

The treatment of co-morbidities in older patients with metastatic cancer

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Abstract

Purpose The purpose of the study was to determine whether older patients with metastatic cancer continue to take medications for the treatment of pre-existing co-morbidities after the diagnosis of metastatic disease.

Methods Between November 2008 and June 2009, patients over the age of 65 with metastatic cancer were interviewed. Medical records were reviewed in order to ascertain current medication use and relevant past medical history. Classes of medication of interest were prospectively defined; these were anti-hypertensives, lipid-lowering drugs, anti-platelet agents, anti-coagulants and bisphosphonates.

Results One hundred patients were recruited, with a median age of 73.5 years (range 65–88); 52% were women. The primary cancer sites were breast, 36%; prostate, 27%; colon, 14%; other, 23%. The median performance status of the patients was 2. The median number of medications was 7 (range 1–17). Eighty-one percent of patients were found to be taking one or more of the predefined medications for treatment of a long-term co-morbidity. Overall 52% of patients had side effects attributed to these medications.

Conclusions Patients with metastatic cancer continue to take drugs for prevention of co-morbidities which are associated with side effects and inconvenience. The benefits of these drugs are likely to be minimal, and medication reviews should be undertaken to address their appropriateness.

Keywords Cancer · Geriatric oncology · Co-morbidities · Polypharmacy

Introduction

The majority of patients who are diagnosed with metastatic cancer from solid tumours have incurable disease, and are managed with the intention of prolonging life with best possible quality [1]. The median survival of such patients with advanced lung, breast and gastrointestinal cancers ranges from 10 to 24 months [2–4]. Most cancers are diagnosed in older people, with 74% of cases in the UK diagnosed in people aged 60 and over, and the absolute number of older patients diagnosed with cancer is likely to increase with the ageing of the population [5, 6]. The prevalence of co-morbidities, such as ischaemic heart disease, also increases with age. Into the future, the management of older patients with cancer and the appropriate management of their co-existing health problems will be a topic of great importance [7].

There are anecdotal reports suggesting that patients with metastatic cancer may continue to take medications for the primary and secondary prevention of concomitant co-morbidities [8]. Given the predicted life expectancy of these patients, they are likely to succumb before the effects of the agents given to reduce these risks become effective. Moreover these medications may be associated with negative effects. The risk of a serious adverse drug reaction increases as more drugs are taken, potentially impairing the patient's quality of life and compromising anti-cancer and symptom control medication [9]. Drug compliance decreases in proportion to the number of drugs prescribed, meaning that anti-cancer and symptom control medication may not be taken because of

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the burden of other medications [10]. The monitoring of the effects of medications given for co-morbidities (cholesterol levels and blood pressure) may also interfere with quality of life. The costs of the medications themselves and of their complications may also be high. The first step in this research is to establish the extent of the problem.

The primary objective of this study was to ascertain the proportion of patients with metastatic cancer who are taking anti-hypertensives, lipid-lowering drugs, anti-platelet agents, anti-coagulants and bisphosphonates.

The secondary objectives were to ascertain the median number of medications taken by patients with metastatic cancers, and where patients are taking anti-hypertensives, lipid-lowering drugs, anti-platelet agents, anti-coagulants and bisphosphonates to establish the indications and any inconveniences/side effects associated with taking the drug.

Methods

Patients with metastatic cancer were recruited from oncology outpatient clinics at the Royal Sussex County Hospital, Brighton and Eastbourne District General Hospital between November 2008 and June 2009. Eligible patients were aged 65 years or over and had been diagnosed with stage IV breast cancer, stage IV colon cancer (assuming not being treated with curative intent), stage IIIB or IV non-small cell lung cancer, stage IV gastric, hepatobiliary or oesophageal cancer, stage IV prostate or bladder cancer or stage III or IV ovarian or endometrial cancer. Patients with germ cell tumours, lymphomas or primary CNS malignancies and those with a life expectancy of less than 8 weeks were excluded. All patients provided written informed consent.

