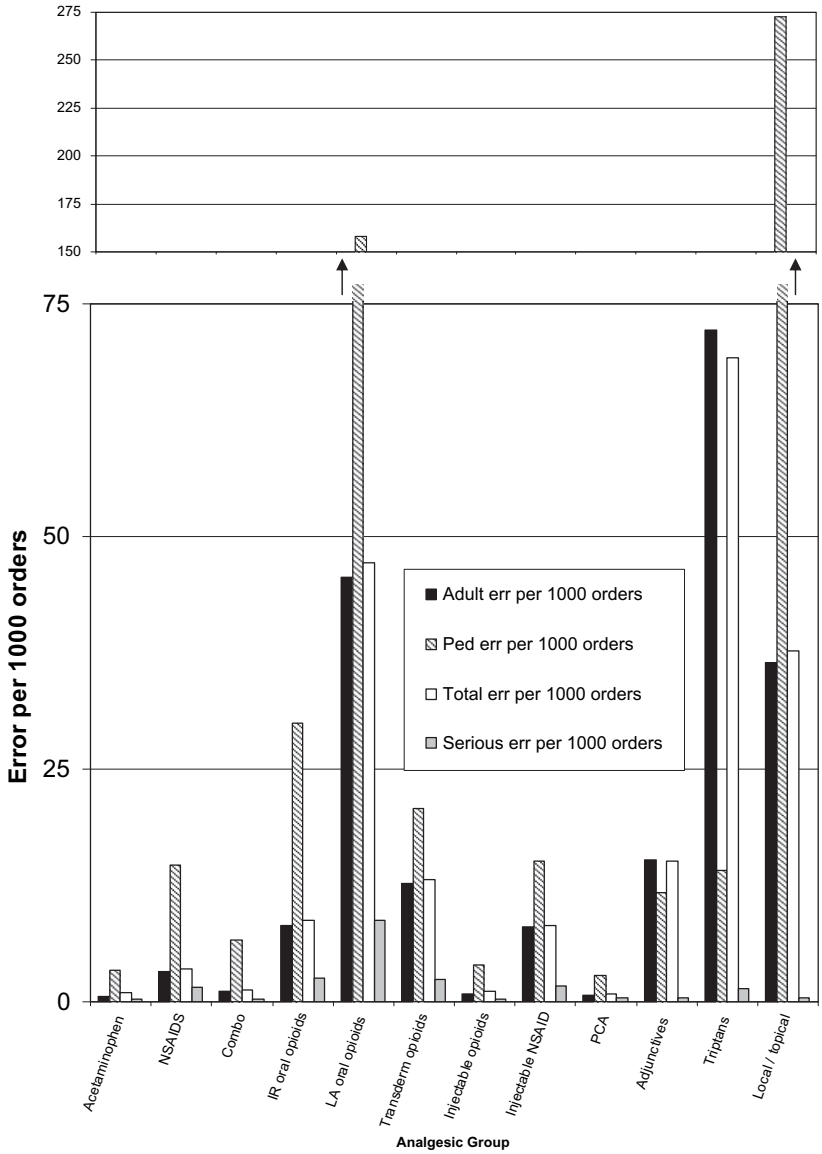

Figure 4. Error rates per 1,000 orders for each analgesic group.

patient safety. It is also helpful to understand the degree to which error-prone characteristics increase risk. We were able to identify clear differences in error rate between analgesic groups based on pharmaceutical characteristics and therapeutic uses. The error-prone analgesic characteristics and uses identified in this study were used in pediatric patients (primarily due to dose-calculation errors and decimal-point misplacement), infrequent use of an analgesic, modified-release dosage forms, the use of atypical dosage regimens, agents administered on an ongoing (around the clock) basis, availability of multiple-dosage forms, and sound-alike drug and dosage form names. These error-prone characteristics appear to compound and contribute to more global causative factors such as lack of patient information or drug knowledge. It is highly likely that a number of the identified error-prone characteristics are not necessarily unique to analgesics and are operative across other drug classes as well.

