

Frequency of Polypharmacy in Advanced Cancer Patients Consulted with the Palliative Service of Imam Khomeini Hospital (Tehran), Iran, 2017

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Abstract

Background: Polypharmacy is defined as the concurrent use of more than four or five medications by an individual. The prevalence of this condition has increased due to the ageing population and the related illnesses. Use of multiple medications would increase the risk of side-effects, drug interactions, and medical costs. The present study aimed to determine the frequency of polypharmacy in the advanced cancer patients. **Methods:** In this cross-sectional study, 92 patients with advanced cancer were selected through convenience sampling from the inpatients and outpatients who referred to the Palliative Care Unit of Imam Khomeini Hospital (Tehran) in 2017. An examining physician completed a researcher-made checklist for all the subjects based on the patients' biography and medical records. Statistical analysis was performed by using SPSS software (version 19.0) through descriptive and analytical tests at the significance level of $p < 0.05$. **Results:** The participants' mean age was 55.5 ± 16.2 years. A minimum of one comorbid disease was seen in 81.5% of the patients ($n=75$), the most prevalent of which were psychiatric disorders. Eighty-eight percent of the patients ($n=81$) were on at least 5 or more medications. Opioids and antacids were the most common medications used by these patients. **Conclusion:** The frequency of polypharmacy and average number of consumed medications were high in patients with advanced cancer. Studying the effectiveness of these medications can highly help the physicians stop or continue prescribing such medications, and guide the focus of attention towards the drugs that can improve the patients' quality of life in the final days.

Keywords: Advanced cancer- comorbidity- palliative care- polypharmacy- quality of life

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Introduction

The aging population and the resulting increase in non-communicable diseases have made the polypharmacy a worldwide problem. Numerous definitions have been proposed such as concurrent use of multiple medications, use of incompatible medications, or inadequate consumption of medication. A number of studies have defined the polypharmacy as the simultaneous consumption of more than four or five medications (Maggiore et al., 2010; Kierner et al., 2016).

Polypharmacy is more common in elderly individuals who make numerous visits to the doctor, receive medications from multiple pharmacies, or have multiple comorbidities (Lees and Chan, 2011). Absence of primary care provider that can coordinate the care services provided by different specialists (Clarfield et al., 2001), as well as the increased use of alternative treatments (Qato et al., 2008) are among the influential factors contributing to polypharmacy. This condition is more prevalent in elderly cancer patients compared with the young counterparts,

or even a control group of the same age without cancer. The number of prescribed medications would increase six months prior to cancer diagnosis apparently due to the early signs of the disease. The number of medications keeps rising as the disease progresses (Balducci et al., 2013).

Polypharmacy by itself is neither good nor bad; however, concurrent consumption of multiple medications increases the side-effects, drug interactions, and medical costs. Meanwhile, medications can increase the chance of survival and independency in elderly patients (Crawford et al., 2009). Larson et al. reported increased risk of cognitive impairment due to polypharmacy (Larson et al., 1987). Ruby et al. revealed that the use of multiple medications would increase the risk of urinary incontinency (Ruby et al., 2005). According to a review, some studies mentioned the effect of polypharmacy on falling of elderly patients (Hajjar et al., 2007).

Medicines management for cancer patients can help reduce the side-effects, avoid drug duplications, prevent the negative effects of medications on cancer and its

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treatment, improve the patients' acceptance toward cancer therapies, as well as manage and reduce the costs. Yet, there is no optimal program to evaluate the medication; which should be performed for all patients at least once a year. Furthermore, it is essential to ask the patients about new medications in each appointment and assess their probable impact on the patient's health. Ideally, the cancer patients should be supervised by a scientific team including clinical pharmacy specialists who are, often, the most qualified people to perform such evaluations (Balducci et al., 2013).

In patients with advanced cancer and short life expectancy, there should be a precise balance between the benefits of a medication and the burden of side-effects. This burden increases in such patients in their final days; while, the previously-prescribed medications for other conditions are still continued, even though they are probably of no use (LeBlanc et al., 2015).

Based on our review of the literature, there was no study in Iran regarding the prevalence of polypharmacy among cancer patients. Therefore, the present study was performed to determine the frequency of polypharmacy in patients with advanced cancer.

