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Off-label prescribing in oncology

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Abstract Off-label prescribing occurs when a practitioner prescribes a drug for a use, or in a manner, not listed in the 'approved product information' (API) for that drug. The literature suggests that this is a frequent occurrence in many areas of medicine, but data are limited in the hospitalized oncology setting. The aim of this study was to quantify the extent of off-label prescribing in a hospitalized oncology population in Australia. The study was conducted at Peter MacCallum Cancer Centre, Australia. On a single day the medication charts of all hospitalized patients were prospectively reviewed. Drug prescribing was assessed for licensing status by comparison with the API as approved by the Therapeutic Goods Administration of Australia. Prescriptions were classified as licensed, off-label or unlicensed. Medication charts of 130 patients were assessed. There were 1351 prescriptions. In 293 (22%) of the prescriptions the drug was either off-label (242, 18%) or unlicensed (51, 4%). Among the 130 patients, 110 (85%) received at least one drug that was prescribed off-label or that was unlicensed. Off-label dosing was the most frequent reason for a drug being off-label (139, 10% of all prescriptions). Off-label due to use for an unapproved indication was found in 118 prescriptions (9%), and off-label due to an unapproved route of administration was found in 38 prescriptions (3%). Off-label prescribing is widespread in the acute hospitalized oncology population, with approximately 22% of all prescriptions being for off-label or unlicensed medication. Such prescribing affects a significant proportion of patients.

Keywords Off-label drug use · Unlicensed drug use · Oncology

Introduction

Patients with cancer are frequently prescribed numerous medications throughout the course of their treatment. Unfortunately, both patients and clinicians often experience limitations in funding availability and the information accessible about medications is commonly inadequate. This is particularly the case when medications are used 'off-label', as reimbursement policies and consumer medication information (CMI) are developed principally from the approved product information (API). In Australia, the API is derived from the marketing approval granted by the Therapeutic Goods Administration (TGA) of Australia. The API contains the approved indications for use, doses and routes of administration. The promotional activities of pharmaceutical manufacturers are restricted to the API, but prescribers are not constrained from prescribing outside the listed usage.

Off-label prescribing occurs when a practitioner prescribes a drug for a use, or in a manner, not listed in the approved product information for that drug. The literature suggests that this is a frequent occurrence in many areas of medicine, particularly in paediatrics [3, 6, 9, 13, 16, 18, 19, 21] and HIV/AIDS [5] treatment.

In our experience, the frequent practice of off-label prescribing in oncology poses added difficulties to an already complex medication regimen. There are limited published data on off-label prescribing in oncology. Two studies from the United States have demonstrated that up to one-half of all chemotherapy is used for an off-label indication [14, 22]. However, chemotherapy is only one component of treatment provided to patients with cancer. It has also been demonstrated that in specialist palliative care units in the United Kingdom approximately one-quarter of medications prescribed are for off-label indications or are given by an off-label route [1, 15, 20]. The present study was conducted to quantify the extent of off-label and unlicensed prescribing in a hospitalized oncology population in Australia.

Methods

Setting and design

This study was conducted at Peter MacCallum Cancer Centre, a tertiary referral cancer hospital in Melbourne, Australia. On a single day in January 2001 the medication charts of all hospitalized patients were prospectively reviewed. Data collection included patient demographics and primary diagnosis, drugs prescribed, form and route of administration, dose, frequency and indication for use of the drug. The indication for use was determined by the clinical pharmacist, in consultation with the treating clinician if clarification was required. Drugs excluded from data collection were intraoperatively administered drugs, clinical trial drugs and standard intravenous fluids.

Definitions

Drug prescribing was assessed for licensing status by comparison with the API, as approved by the TGA of Australia. The 2001 electronic Australian Prescription Product Guide (APPG) was utilized for reference to the API [17]. Prescriptions were classified as:

1. Licensed: where indication, dose *and* route of administration *all* met those contained in the API.
2. Off-label: where any of indication, dose *or* route of administration did not meet those contained in the API.
3. Unlicensed: the drug prescribed was not registered in Australia, i.e. the drug had not been approved by the TGA and, therefore, was not listed in the APPG.

Analysis

Data were analysed to determine the proportion of drugs that were used off-label or that were unlicensed and to determine the percentage of patients receiving off-label and unlicensed medication.

Results

On the day of the review, the medication charts of 130 patients were assessed; this included both day-stay and longer-term hospitalized patients. There were 1351 prescriptions for 231 different medications. Of the 1351 prescriptions 47 were for 22 chemotherapy or hormonal medications used to directly treat or prevent a primary cancer. The 231 medications were prescribed for 320 different indications. In 293 (22%) of the prescriptions the drug was either off-label (242, 18%) or unlicensed (51, 4%). Of the 130 patients, 110 (85%) received at least one drug that was prescribed off-label or that was unlicensed.

The most frequent reason that a drug was assessed as being off-label was that the dose prescribed did not comply with the API (139, 10% of all prescriptions). Off-label due to use for an unapproved indication was found in 118 prescriptions (9%), and off-label due to an unapproved route of administration was found in 38 prescriptions (3%). There were 53 prescriptions (4%) that were off-label for more than one reason; for example, due to an unapproved indication *and* dose (see Fig. 1). Of the 47 prescriptions for chemotherapy or hormonal medications, 14 (30%) were off-label, 5 for an unapproved indication and 13 for an unapproved dose; 4 prescriptions were off-label for both dose and indication.

The drugs most frequently used off-label are listed in the Table 1. The drug most frequently prescribed off-label was metoclopramide, a drug routinely used for the treatment and prevention of nausea and vomiting. The recommended dose in the API is 10 mg three times daily for oral, intramuscular and intravenous administration. We found that prescribers commonly prescribed up to 20 mg for administration up to every 4 hours. This dosing schedule is accepted as a standard dosing regimen, but is not included in the API.

Similarly, the combination product of sulphamethoxazole and trimethoprim is used as standard practice for the prevention of *Pneumocystis carinii* pneumonia. However, neither this indication nor the dosage used is listed in the API. Lorazepam is an anxiolytic frequently used as an adjunctive antiemetic agent in oncology. The commonest route of administration is the sublingual route, which is

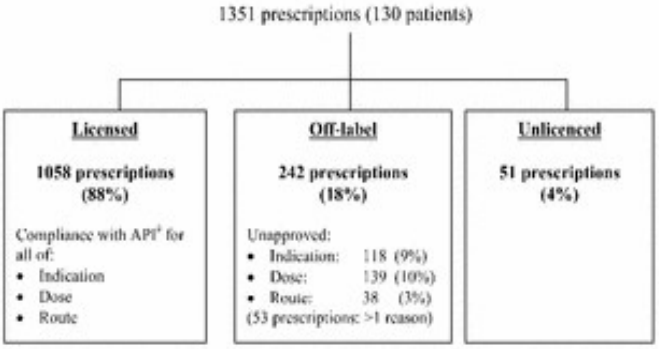

Fig. 1 Extent of off-label and unlicensed prescribing in a hospitalized oncology population