Infrequently Prescribed Analgesics

Less frequently prescribed analgesics were associated with higher rates of prescribing errors, strongly suggesting that lack of familiarity with analgesics results in greater risk for errors. We have observed higher error rates when new medications are introduced into our organization, or older agents are used in new or uncommon ways. The implications of this finding—most errors occur with commonly used agents, while errors occur at a higher rate with less commonly used agents—has obvious implications for designing risk-reduction strategies.

Modified Dosage Forms

The problem of errors involving modified dosage forms has been reported.[6,18,23] Errors involved both failure to specify the product dosage form and incorrect product use. Poor prescriber understanding of the nature and importance of modified dosage forms is common,

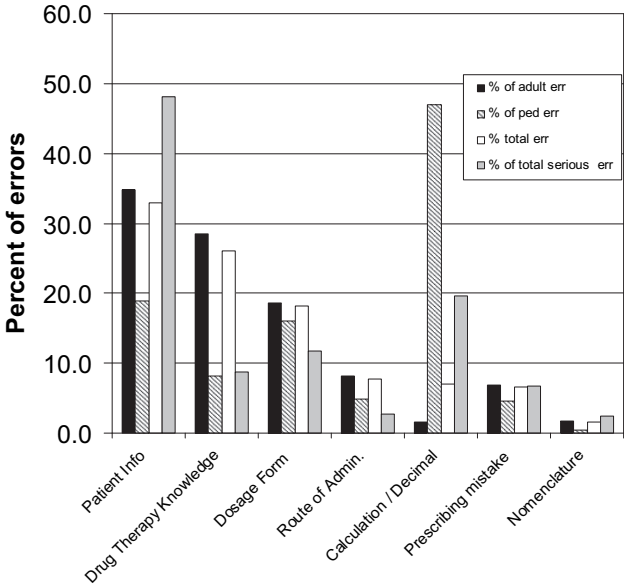

Figure 5. Global factors contributing to errors as a percent of total errors.

leading to error. For example, consistent with the recent Food and Drug Administration communications,[1] we found fentanyl patches ordered in high doses for opioid-naïve patients, use in acute short-term pain, and inappropriately rapid dosage escalation.

Analgesic Dosing Regimens

The vast majority of analgesic prescriptions in hospitals are prescribed as needed for pain at a fixed frequency (eg, every 4 hours as needed), and other regimens are less familiar to prescribers. The contribution of atypical dosage regimens to error was well illustrated by the detected triptan errors (represented by sumatriptan). The most common errors often involved dosing of sumatriptan at a set interval, usually every 6 to 24 hours as needed instead of the appropriate but unusual atypical dosing regimen used for triptans (eg, administering a dose and repeating the dose in 2 hours if response is inadequate up to a daily maximum total dose). Similarly, the unusual dosage regimens for fentanyl patches (every 3 days) and lidocaine patches (recommended to be applied each day for 12 hours and then removed for 12 hours) were commonly ordered in error. A common theme noted for atypically dosed agents was the misapplication of the common dosing pattern of ordering analgesics as needed for pain. Of note was the relatively low error rate for PCA in the study despite having complex and unusual dosage regimens. We attribute low PCA error rates to the mandatory use of a preformatted standardized order sheet for all PCA orders in our organization.

Similar to atypically dosed agents, when ordering medications or dosage forms used for ongoing pain, prescribers again frequently applied, inappropriately, the more common as needed analgesic dosing patterns. The LA opioids, fentanyl patches, adjunctive agents, and capsaicin are all used on a continuous basis and were often inappropriately or inadvertently ordered as needed when prescribing these agents.

Route of Administration

Prescribing errors related to the route of administration and duplicate or redundant analgesics comprise an important proportion of medication errors.[6,18,23] Availability of analgesics that are administered by multiple routes or dosage forms resulted in 3 major types of errors: failure to adjust doses for route of administration; disruption of dosage form when administered by prescribed route; and inappropriate concurrent administration by multiple routes. Analgesics, either the same drug, or a drug in the same class (eg, NSAIDs), were commonly ordered to be inappropriately given concurrently by multiple routes.[12,23]

Look-Alike–Sound-Alike Medication Names

Analgesics are commonly involved in look-alike–sound-alike errors,[6] and it is not surprising such characteristics were found to contribute to higher error rates. Oxycodone was commonly involved due to the similarity of the generic name and the brand name Oxycontin (Purdue Pharma, Stamford, CT). Similar, but fewer errors occurred with confusion between MSContin (Purdue Pharma) and Oxycontin.

