Chemotherapy and community dispensed drugs show frequent interactions in a continuous screening programme

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Background

A previous retrospective study into drug-drug interactions between anticancer agents administered in our hospital and community pharmacy dispensed drugs identified a prevalence of clinically relevant interactions of 18%. In general, the hospital pharmacy and community pharmacy care systems are not automatically linked in the Netherlands. Therefore, potential drug-drug interactions may not be noticed. We developed a continuous screening programme for all patients eligible for systemic antineoplastic treatment, in which we perform a medication review prior to the first round of chemotherapy.

Purpose

To identify drug-drug interactions between cytotoxic agents and community pharmacy dispensed medication before the start of chemotherapy, and to develop clinical rules for their management.

Materials & Methods

Prior to chemotherapy, a medication review was performed on the current medication list from the community pharmacy. Both ambulatory and clinical oncology patients were included from June 2010 until September 2011. 412 screenings were performed in 365 patients.

Total number of patients	365
Male/female	167/197
Age	
Median age males (range)	60 (18-83)
Median age females (range)	58 (18-93)
Types of cancer n (%)	
Breast	91 (25)
Colorectal	85 (23)
Non-Hodgkin lymphoma (NHL)	53 (15)
Acute myeloid leukemia (AML)	17 (5)
Hodgkin lymphoma	17 (5)
Ovarian	17 (5)
Multiple myeloma (MM)	11 (3)
Pancreas	11 (3)
Prostate	10 (3)
Testis	9 (2)
Other	44 (12)

Table 1
Patient characteristics

Results

80 potentially relevant interactions were observed in 57 patients (16 %). Most frequent interactions, their possible clinical effects and proposed management were:

A) coumarins with cytostatics (n=17), resulting in a possible increased anticoagulation. Clinical management involves additional INR (international normalized ratio) checks.

B) protease inhibitors with anthracyclins and vinca-alkaloids (n=13) resulting in possible augmented toxicity. Management consists of prophylactic GCSF (granulocyte colony-stimulating factor) and monitoring for neuropathy.

C) ciprofloxacin with anthracyclins, etoposide/teniposide and oxazaphosphorins (n=8), leading to reduced exposition to the fluorchinolon. In the case of prophylactic treatment, no action is needed, whereas in therapeutic use, switching to another antibiotic should be considered. Overall, 24 interactions involved CYP inducing or inhibiting co-medication. In 11 of these, a switch to a non-CYP influencing drug was feasible. In 3 cases, anti-epileptics or anti-depressants were involved, requiring additional monitoring of serum levels. These results warrant a timely execution of interaction screening, preferably days before the start of chemotherapy.

Interaction	Description	Number of cases	Proposed clinical management
Cytostatic – coumarin	Increased coagulation	17	Additional INR checks and subsequent adjustment of coumarin dose
Doxorubicin/vincristine/vinblastin – protease inhibitors	Increase in toxicity of the cytotoxic	13	Start GCSF prophylaxis and monitor for neuropathy (in case of vinca-alkaloids)
Doxorubicin/cyclophosphamide/ etoposide - ciprofloxacin	Decrease in ciprofloxacin exposure	8	Ciprofloxacin in therapeutic use: consider switching to an antibiotic from a different class. Ciprofloxacin in prophylactic use: no action needed
Methotrexate - co-trimoxazole	Possible increase in MTX toxicity	4	Consider switching to another antibiotic, or start chemotherapy after completion of co-trimoxazole course. In case of prophylactic (chronic) co-trimoxazole, switch to another antibiotic at least three days before starting MTX .
Cytostatic - hydrochlorthiazide	Possible decrease in clearance of cytostatic	3	No additional action is needed because all patients are regularly monitored for myelosuppression
Irinotecan - dexamethasone	Decrease in serum levels of irinotecan and its active metabolite	3	No action because this is a desired interaction, dexamethasone is prescribed to lower irinotecan side-effects
Cytostatic – TNF alpha inhibitor	Additive myelosuppressive effects	2	Stop TNF alpha inhibitor for the duration of chemotherapy
Cytostatic – carbamazepin/valproic acid	Possible decrease in anti-epileptic serum levels	2	Monitor serum levels of the anti-epileptic drug during the chemotherapy, and adjust dosage accordingly

Table 2
Most frequent potentially relevant interactions

GCSF = granulocyte colony stimulating factor, INR = international standardized ratio, MTX = methotrexate, TNF = tumour necros is factor

Conclusions

The high prevalence of potential drug-drug interactions between anti-cancer agents and community dispensed drugs stresses the need for an optimal medication surveillance and data exchange between clinic and community.