The researcher (JC) interviewed each patient to ascertain current medication use of prescription drugs. Directed questions were asked to ascertain use of anti-hypertensives, lipid-lowering drugs, anti-platelet agents, anti-coagulants and bisphosphonates. (The use of bisphosphonates for the treatment of metastatic bone disease was recorded separately.) Patients were also asked supplementary questions on their past medical history and indications for treatment, as well as pre-selected questions regarding inconveniences/side effects associated with taking the drugs. The medical records were reviewed, and a general practitioner was contacted in order to confirm the current medication use, and where relevant the exact indication for the medication.

One hundred participants were recruited into the study. This was an exploratory study; formal power calculations were not performed. Data were summarised using appro-

appropriate descriptive statistics: number of observations, median, minimum and maximum for continuous data and number of observations and percentage within each category for categorical data.

Results

One hundred and two patients were approached to be involved in the study, and 100 agreed to participate (acceptance rate 98%).

Demographics

The median age of the 100 recruited patients was 73.5 years (range 65–88 years), 52% of participants were women. The most common primary cancer sites were breast, prostate and colon cancer (Table 1). The median performance status of the patients was 2. The median number of sites of metastatic disease was 1, and 12% of patients had three or more metastatic sites.

Medications

The median number of medications the patients were taking was 7 (range 1–17). Eighty-one percent of participants were found to be taking one or more of the drugs in the selected groups of medications: anti-hypertensives, lipid-lowering drugs, anti-platelet agents, anti-coagulants and bisphosphonates (the latter for indications other than cancer). As shown in Table 2, the most commonly used group of medications were anti-hypertensives, with 71% of patients taking one or more of these drugs. Of these 71 patients, 52% were taking one anti-hypertensive, 27% were taking two, 15% were taking three, and 6% were taking four anti-hypertensive drugs. The second most commonly used drugs were lipid-lowering drugs (33%). The majority of the other medications participants were taking were for palliative treatment of cancer and symptom control (most commonly analgesia).

Indications for medications

All of the 71 participants taking anti-hypertensives had a history of high blood pressure; 18 of these patients had a history of cardiovascular disease (angina, myocardial infarction, cerebrovascular accident or transient ischaemic attack). Of those 33 patients taking lipid-lowering drugs, 15 (46%) had a history of cardiovascular disease. Of the 32 patients taking anti-platelet treatment, two patients (6%) had a drug-eluting coronary stent, two patients (6%) had atrial fibrillation, 12 patients (38%) were prescribed anti-platelets for secondary prevention of cardiovascular dis-

Table 1 Demographics of participants ($n=100$)

	Male	Female	Total
Number	48 (48%)	52 (52%)	100 (100%)
Tumour type			
Stage IV breast cancer	0 (0%)	36 (36%)	36 (36%)
Stage IV colon cancer	8 (8%)	6 (6%)	14 (14%)
Stage IIIB or IV non-small cell lung cancer	3 (3%)	1 (1%)	4 (4%)
Stage IV oesophageal cancer	3 (3%)	1 (1%)	4 (4%)
Stage IV prostate cancer	27 (27%)	0 (0%)	27 (27%)
Stage IV renal cancer	4 (4%)	1 (1%)	5 (5%)
Other	3 (3%)	7 (7%)	10 (10%)
Number of sites of metastatic disease			
1	37 (37%)	21 (21%)	58 (58%)
2	10 (10%)	20 (20%)	30 (30%)
≥ 3	1 (1%)	11 (11%)	12 (12%)
Treatment			
Active supportive care alone	10 (10%)	7 (7%)	17 (17%)
Cytotoxic chemotherapy	11 (11%)	18 (18%)	29 (29%)
Radiotherapy	1 (1%)	2 (2%)	3 (3%)
Targeted therapy	2 (2%)	2 (2%)	4 (4%)
Hormone therapy	26 (26%)	24 (24%)	50 (50%)
Performance status			
0	5 (5%)	5 (5%)	10 (10%)
1	13 (13%)	12 (12%)	25 (25%)
2	13 (13%)	19 (19%)	32 (32%)
3	16 (16%)	16 (16%)	32 (32%)
4	1 (1%)	0 (0%)	1 (1%)

ease, and 13 patients (41%) had been prescribed aspirin for primary prevention of cardiovascular disease. Of the eight patients taking anti-coagulants, four (50%) had a history of venous thromboembolic disease, three (38%) had atrial fibrillation, and one (12%) had a history of myocardial infarction.

