Original Article

Oral Antineoplastic Handling at Health Care Institutions in the United States: Survey of Nurses and Pharmacists

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Abstract

Purpose: To characterize and identify trends in current practices for ordering, handling, dispensing, administering, and disposing of oral antineoplastics.

Methods: An electronic survey was designed and sent to pharmacists and nurses via professional society listservs.

Results: One hundred and twenty-three practitioners responded to the survey. Of those responding, 76% described having an official policy regarding the handling of oral antineoplastics. Prescribing was limited to attending physicians or oncologists the majority of the time (42% and 98%, respectively), with 11% accepting telephone orders for oral antineoplastics. Personal protective equipment was required by many of the respondents; 70% required gloves be worn. Patient contact precautions were utilized by 79% of practitioners, of which 81% followed similar precautions for targeted therapies. Compounding was required to be performed in a biological safety cabinet by 88% of respondents, and 83% required decontamination of supplies and equipment after exposure to oral antineoplastics.

Conclusion: Although practices varied slightly, the majority of respondents follow available guidance when handling oral antineoplastics.

Key Words—antineoplastic, chemotherapy, handling, hazardous, tyrosine kinase inhibitor

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Many antineoplastic drugs are considered to be high-alert medications by the Institute for Safe Medication Practices (ISMP) and are considered hazardous by the National Institute for Occupational Safety and Health (NIOSH).^{1,2} Traditionally, antineoplastics were administered intravenously and mainly consisted of cytotoxic chemotherapy agents. In recent years, however, more antineoplastic medications have become available in oral formulations. As of 2008, it was reported that approximately 25% of chemotherapy in the pipeline was planned as oral medications.³ Many of these oral drugs are no longer cytotoxic chemotherapy agents, but are targeted therapies with properties distinct from cytotoxic agents. Most notably, targeted therapies (ie, tyrosine kinase inhibitors, monoclonal antibodies) affect distinct proteins

or receptors on the surface of or inside cancer cells. Targeted therapies block specific signaling pathways involved in cell processes (ie, proliferation, maturation, etc), whereas cytotoxic chemotherapy affects most rapidly dividing cells, regardless of whether or not they are malignant. This targeted approach decreases the amount of collateral damage to normal cells in the body that is typically seen with traditional chemotherapy. The adverse effects of targeted therapies in patients have been well documented, however less is known regarding risks related to handling, administering, and disposing of these medications.

In the past, oral antineoplastic medications made up the minority of anticancer treatments that were administered to patients, especially in the hospital setting. This has largely changed with the proliferation of new

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Table 1. Summary of recommendations for safe handling of oral antineoplastics for health care providers⁴**Storage**

Oral chemotherapy medications should be stored separately from non-cytotoxic agents and in a manner to prevent accidental exposure.

Handling

Correct personal protective equipment (PPE) should be used to minimize exposure including gloves for dispensing and manipulating.

Compounding, crushing, cutting, and splitting should be completed in a biological safety cabinet (BSC).

Equipment used to handle cytotoxic agents should not be used for non-cytotoxic agents.

Doses for liquid or powder oral chemotherapy should be prepared in unit doses, ready for administration.

A plan should be in place to handle spills or accidental exposures.

Disposal

All personal protective equipment (PPE) should be disposed of as cytotoxic waste.

All non-disposable equipment exposed to chemotherapeutic agents should be washed or decontaminated after use.

Training/Competencies

Those who handle oral chemotherapeutic agents should be trained and competent to treat accidental exposures and to dispose of cytotoxic medications.

Those who come in contact with oral chemotherapeutic agents or waste from patients receiving these agents should undergo training.

oral targeted therapies. With this expansion of use, the National Comprehensive Cancer Network developed a task force to address issues associated with oral antineoplastics.³ More recently, an international group of pharmacy practitioners with various clinical backgrounds developed recommendations that specifically address the use of oral agents in the hospital setting, as well as handling precautions for health care providers (Table 1).⁴ Recommendations from the pharmacy practitioners pertained to the storage, handling, disposal, and training related to oral chemotherapy. Specific recommendations included the use of personal protective equipment (PPE); use of a biological safety cabinet (BSC) to compound, crush, cut, or split oral chemotherapy; use of separate equipment/decontamination of equipment; and recommended training procedures for persons who come in contact with these medications. The purpose of this survey was to provide information on common practices for ordering, handling, dispensing, administering, and disposing of oral antineoplastics. This study attempts to characterize the implementation of the recommendations that relate to the handling and administration of oral antineoplastic agents and identify trends in medication use processes for these medications, including the newer targeted therapies.