Implications for Risk Reduction

There is expanding, though incomplete, information on utility of interventions designed to reduce preventable ADE from medications and specifically for pain medications.[1,2,6,8,13,22,28,29] Recommendations specific to a number of error-prone medication characteristics and uses identified in this study are available, including analgesic use in general,[23] medication use in pediatrics,[8,13,22,29] controlled-release dosage forms,[6,18,23] dosage calculations and decimal-point errors,[6,14,17,28] routes of administration,[6,19] and for sound-alike, look-alike medications.[6] Computerized prescriber order entry (CPOE) systems have been promoted as one solution to the problem of prescribing errors. Such systems have been demonstrated to reduce, but not eliminate, errors and to create some new risks. Even with advanced technologies such as CPOE, other safety-oriented medication-use systems processes and controls, including limiting number of similar medications available for use through formulary controls, and order review by pharmacists and nurses, will continue to be important patient safeguards.[6,8,13,20,23,25,29,30]

On a longer-term basis, efforts to improve analgesic product design, naming, and packaging are necessary systems-based changes to reduce patient risk.[2,6] Marketing and promotional practices also appear to compound inadequate caregiver knowledge.[25] Our experiences strongly support the application of multifaceted safety engineering and design practices into pharmaceutical product development, and the inclusion of safety considerations in product naming and labeling.

Study Limitations

Study limitations include use of a definition of error that differs somewhat from that used by others but one that is consistent with our previous studies over the past 20 years.[14-19] We focused on prescribing errors

Table 3. Analgesic Characteristics Associated With Prescribing Errors and Commonly Involved Analgesic Groups

Medication Characteristic	*Example Error*	*Total Number of Errors Attributed to Characteristic*	*Specific Analgesics and Analgesic Groups With Major Contribution of Medication Characteristic to Errors (% of Orders for Drug With Errors Due to Medication Characteristic)*
Dosage forms available for multiple administration routes	Morphine 2 mg by mouth every 4 hours as needed for pain in an adult	209 errors (10.2% of total errors)	Morphine Injection and IR oral: 87 errors (.06% of orders) Ketorolac injection and oral NSAID: 108 errors (.12% of orders)
Modified dosage forms	Morphine LA 100 mg per feeding tube every 12 hours	202 errors (9.9% of total errors)	Morphine LA: 97 errors (2.03% of orders) Oxycodone LA: 18 errors (.48% of orders)
Atypical dosage regimen	Sumatriptan 25 mg every 6 hours as needed for headache	155 errors (7.6% of total)	Triptans: 84 errors (5.7% of orders) Fentanyl patches: 36 of 56 errors (.84% of orders) Lidocaine patches: 35 errors (3.63% of orders)
Sound-alike–look-alike medication names	Oxycodone 30 mg by mouth every 12 hours (instead of OxyContin)	143 errors (7.0% of total)	Morphine LA: 20 errors (.42% of orders) Oxycodone LA: 114 errors (3.03% of orders)
Analgesics dosed only on an ongoing basis (only appropriate as non–as needed)	Pregabalin 75 mg by mouth every 12 hours as needed for pain	143 errors (6.7% of total)	Morphine LA: 67 errors (1.4% of orders) Oxycodone LA: 44 errors (1.17% of orders) Adjunctive agents: 22 errors (.34% of orders)

with clear patient risks within our organization, and we did not include most very-low-risk processes, rules-based, or missing prescription-component errors, as such errors are consistently stopped from being further processed and medications from being dispensed and administered in our organization. The institution has a robust system for capturing prescribing errors corrected by pharmacists, designed to require minimal effort to report an error. However, error detection was likely not complete in that with more complete pharmacist access to patient information, patient-care teams, and patients, it is likely more cases of therapeutic-mismanagement errors such as undertreatment and unnecessary therapy, could be identified.[9,12,13,22,28,29] This limitation is concerning, as errors in therapeutic decision-making have been reported to have a greater likelihood of producing patient harm than the type of dosing errors found to be so frequent in this study.[28] An additional limitation to consider is changeover time at the study hospital, which included increased use of standardized preprinted order sets, staff education, and medication-system controls.