Associated side effects/inconvenience of taking medications

Of those patients taking anti-hypertensives, 19 (27%) reported dizziness on standing (postural hypotension). Lipid-lowering drugs were associated with muscle aches

Table 2 Number of patients on medications and their indications and side effects ($n=100$)

	No. (%)		
	Patients on medication	Patients on medication with side effects	Patients on medication with history cardiovascular disease ^a
Anti-hypertensives	71 (71%)	19 (27%)	18 (25%)
Lipid-lowering drugs	33 (33%)	3 (9%)	15 (46%)
Anti-platelet agents	32 (32%)	24 (75%)	15 (47%)
Anti-coagulants	8 (8%)	5 (63%)	–
Bisphosphonates	4 (4%)	2 (50%)	–
Any of the above	81 (81%)	42 (52%)	–

^a Cardiovascular disease (including angina, myocardial infarction, cerebrovascular accident and transient ischaemic attack)

in three (9%) patients, and 14 (42%) reported six monthly cholesterol checks. Patients taking anti-platelet agents were questioned about whether they suffered from indigestion or reflux (gastritis), and whether they bruised easily. Overall, 24 patients (75% of those taking aspirin) reported side effects: 14 participants (44%) reported bruising easily, one (3%) suffered from gastritis, and nine (28%) reported both. Five (63%) of the patients taking anti-coagulants reported easy bruising, and INR monitoring in those on warfarin was being performed weekly in one patient, fortnightly in three patients, and six weekly in the remaining two patients. Two of the four patients taking bisphosphonates (for reasons other than cancer) reported indigestion or reflux (gastritis).

Discussion

The study found that 81% of participants were taking one or more of the preventative medications selected: anti-hypertensives, lipid-lowering drugs, anti-platelet agents, anti-coagulants and bisphosphonates. The most commonly prescribed were those used in the secondary prevention of cardiovascular disease with 71% of participants taking anti-hypertensives, 33% taking lipid-lowering drugs and 32% taking anti-platelet agents. The median number of medications that patients in the study were taking was 7. This puts patients at a high risk of adverse drug reactions (ADRs), with one study suggesting that the risk of ADRs in patients taking seven or more medications is 82% [11]. Previous research also suggests that patients taking multiple medications are less likely to be compliant with their medications [12]. In the patient population in this study, this may mean worse compliance with anti-cancer and symptom control medications. Overall 52% of patients had side effects attributed to these medications, including problems with bruising, dizziness and indigestion, and many patients were also undergoing additional blood tests for monitoring of lipid levels or anti-coagulant effects. These may all have negative impacts on quality of life.

These results raise the question of why these patients continue to take these medications and why no one has recognised the risks and stopped them despite frequent interactions with health professionals. One reason for this could be limited communication between those involved in primary and secondary care. Whilst a patient's oncologist may be in a good position to judge prognosis and whether a medication is appropriate, he or she may defer to a patient's GP regarding such medications which are usually initiated in primary care. Thus neither party may feel that they have ownership of the problem. Another reason that doctors may be reluctant to address the issue is the apprehension about the response they may get when the conversation is

approached. Patients may raise many difficult questions that the doctor may wish to avoid [8], for example: "am I not worth treating anymore?", "I was told I should take this for the rest of my life, does this mean I am going to die?" and "won't I get ill without the tablets?" It is important that doctors are able to answer these questions sensitively and honestly and to be able to recognise the potential psychological impact for a patient.

This study confirms that a problem exists: Many patients with cancer continue to take drugs for primary and secondary prevention of co-morbidities for perceived long-term benefit even after they have been diagnosed with metastatic disease. The reduction in risk that they offer is unlikely to be significant to the patients given their limited life expectancy. Many patients reported suffering from side effects and were inconvenienced by the monitoring of the effects of the medications. These findings indicate that regular medication reviews (involving both primary and secondary care) should be conducted in this patient population to ensure that all medication use is appropriate and necessary.

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Ethical approval Ethical approval was obtained from Brighton East Research Ethics Committee (08/H1107/107) and by local research and development departments: 08S 012 RIN (Brighton and Sussex University Hospitals), T 08-36 (East Sussex Hospitals Trust). All participants gave informed consent.

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