SHORT COMMUNICATION

Towards safety of oral anti-cancer agents, the need to educate our pharmacists

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Abstract
Introduction: The global prevalence of cancer is rising. Use of oral anticancer medications has expanded exponentially. Knowledge about these medications as well as safe handling guidelines has not kept abreast with the rapidity these medications are applied in clinical practice. They pose serious hazards on all personal involved in handling these medications as well as on patients and their caregivers. We addressed the gaps in knowledge and safe handling of oral anticancer agents among pharmacists in institutional based cancer care. Materials and Methods: We used a 41 item questionnaire to explore three domains, pharmacists’ knowledge, safe handling practice and confidence and self-improving strategies towards these agents among pharmacists in multicentre specialized cancer care. Results: Participants included 120 pharmacists dedicated to handle and dispense oral anticancer agents. About 20% of Pharmacists have adequate knowledge about oral anticancer agents. Less than 50% apply safe handling practice adequately. Only a quarter are confident in educating cancer patients and their caregivers about Oral Anti-Cancer Agents. Conclusions: Pharmacists’ knowledge about Oral Anticancer agents needs to be improved. Safe handling and dispensing practice of these medications should be optimized. Pharmacists’ confidence towards educating patients and their caregiver needs to be addressed. Enhancing safety of oral anticancer agents should be a priority. Involving all key players, research and quality improving projects are needed to improve all aspects of the safety of oral anticancer agents.

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1. Introduction

The cancer burden is rising in many developing countries. It is projected that cancer incidence will increase form 12.7 million in 2008 to 22.2 million by 2030 (Bray et al., 2012). The first oral anti-cancer chemotherapy dates back to the 1940’s of the last century. The therapeutic use of Nitrogen Mustard for certain hematological malignancies was first reported by Goodman
et al. (1984). With the increasing understanding of cancer biology and molecular genetics a variety of Oral Anti-Cancer Agents (OAA) are developed targeting key cellular mechanisms involved in tumour resistance to conventional therapies. It is estimated that 25% of all targeted anticancer agents will be oral medications and more than 400 oral agents are in the development pipeline (Weingart et al., 2008). They are used as single agents or in combinations to treat a variety of different cancers. In the last decades a tremendous expansion in the indications of OAA has taken place in solid tumours and hematological malignancies (Timmers et al., 2012). They belong to different classes of medications with different modes of action and different toxicity profiles. The OAA have many potential advantage including reducing costs by decreasing the utilization of valuable resources such as beds, infusion areas and health care providers time. It is also preferred by many patients as it reduces the need and risks of invasive devices such as central venous catheters, save time, easy of administration and more gives them a feel of control of their mediations (Schott et al., 2011; Liu et al., 1997; O'Neill and Twelves, 2002). There are however several challenges associated with the increasing use of OAA pertinent to patients, caregivers, health care providers and hospital safety systems. Patients concerns include adherence, understanding complex schedules, different side effect profile, interactions with foods and other medications and increase reliance on them to manage these medications. The health care providers particularly pharmacists are facing the challenges of updating their knowledge, reducing medications errors, safe handling, educations of patient and their caregivers and managing side effects. The safe handling policies and procedures for OAA are not well developed as the parenteral anticancer agents. The practice of dispensing anti-cancer agents is variable. In many countries such as the United States and Canada, these agents are dispensed and managed primarily by a community Pharmacists. It is therefore not surprising that the published studies addressed these challenges in all aspects of OAA imposed on community Pharmacists. In other countries the OAA are dispensed only in cancer centres or specialized hospitals with cancer care facility and not dispensed in community Pharmacy. We intended to address these issues facing specialized Oncology Pharmacists dealing routinely with OAA in the latter setting of specialized centres with cancer care facility.

2. Material and methods

Pharmacists involved in dispensing and handling OAA at three tertiary care centres with oncology services namely King Fahad Medical city, King Saud Medical City and King Faisal Specialist Hospital and Research Center in Riyadh, Saudi Arabia, were included. All participants gave verbal consent and participation was voluntary. The study was cross sectional and extended from March 2013 to May 2014. King Faisal Hospital had a dedicated Oncology Pharmacy and the first two centres had dedicated pharmacists in the main outpatient pharmacy dispensing and managing the OAA. We designed a structured questionnaire consisting of 41 questions testing 3 domains namely safe handling of OAA including patients caregivers’ education, Knowledge of OAA medication (usage, indications, side effects, and drug interactions) and Pharmacists Attitudes (Confidence towards dispensing OAA and self-improvement strategies). Multiple choice questions were used for testing the domains of OAA knowledge. While the answers for the safe handling domain included true, false and choose what were applicable. All correct/incorrect and don’t know answers are expressed in percentages. The face value of the questionnaire was validated by 4 pharmacists and revised by a medical oncologist. The main revision was to include only OAA that are standard treatment and available for several years and in all three centres. The knowledge questions excluded newly approved medications (within the last 1 year) even if available at one of the centres. One hundred and twenty Pharmacists answered the questionnaire.