METHODS

An electronic survey was developed to characterize common practices at health care institutions in the

United States (Appendix). The survey questions related to handling/administration were developed using the available guideline recommendations (Table 1). Additional questions related to demographics and ordering/prescribing of these medications. *Survey Monkey* was used to administer the survey. A link to the survey was sent electronically to practitioners via nursing and pharmacy society listservs (ie, Oncology Nursing Society Chemotherapy Special Interest Group, National Association of Clinical Nurse Specialists, American Society of Health-System Pharmacy, and American College of Clinical Pharmacy) in December 2011 and again in January 2012. Results of the survey were confidential and de-identified. The survey was voluntary; response to the survey indicated consent. The local institutional review board approved the survey. Data were evaluated using descriptive statistics, and all completed surveys were included in the analysis. A post hoc analysis comparing results based on hospital size, number of oncology beds, respondent practice site (academic vs community vs government), and respondent position (pharmacist vs nurse) was conducted. The chi-square test was utilized to compare results. All statistical comparisons were made with Microsoft Office *Excel* (2007).

RESULTS

The survey was distributed to 13,519 pharmacists and nurses via listservs. A total of 123 completed

surveys were returned. Respondent demographics are described in Table 2. The majority of respondents were pharmacists (72%) practicing in a community-based hospital setting.

Trends in Prescribing

Although prescribing practices varied, the majority of respondents noted that most institutions allowed oncologists (98%) to prescribe oral antineoplastics (including chemotherapy and targeted therapies) with 42% allowing all attending physicians to order these medications. Less than 10% of respondents' institutions accepted orders from resident physicians (8%), intern physicians (4%), or pharma-

cists (<1%). In a subgroup analysis comparing institutions by the number of oncology beds, a statistically significant difference was noted in responses from those at institutions with fewer than 20 oncology beds and those with 40 or more oncology beds. More hospitals with a large number of oncology beds (40 or more) allowed antineoplastic orders from any attending physician compared to those with fewer beds (less than 20) (61% vs 19% respectively: $P = .007$; after Bonferroni correction for multiple comparisons, $P = .021$) (Table 3). A small number of practices (11%) accepted telephone orders for oral antineoplastic medications. Upon subgroup analysis, a difference in responses was seen based on the practice setting (Table 3). Telephone orders were not accepted in 84% of community hospitals, 98% of academic hospitals, and 81% of government hospitals. After analysis and Bonferroni correction for multiple comparisons, a difference was found between the community and government hospitals ($P < .001$, Bonferroni correction $P < .001$) and between academic and government hospitals ($P = .006$, Bonferroni correction $P = .019$). Pharmacists specially trained in oncology reviewed orders in (51%) of the respondents' institutions. Again, a difference was detected based on respondents' position (pharmacist vs nurse). Forty percent of the pharmacists responding stated that specially trained pharmacists review all oral oncology orders compared to 95% of nurses ($P = .008$) (Table 3).

Trends in Handling

Overall, 76% of respondents described having a hospitalwide policy regarding the handling and administration of oral antineoplastics. Ninety-eight percent required PPE while handling oral antineoplastics, with most requiring a single pair of gloves (70%). Other required PPE included double pair of gloves (28%), gowns (28%), mask (16%), goggles (4%), and face shields (<1%). An additional trend in handling requirements included that the manipulation of oral antineoplastic dosage forms be performed in a BSC. Overall, BSCs were required for compounding of oral antineoplastics in 88% of institutions. Seventy-six percent of institutions required that a BSC be used when crushing and 72% when cutting/splitting. Liquid oral antineoplastics were dispensed in single-dose oral syringes in 80% of respondents' institutions. Disposal of supplies in designated chemotherapy buckets was required by 78% of respondents' institutions and decontamination of reusable supplies was required in 83%.