Materials and Methods

This cross-sectional study was performed on 92 patients with advanced cancer who had referred to the Palliative Care Unit of Imam Khomeini Hospital in Tehran during the year 2017. The study was registered and ethically approved by the Ethics Committee of Tehran University of Medical Sciences (IR.TUMS.IKHC.REC.1396.3097).

The participants were selected through convenience sampling method. The examining physician completed a researcher-made checklist for the subjects based on their medical records. The inclusion criteria were being diagnosed with advanced cancer and having referred to the Palliative ward, and the exclusion criterion was unwillingness to participate.

A palliative care physician examined the patients according to their medical records, and completed a researcher-made checklist about the demographic information (age and sex), the number and types of comorbid diseases, and the number and type of prescribed medications. Polypharmacy, in this study, was considered as the concurrent use of five or more medications. The

Table 1. Frequency of Comorbidities in Advanced Cancer Patients Referred to the Palliative Care Unit of Imam Khomeini Hospital, Tehran, 2017

Comorbidity	n (%)
Cardiovascular Dx	24 (26.1)
Diabetes	10 (10.9)
Hypertension	30 (32.6)
Thyroid Dx	4 (4.3)
Psychiatric Dx	31 (33.7)
Auto Immune Dx	1 (1.1)
Other Dx	39 (42.4)

patients' anonymity was maintained during the data collection process, and the cumulative method was employed for data analysis.

The sample size was determined to be 92 individuals assuming $\alpha=0.05$, $\beta=80\%$, and $d=0.1$ (effect size) with respect to the 40% prevalence of polypharmacy as reported by previous foreign studies. The obtained data were statistically analyzed by using SPSS software (version 19.0) through descriptive statistics (frequency, mean, median, standard deviation, minimum, and maximum), and analytical tests (Mann-Whitney, Chi-Square and Spearman's correlation). The P values <0.05 were considered to be statistically significant.

Results

The findings revealed the participants' mean age to be 55.5 ± 16.2 years (min=18 and max=90). Male patients constituted 52.2% (n=48), while females comprised 47.8% of all patients (n=44). Thirteen subjects were single (14%) and 79 were married (86%). Of all patients, 81.5% had at least one additional disease (n=75). Regarding the type of cancer, the findings showed that out of 92 studied cases, 21 had colon cancer (22.82%), 15 had gastric cancer (16.3%), and 11 had breast cancer (11.95%). The most commonly-reported comorbidities were psychiatric disorders (33.7%, n=31) and hypertension (32.6%, n=30) (Table 1). With respect to the number of comorbidities, no statistically significant difference was found between the two sexes (P=0.77). But, this number was significantly and positively related to the age (P<0.001, r=0.4). Concurrent use of five or more medications was detected in 88% of patients (n=81). The most frequently used medications were opioids and antacids, both of which were used by 75% of patients (n=69) (Table 2). The mean number of drugs used by patients was 7.7 ± 3.2 , with the median of 7.

Table 2. Frequency of Drug Usage in Advanced Cancer Patients Referred to the Palliative Care Unit of Imam Khomeini Hospital (2017)

Drug	n (%)
Cardiovascular	19 (20.7)
Antihypertensive	26 (28.3)
Anti-Diabetic	6 (6.5)
Steroid	24 (26.1)
Antibiotic/Antifungal	52 (56.5)
NSAID	14 (15.2)
Anticoagulant	41 (44.6)
Laxative	44 (47.8)
Sedative, Psychoactive	37 (40.2)
Antacid	69 (75)
Antiemetic	40 (43.5)
Acetaminophen	34 (37)
Hormonal	5 (5.4)
Gabapentin	13 (14.1)
Opioids	69 (75)
Others	67 (72.8)

There was no statistically significant difference between men and women regarding the number of prescribed medications ($P=0.85$). This number was not significantly related to the age ($P=0.59$).

Discussion

This cross-sectional study was conducted on 92 advanced cancer patients with a mean age of 55.5 ± 16.2 years, 88% of whom were on five or more medications, and the most frequently used medications were opioids and antacids. More than 80% of them had at least one comorbid disease, the most common of which were psychiatric disorders.