Statistical Considerations: Descriptive statistics was used applying SSPS version 21.

3. Results

The characteristics of the participants are shown in Table 1.

| Domain 1 | Dispensing and Safe Handling | 98 | 22 |
| Gender | Female | 64% | N = 77 |
| | Male | 36% | N = 43 |
| Job description | Oncology pharmacist | 12% | N = 14 |
| | Clinical pharmacist | 2.6% | N = 3 |
| | Pharmacy manager | 85.4% | N = 103 |
| Years of experience | Less than 3 years | 37% | N = 44 |
| | 3–6 years | 38% | N = 46 |
| | 7–10 years | 11% | N = 13 |
| | More than 10 years | 14% | N = 17 |
| Degree | Bachelor Degree | 88% | N = 106 |

Table 1 Participants’ characteristics.
agreed they would participate in further educations about OAAs and online learning was the preferred method to enhance knowledge. These results are shown in Table 4.

4. Discussion

OAAs are different from many medications as they pose risks to health care providers, patients and their caregivers even with what is considered a standard use. Special precautions are required for safe dispensing and handling of these medications. Pharmacists are at the frontline in providing care when it comes to oral medications and contribute to overall safety and outcomes of these therapies. Our study highlights that there are serious gaps in Pharmacists Knowledge about OAAs and there is a general lack of confidence and ability to educate patients and their caregivers. Previous published studies have focused on community pharmacists as handling and dispensing these medications take place primarily in the community setting. In a study across Canada only 24% knew about the common dosing and less than 10% felt confidence in educating patients and caregivers about OAAs (Abbott et al., 2014). In a US study community Pharmacists fared better knowledge about dosing principles but knowledge about side effects remained suboptimal (45%) (O’Bryant and Crandell, 2008). Pharmacists expressed they did not receive adequate education at the undergraduate level 55% in our study and 59% in the Canadian study (Abbott et al., 2014). Our study showed a low confidence towards dispensing OAAs, similarly in the US study the confidence towards dispensing was scored as 2.4/5 on a five point scoring system (O’Bryant and Crandell, 2008). These studies including ours highlight important fact that knowledge gaps and suboptimal confidence are a concern among community and specialized pharmacists. The pharmacists uniformly agree that they need further education to boost their knowledge and confidence towards OAAs and to improve their ability to educate their patient and caregivers.

When it comes to safe handling practices our study highlights important differences between community and hospital based practice. Safety guidelines exists in hospital practice for OAAs evidenced by three quarters of Pharmacists acknowledging awareness of safety principles, higher rate of separate counting trays, use of protective clothing and double checking. Almost 95% of US community pharmacist were not using a separate counting tray compared to 93% using a separate tray in the specialized setting (O’Bryant and Crandell, 2008). Higher percentage have attended educational courses 70% in our study compared to 16% in the US pharmacist study (O’Bryant and Crandell, 2008). Despite safe handling principles and guidelines exists at facilities caring for cancer patients our study indicates their implementations remains suboptimal. It highlights that the interventions need to be tailored according to gaps in knowledge and deficiencies in safe handling and dispensing practice. Dispensing errors constitute about 15% of the Medication related errors. Studies have shown higher prescription of errors are related to OAAs (Weingart et al., 2010). Studies have shown pharmacists not applying safety standards are at risk of greater exposure to these cytotoxic medications. Urine samples taken from personal handling these medications have shown measurable amounts of these medications in 40% to two thirds of the personal who included pharmacists and other personal handling these medications (Pethran et al., 2003; Schreiber et al., 2003). Interventions by well-trained pharmacists have shown to improve the outcomes of many medical conditions (Machado et al., 2008; Chisholm-Burns et al., 2010).

Therefore improving knowledge and safe handling practices are imperative and will undoubtedly improve patient outcomes and safety of the providers.