Table 2. Demographic information of survey respondents regarding oral antineoplastic handling (n = 123)

Demographics	n (%)
No. of beds at institution	
100-249	48 (39)
250-499	38 (31)
500-749	24 (20)
750+	13 (10)
No. of oncology beds	
0-9	22 (18)
10-19	14 (11)
20-29	23 (19)
30-39	26 (21)
40-49	8 (6)
50+	23 (19)
Unknown	7 (6)
Practice setting	
Community	63 (51)
Academic	43 (35)
Government	16 (13)
Pediatric	1 (1)
US geographic region	
South	40 (33)
Midwest	35 (28)
West	26 (21)
Northeast	22 (28)
Respondent position	
Pharmacist	89 (72)
Nurse	24 (19)
Physician's assistant/nurse practitioner	8 (7)
Unknown	2 (2)

Table 3. Significant results of analysis of survey respondent subgroups

	Oncology beds				Setting				Respondent		
	0-19 (n=36)	20-39 (n=49)	40+ (n=31)	P	Community (n= 63)	Academic (n=43)	Government (n=16)	P	Pharmacist (n=89)	Nurse (n=24)	P
Who can prescribe antineoplastics?											
Residents	2	5	2	.700							
Interns	1	2	1	.938							
Attendings	7	24	19	.018*							
Oncologists	33	49	31	.750							
Physician's assistant/nurse practitioner	5	10	8	.507							
Fellow	0	1	0	.484							
Pharmacist	0	0	1	.233							
Telephone orders for oral antineoplastics may be taken by nursing or pharmacy.											
No					53	42	13	.023**			
All oral antineoplastic orders are reviewed by pharmacists specialized in oncology.											
Yes									36	20	.008

*After analysis and Bonferroni correction, the difference was between the groups 0-19 and 40+ ($P = .007$ and $.021$ after Bonferroni correction).

**After analysis and Bonferroni correction, the difference was between community and government ($P < .001$) and academic and government ($P = .006$) ($P < .001$ and $P = .019$ after Bonferroni correction).

Trends in Administration

Sixty-two percent of respondents required patient consent prior to starting new antineoplastics, while 15% required consent when continuing therapy after inpatient admission. Seventy-two percent allowed non-oncology nurses to administer oral antineoplastics. Special training for nurses was available at most of the institutions (72%). Administration required a witness at 41% of respondents' institutions. Eighty-nine percent required all oral antineoplastic medications to be labeled as a "chemotherapy agent" or with other special precautions, and 79% of respondents placed patients on precautions to alert staff and families of potential risks from exposure when handling body fluids. Of these institutions requiring precautions for oral antineoplastics, 81% required the same precautions for patients on oral tyrosine kinase inhibitors. Forty-seven percent required precautions for hormone agents, and 13% of respondents did not require any precautions.

DISCUSSION

Overall, many of the recommendations addressed in the survey relating to the handling and administration of oral antineoplastics put forth by the international pharmacy panel have been implemented at the majority of institutions responding to the survey.

Recommendations with the highest rates of implementation included the use of PPE when handling these medications and the use of a BSC when compounding. All of the items included in the recommendations (Table 1) that were assessed by the survey were implemented in more than 70% of respondents' institutions. These published recommendations were specifically for oral cytotoxic chemotherapeutic agents as a whole and did not address any of the new targeted therapies, many of which are quickly moving to the front lines of cancer treatment. Despite the paucity of information regarding hazards of handling these new agents, many institutions have implemented precautions for pharmacy and nursing similar to those practiced with traditional oral chemotherapy agents. Many of the institutions represented in this survey limited prescribing of oral targeted therapies to attending physicians and oncologists. This is possibly to prevent ordering of these medications by medical staff unfamiliar with their adverse effects and drug-drug interactions.