Polypharmacy is more prevalent in cancer patients than in the individuals of the same age without cancer (Jorgensen et al., 2012). A systematic review in 2015 reported the prevalence of polypharmacy to be 65-91% in long-term care facilities (Jokanovic et al., 2015). The Danish Cancer Registry reported a prevalence of 35% for polypharmacy in cancer patients (Jorgensen et al., 2012). Other studies reported the prevalence rates ranging from 16% to 94.3%. These differences can be due to the differences in the age group, the patients' clinical conditions, research design, or the definition of polypharmacy (Corcoran, 1997).

In the present study, the average number of prescribed medication was 7.7 ± 3.2 , with the median of 7. In this regard, previous studies reported an average usage of 9.1 medications in outpatients over 70 years old under chemotherapy (Sokol et al., 2007), 4.6 in patients with advanced cancer (LeBlanc et al., 2015), and average range of 5-7 in elderly cancer patients (Lees and Chan, 2011). Certainly, previous studies reported higher number of medications being used in comparison with our findings, which could be due to the higher participants' age range in those studies. Although, the present study found no association between the number of used medications and age, some studies did indicate an increase in the number of medications by aging (Bushardt et al., 2008).

Opioids and antacids were the most commonly-used medications among our participants. In this regard, another study reported the most commonly-used drugs in the end-stage cancer patients to be antihypertensive and lipid-lowering drugs, anticoagulants, antiplatelet agents, and bisphosphonates (Cashman et al., 2010). The reason for high consumption of preventive drugs in the aforementioned study was stated to be the lack of coordination between the healthcare service providers in the primary and secondary levels. Moreover, other studies identified opioids, psychoactive drugs (Kierner et al., 2016), morphine and other painkillers, as well as antiemetic drugs (Nauck et al., 2004) as the most frequently-used medications in the patients with advanced cancer.

Considering that psychoactive drugs are sometimes administered to relieve symptoms such as nausea and pain, these findings were consistent with those of the present study due to the similarity of patients in terms of cancer stage. A study reported the cardiovascular and hypertensive drugs as the most common medications in

cancer patients (Sokol et al., 2007). Such a difference could be related to the cancer stage, since the patients in that study were neither in the final stages of the disease, nor under chemotherapy. In patients with advanced cancer, consumption of certain medications for symptom therapy such as antiemetic, antacid or analgesic drugs can improve their quality of life by relieving the symptoms. However, some preventive medications (e.g. heparin, statins, etc.) still require more extensive research to identify their specific benefits and harms.

Currow et al., (2007) studied the patients with terminal illnesses and found that the symptom-specific medications increased as death approached; while, the medications for comorbid medical conditions decreased. They also reported that the patients with better performance received more symptom-specific medications (SSMs); while, the elderly patients received more medications for their comorbidities.

In a study on cancer patients undergoing abdominal or pelvic surgery, 39 patients had to take low-molecular-weight heparin (LMWH) to prevent venous thromboembolism (number needed to treat [NNT]=39), 71 patients had to take heparin to prevent the deep vein thrombosis (DVT) incidence in one individual (NNT=71). Furthermore, use or non-use of heparin made no statistically significant difference in the incidence of pulmonary embolism (PE) and all-cause mortality (Fagarasanu et al., 2016). Moreover, another study on the effectiveness of statins in preventing atherosclerotic cardiovascular disease showed that 18 individuals had to be treated with statins for a period of 10 years to prevent one person from developing cardiovascular disease (10-year NNT=18) (Egan et al., 2016). These findings imply the necessity of noticing the NNT of drugs which are prescribed for the patients with advanced cancer.

The current study evaluated the frequency of polypharmacy in one of the main palliative care centers in Iran. However, to develop nationwide strategies regarding the polypharmacy, it is necessary to consider other diagnostic medical centers as well to estimate the nationwide prevalence of this condition. Further studies are highly recommended to calculate the NNT of preventive drugs among Iranian patients with advanced cancer. We also suggest conducting a study on the prevalence of polypharmacy in the Iranian National Cancer Registry, as well as designing and implementing comparative interventions to reduce the prevalence and complications of this condition.

According to the current results, the frequency of polypharmacy and average number of used medications is high. Studying the effectiveness of these medications can help deciding to stop or continue their prescription; so as to reduce the financial and mental burden imposed on patients by polypharmacy, as well as the probable side-effects. Moreover, extra complications can be avoided merely by focusing on medications that would improve the cancer patients' quality of life during the advanced stages of the disease.

Conflict of Interest

None to declare.

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