Table 2  Safe handling and dispensing of anti-cancer agents.

| Domain 1 Safe handling and dispensing of anti-cancer agents | No of questions | Correct (%) | Incorrect (%) | I don’t know (%) |
|------------------------------------------------------------|----------------|-------------|---------------|-----------------|
| Dispensing and safe handling of OCDs                       | 8              | 48          | 32            | 20              |
| Know and apply the safety principles of dispensing and safe handling | 1              | 75          | 18            | 7               |
| Recommendation for safe handling                            | 1              | 37          | 33            | 30              |
| Directions to patients and care givers about safe handling  | 1              | 20          | 39            | 40              |
| Strategies to improve safe handling                         | 1              | 35          | 34            | 31              |
| Safe dispensing (if the patient unable to swallow)          | 1              | Yes         | No            |                 |
| Separate counting tray for oral chemotherapy drugs          |                | 93          | 7             |                 |
| Required double checking                                     | 1              | Yes         | No            |                 |
| Wearing Glove during dispensing                              | 1              | Yes         | No            |                 |
|                                                            |                | 34          | 66            |                 |

Table 3 Knowledge of pharmacists about oral anticancer agents.

| Domain 2 | Number | Correct (%) | Incorrect (%) | I don’t know (%) |
|----------|--------|-------------|---------------|-----------------|
| Drug knowledge A-General knowledge                          | 30            | 23          | 35            | 42              |
| B-Side effects                                               | 11            | 23          | 35            | 42              |
| C-Dosing knowledge                                           | 7             | 14          | 36            | 50              |
| D-Drug drug interaction                                      | 4             | 18          | 50            | 32              |
|                                                            | 8             | 22          | 45            | 33              |

(ASCO/ONS) guidelines for safe administration and management of oral chemotherapy (Neuss et al., 2013). These guidelines intended to involve all the stakeholders, to be comprehensive and applicable to individuals and institutions. In a recent multinational study by the International Medication safety Practice (ISMP) and International Medication safety Practice Canada (ISMPC) addressing system based safeguards in Oncology practice identified OAAs as a key areas that needs improvement (Greenall et al., 2015). How to implement and adapt these guidelines and monitor their applications remains a major challenge. It is imperative to conduct research and quality improvement programs in different practice settings involving OAAs. These studies and quality projects will help in identifying areas of deficiency in knowledge and safe handling and will aid in the development of best assessment tools and interventions applicable to the relevant practice. A proposed schema for the potential improvement of the overall safety of the OAAs from a pharmacists perspective is shown in Fig. 1. Our studies’ results do have limitations which include the lack of a validated assessment tool, the inability to cover all aspects to safety and cross comparisons to a different practice in our

### Table 4: Attitude and self improvement.

| Domain            | No of questions | Confident | Somewhat confident | Neutral | Not confident | I don’t know |
|-------------------|-----------------|----------|--------------------|---------|---------------|--------------|
| Pharmacist attitude | 4               | 18%      | 8%                 | 16%     | 14%           | 44%          |
| Confident about dispensing oral chemotherapy | 1               | Yes      | No                 | I’m not sure | 17%           |              |
| Education about oral anti-cancer agents (College or postgraduate) | 1               | 28%      | 55%                | No      | I don’t know | 7%           |
| Attend a course or continuing education | 1               | Yes      | 70%                | Online courses video seminars | 23%           | No response |
| Preferred format of continuing education | 1               | 7%       | 23%                | Lectures written materials | 63%           |              |

**Figure 1** Towards better safety of oral anticancer agents.
analysis. Despite these limitations we still believe limited studies have addressed these issues and seem to reach a similar conclusion. We provide a prospective of practice different from the community pharmacy practice and highlight the complexity of this subject.

5. Conclusions

The global burden of cancer is increasing. The expanding use of OAAs is posing major concerns on safety of personal, patients and their caregivers. The standards and guidelines for safe handling and dispensing of these agents a not abreast with the rapid and wide applications of these medications in clinical practice. After collaborative initiatives more comprehensive guidelines addressing safe handling and dispensing of OAAs have been developed, however their uniform implementations remains a major challenge. More studies are needed to identify the areas for improvement relevant to each practice. Pharmacists will remain a key player in safe handling and dispensing these medications as well as educating patients and caregivers. The published studies highlights major gaps in OAAs and safe dispensing. Medical schools, policy makers, institutions, researchers and patient advocates need to work together to improve pharmacists’ knowledge and competency as well as the safety of pharmacists, patients and caregivers handling the OAAs.

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