The use of near-miss error data has a number of limitations as well as advantages.[3,27] Near-miss errors may not accurately reflect those errors which result in actual risk to patients in a specific environment, as patient harm from error is usually the end result of multiple complex systems failures.[10,21] Despite these limitations, near-miss error reporting and evaluation are widely used in high reliability organizations to drive safety efforts.[4,8,9,11,26,27,29] Use of near-miss error reports may be particularly meaningful for analgesics, as 37% of errors with opioids and 15% of nonopioid analgesic errors result in some patient harm, compared to 1 to 5% of prescribing errors in general.[5] As recommended by the Institute of Medicine,[2] a multimodal method of tracking medication errors and adverse events,[6,7,27] including near-miss errors, should be employed on an ongoing basis to monitor and improve medication safety.

The applicability of the study results to other organizations may be limited by differences in medication-systems features such as CPOE and pharmacist deployment. Despite the study limitations, we believe that medication-use processes have many common elements across organizations and the findings of this study are broadly applicable.

Conclusion

Prescribing errors involving analgesic medications are common and present significant risk to hospitalized patients. Errors with analgesic medications are related to identifiable problem-prone factors compounding inadequate consideration of patient-specific information, inadequate prescriber drug-therapy knowledge, and in pediatric patients, errors in dose determination. The information provided should be useful in guiding improvements in analgesic-therapy safety.

Acknowledgments

The authors thank the pharmacists of Albany Medical Center for the identification of errors and reporting of the data.

No specific internal or external funding was used in the completion of this study.

Both authors had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. The authors have no potential conflicts of interest or financial interests to declare.

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Appendix A

Potential Severity Classifications for Order Errors (Adapted from reference 11)

Note: Classification system provides for assigning a generalized, population-based assessment of risk. It is recognized that errors rated as fatal or severe may produce little or no adverse effects in some patients, just as it is recognized that errors rated as significant may produce life-threatening adverse effects in some patients.

A. Potentially Fatal or Severe Adverse Outcomes (cardiovascular arrest, serious arrhythmia, stroke, life-threatening metabolic abnormality, therapeutic failure in life-threatening illness. Example: Tenfold morphine overdose in a nonventilated, opioid naïve patient).
   1. A dose or dose delivery ordered for 10-fold or greater overdose of medication with low therapeutic index.
   2. A dose or dose delivery ordered for a medication with a very low therapeutic index that would potentially produce severe or fatal adverse effects in a substantial proportion of patients.
   3. A drug, dose, or dose delivery ordered which would produce severe or fatal toxicity in a substantial proportion of patients with similar medical characteristics.
   4. A drug, dose, or dose delivery ordered for a medication for a life-threatening illness or severe disorder that would potentially result in therapeutic failure in a substantial proportion of patients.
   5. Drug or dose form ordered to be administered by route or method that would potentially result in fatal or severe toxicity in a substantial proportion of patients.

B. Potentially Serious Outcomes (significant cardiovascular decompensation, metabolic disorder requiring urgent treatment, inadequate, incomplete or significantly delayed therapeutic response in serious or severe illness. Example: Ordering aspirin in patient with history of significant aspirin-induced bronchospasm).
   1. A dose or dose delivery ordered for 4- to 10-fold overdose of medication with low therapeutic index.
   2. A dose or dose delivery ordered for a medication with a very low therapeutic index that would potentially produce serious adverse effects in a substantial proportion of patients.
   3. A drug, dose, or dose delivery ordered which would produce serious toxicity in a substantial proportion of patients with similar medical characteristics.
   4. A drug, dose, or dose delivery ordered for a medication for a serious illness that would potentially result in therapeutic failure or suboptimal response in a substantial proportion of patients.
   5. Drug or dose form ordered to be administered by route or method that would potentially result in serious adverse events in a substantial proportion of patients.