In 2007, a survey of 54 comprehensive cancer centers in the United States focused on prescription requirements and patient education related to oral chemotherapy and found that practice varied among the 42 respondents.⁵ Prescribing practices were not standardized among the institutions and only a third

required informed consent. The rates of consent in the current study are twice what were originally reported; however, the number of respondents is larger in the current survey. The previous study also did not address handling or administration practices.

There are several limitations to this study. The survey included the potential for multiple responses from one institution. The authors were unable to monitor this due to the confidential nature of the survey. Moreover, there was a relative lack of response from nursing professionals that may have biased the results toward practices within the pharmacy. This may be evident by the differences noted in the response to the question regarding review of orders by specially trained pharmacists. Nursing may not be aware that pharmacists not specially trained in oncology were verifying orders for these medications, which may account for the difference in the responses between nurses and pharmacists. Other health care professionals were not represented in this study, as the survey was sent to pharmacy and nursing listservs. Lastly, the survey did not address all recommendations in the guideline but rather focused on specific aspects of the handling and administration of antineoplastic medications. The survey also included questions regarding the prescribing/ordering processes that were not addressed in the guideline. Nonetheless, the results indicate that many institutions have taken steps to address the prescribing, handling, and administration of oral antineoplastics. Overall, many institutions have incorporated similar precautions for both oral chemotherapy agents and the newer targeted therapies.

CONCLUSION

Although oral antineoplastic handling practices vary slightly, the majority of respondents follow available guidance when handling and administering oral antineoplastics. Prescribing requirements have not been addressed in the available recommendations, but trends do exist in practices throughout the United States. More research and guidance are needed to determine the level of risk from the new generation of targeted therapies and to determine whether currently instituted precautions are necessary. Until then, many institutions have adopted a conservative approach to the handling of these new medications similar to that for the traditional oral cytotoxic agents.

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APPENDIX

Table A1 Survey questions

1. A hospitalwide policy exists regarding handling and administration of oral antineoplastics. Yes/No
2. Who can prescribe oral antineoplastics (chemotherapy/targeted therapy)?
3. Oral antineoplastic precautions are followed for: Oral tyrosine kinase inhibitors (ie, imatinib, dasatinib, sunitinib, erlotinib, etc) Hormone agents (ie, anastrozole, letrozole, tamoxifen) No precautions are followed for any oral antineoplastic agents Other (please specify)
4. The following personal protective equipment is required when administering oral antineoplastics (chemotherapy/targeted therapy): Single gloves Double gloves Gown Mask Goggles Other (please specify)
5. With regards to oral chemotherapy, the following is/are required to be completed in a biological safety cabinet: Compounding (making an oral solution) Crushing Cutting/splitting Other (please specify)
6. Doses for oral antineoplastics in the liquid form are required to be dispensed in single dose oral syringes. Yes/No
7. Packaging and supplies for oral antineoplastics are disposed in specially designated chemotherapy buckets. Yes/No
8. Decontamination of counting trays, counters, and other equipment is completed thoroughly after use when dispensing oral antineoplastics. Yes/No
9. Telephone orders for oral antineoplastics may be taken by nursing or pharmacy. Yes/No
10. Patient consent is required prior to the following: Starting a new oral antineoplastic Continuing therapy after inpatient admission Other (please specify)
11. Who of the following may administer oral antineoplastics? Oncology nurses Non-oncology nurses Other (please specify)
12. If non-oncology nurses are permitted to administer oral antineoplastics, special training is provided for non-oncology nurses regarding administration and handling of oral antineoplastics. Yes/No
13. Administration of oral antineoplastics requires a witness (ie, 2 RNs are required to verify and document drug administration). Yes/No
14. After receipt of oral antineoplastics, patients are placed on precautions to alert staff and families of the potential risk of exposure when handling body fluids (ie, urine, emesis). Yes/No
15. All chemotherapy orders, including oral antineoplastics, are reviewed by a pharmacist specialized in oncology. Yes/No
16. Oral antineoplastics (including tyrosine kinase inhibitors and hormonal agents) dispensed from the pharmacy are labeled with "chemotherapy agent" or other special handling precautions. Yes/No