C. Potentially Significant Adverse Outcomes (symptomatic hypotension, metabolic abnormality requiring treatment, suboptimal therapeutic response, gastrointestinal upset, dizziness. Example: Ordering full dose ketorolac around the clock for a patient taking ibuprofen at full analgesic doses around the clock).
   1. A dose or dose delivery ordered for 1.5- to 4-fold overdose of medication with low therapeutic index.
   2. A dose or dose delivery ordered for a medication that would potentially produce some adverse effects in some proportion of patients.
   3. A drug, dose, or dose delivery ordered which would produce adverse effects in some proportion of patients with similar medical characteristics.
   4. A drug, dose, or dose delivery ordered for a medication that would potentially result in reduced, incomplete or delayed therapeutic response in some proportion of patients.
   5. Drug or dose form ordered to be administered by route or method that would potentially result in adverse events in some proportion of patients.

Appendix B. Analgesic Order Numbers, Prescribing Errors, and Error Rates per 1,000 Orders

Analgesic Group and Analgesic Drug	Adult Orders	Adult Errors	Adult Errors per 1,000 Orders	Adult Serious Errors	Adult Serious Errors per 1,000 Orders	Ped Orders	Ped Errors	Ped Errors per 1,000 Orders	Ped Serious Errors	Ped Serious Errors per 1,000	Total Orders	Total Errors	Total Errors per 1,000 Orders	Total Serious Errors	Serious Errors per 1,000 Orders
Acetaminophen	95,793	51	.53	14	.15	16,507	56	3.39	10	.61	112,300	107	.95	24	.21
Oral NSAIDS															
Ibuprofen	58,140	145	2.49	78	1.34	1,980	24	12.12	5	2.53	60,120	169	2.81	83	1.38
Celecoxib	1,687	21	12.45	4	2.37	45	5	111.11	0	0	1,732	26	15.01	4	2.31
Naproxen	807	17	21.07	5	6.20	13	1	76.92	0	0	820	18	21.95	5	6.10
Indomethacin	620	8	12.90	3	4.84	0	0	0	0	0	620	8	12.90	3	4.84
Diclofenac	320	4	12.50	1	3.13	0	0	0	0	0	320	4	12.50	1	3.13
Nabumetone	165	4	24.24	1	6.06	0	0	0	0	0	165	4	24.24	1	6.06
Totals NSAID	61,739	199	3.22	92	1.49	2,038	30	14.72	5	2.45	63,777	229	3.59	97	1.52
Combination products															
Acetaminophen + hydrocodone	113,241	89	.79	27	.24	3,373	10	2.96	2	.59	116,614	99	.85	29	.25
Acetaminophen + oxycodone	67,617	50	.74	8	.12	896	2	2.23	0	0	68,513	52	.76	8	.12
Acetaminophen + Codeine	11,316	23	2.03	5	.44	2,948	32	10.85	6	2.04	14,264	55	3.86	11	.77
Acetaminophen + propoxyphene	5,373	52	9.68	7	1.30	49	2	40.80	0	0	5,422	54	9.96	7	1.29
Acetaminophen + caffeine + Butalbital	1,451	5	3.45	0	.00	6	2	333.33	0	0	1,457	7	4.80	0	.00
Aspirin + caffeine + Butalbital	18	3	166.67	1	55.56	0	0	0	0	na	18	3	166.67	1	55.56
Totals combo	199,016	222	1.12	48	.24	7,272	48	6.60	8	1.10	206,288	270	1.31	56	.27
Tramadol	3754	48	12.79	2	.53	33	0	0	0	0	3787	48	12.67	2	.53
Imediate release (IR) oral opioids															
Oxycodone IR	10,213	27	2.64	8	.78	187	0	.00	0	.00	10,400	27	2.60	8	.77
Morphine IR	4,759	82	17.23	16	3.36	186	11	59.14	2	10.75	4,945	93	18.81	18	3.64
Methadone	1,459	7	4.80	6	4.11	102	3	29.41	3	29.41	1,561	10	6.41	9	5.77
Hydromorphone	1,164	12	10.31	8	6.87	49	0	.00	0	.00	1,213	12	9.89	8	6.60
Codeine	62	12	193.55	1	16.13	45	3	66.67	0	.00	107	15	140.19	1	9.35
Propxyphene	49	2	40.82	2	40.82	0	0	0	0	.00	49	2	40.82	2	40.82
Buprenorphine	9	2	222.22	0	.00	0	0	0	0	.00	9	2	222.22	0	.00
Oral IR Opioids totals	17,715	144	8.13	41	2.31	569	17	29.88	5	8.79	18,284	161	8.81	46	2.52
Long acting (LA) oral opioids															
Morphine SR	4,668	205	43.92	26	5.57	102	11	107.84	4	39.22	4,770	216	45.28	30	6.29
Oxycodone SR	3,745	179	47.80	45	12.02	12	7	583.33	0	0	3,757	186	49.51	45	11.98
LA oral opioids totals	8,413	384	45.64	71	8.44	114	18	157.89	4	35.09	8,527	402	47.14	75	8.80
Transdermal Fentanyl	4,083	52	12.74	10	2.45	192	4	20.83	0	0	4,275	56	13.10	10	2.34
Injectable opioids															
Morphine	120,365	149	1.24	20	.17	10,454	43	.41	22	2.10	130,819	192	1.47	42	.32
Fentanyl	76,681	30	.39	16	.21	1,814	8	4.41	6	3.31	78,495	38	.48	22	.28
Hydromorphone	26,454	25	.95	14	.53	578	1	1.73	0	0	27,032	26	.96	14	.52
Nalbuphine	8,272	4	.48	1	.12	93	0	0	0	0	8,365	4	.48	1	.12
Butorphanol	2,651	2	.75	0	0	2	0	0	0	0	2,653	2	.75	0	0

Appendix B. Continued

Analgesic Group and Analgesic Drug	Adult Orders	Adult Errors	Adult Errors per 1,000 Orders	Adult Serious Errors	Adult Serious Errors per 1,000 Orders	Ped Orders	Ped Errors	Ped Errors per 1,000 Orders	Ped Serious Errors	Ped Serious Errors per 1,000	Total Orders	Total Errors	Total Errors per 1,000 Orders	Total Serious Errors	Serious Errors per 1,000 Orders
Meperidine	988	6	6.07	2	2.02	3	0	0	0	0	991	6	6.05	2	2.02
Injectable opioids totals	235,411	216	.92	53	.23	12,944	52	4.02	28	2.16	248,355	268	1.08	81	.33
Injectable NSAID- Ketorolac	25,783	207	8.03	46	1.78	728	11	15.11	0	0	26511	218	8.22	46	1.74
PCA															
Fentanyl PCA	5,807	2	.34	0	0	68	0	0	0	0	5,875	2	.34	0	0
Morphine PCA	3,516	6	1.71	5	1.42	278	1	3.60	1	3.60	3,794	7	1.85	6	1.58
Hydromorphone PCA	2,481	1	.40	0	0	0	0	0	0	0	2,481	1	.40	0	0
PCA totals	11,804	9	.76	5	.42	346	1	2.89	1	2.89	12,150	10	.82	6	.49
Adjunctives															
Gabapentin	5,385	79	14.67	0	0	169	2	11.83	2	11.83	5,554	81	14.58	2	.36
Pregabalin	988	18	18.22	1	1.01	2	0	0	0	0	990	18	18.18	1	1.01
Adjunct totals	6,373	97	15.22	1	.16	171	2	11.70	2	11.70	6,544	99	15.13	3	.46
Triptans- Sumatriptan	1344	97	72.17	2	1.49	71	1	14.08	0	0	1415	98	69.26	2	1.41
Local Anesthetics / Topical															
Lidocaine patch	962	37	38.46	0	0	1	1	1,000	0	0	963	38	39.46	0	0
Phenazopyridine	720	1	1.39	0	0	0	0	.00	0	0	720	1	1.39	0	0
Benzocaine	221	29	131.22	0	0	3	1	333.33	0	0	224	30	133.93	0	0
Lidocaine PO	122	6	49.18	1	8.20	7	1	142.86	0	0	129	7	54.26	1	7.75
Capsaicin	30	2	66.67	0	0	0	0	.00	0	0	30	2	66.67	0	0
Local / topical totals	2,055	75	36.50	1	.49	11	3	272.73	0	0	2,066	78	37.75	1	.48
Total- all drugs	673,283	1801	2.68	386	.57	40,996	243	5.93	63	1.54	714,279	2044	2.87	449	.63