POTENTIAL DRUG-DRUG INTERACTIONS IN HYPERTENSIVE PATIENTS

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Background and Importance. Hypertension is among the most frequently diagnosed chronic medical condition in adults. Treatment of hypertension requires one or more drugs (usually thiazide, angiotensin converting enzyme inhibitor (ACEI), angiotensin-II-receptor blocker (ARB), calcium channel blocker (CCB) and/or beta-blockers). Potential drug-drug interactions (pDDIs) are highly prevalent in hypertensive patients receiving multidrug therapy. Knowledge about pDDIs may help physicians minimize adverse effects by careful choice of drugs.

Aim and Objectives. To analyse pDDIs among hypertensive patients and evaluate the mechanism and severity of potential outcomes of such interactions.

Materials and Methods. We conducted a cross-sectional study during a two months period, which included 350 patients with hypertension, treated in university hospital, who had ≥ 2 medications prescribed. Approval was granted by the Ethics Committee of the hospital. Medication prescriptions were analysed for clinically relevant pDDIs using Lexi-Interact database (Lexi-Comp, Inc, Hudson, Ohio. Statistical analysis was performed using the software PASW Statistics (PASW Inc., Chicago, IL, USA) version 22 and Microsoft Excel® 2010.

An expert group, consisting of two clinical pharmacists and two hospital pharmacists, assessed the benefits and risks of each prescribed drug by using the Medication Appropriateness Index. Discontinuation or substitution with another drug with less interacting potential was suggested.

Results. A total of 350 patients were included in this study, with average age 77 (36-98) years and 6.1 (2.5) medications. The majority of patients (86.0%) had at least one clinically significant pDDI, average was 3.78 (3.90) (range 1-25).

Suggestions for treatment change aimed mainly at eliminating drug duplications, reducing the use of thiazide diuretics, sulfonylureas, alpha-lipoic acid and pentoxiphylline and increasing the use of calcium-channel blockers, when appropriate. pDDIs would have decreased to 2.10 (2.52), p<0.001, yet male gender, ≥ 6 medications, cardiovascular diseases, diabetes, benign prostatic hyperplasia, would be predictive of ≥2 pDDIs. The main potential adverse outcomes of pDDIs were hypotension, renal failure, hypoglycemia, bradycardia and lactic acidosis.

Characteristic	Value
Age, years (median (range))	77 (36-98)
Gender female, number (%)	180 (51.4)
The number of medications per patient, mean (SD) (range)	6.1 ((2.5) (3-15)
The number of comorbidities per patient, mean (SD) (range)	3.1 (1.5) (1-10)
Most prevalent comorbidities, number (%)	
Arterial hypertension	350 (100.0)
Angina pectoris	101 (28.9)
Diabetes mellitus	80 (22.9)
Anxiety	64 (18.3)
Dyslipidemia	60 (17.1)
BPH	42 (12.0)
Dyspepsia	37 (10.6)
Infectious disease	32 (9.1)
Osteoporosis	31 (8.9)
Heart failure	30 (8.6)
Atrial fibrillation	24 (6.9)

Interactions	Before medication review Mean (SD)	After medication review Mean (SD)	p-value
Nr of interactions	3.78 (3.90)	2.10 (2.52)	<0.001
X	0.05 (0.29)	0.0 (0.0)	0.003
D	0.18 (0.58)	0.02 (0.15)	<0.001
C	3.55 (3.67)	2.09 (2.48)	<0.001
ACEI	1.08 (1.27)	0.65 (0.98)	<0.001
Beta-blockers	0.71 (1.11)	0.42 (0.70)	<0.001
Benzodiazepines	0.16 (0.71)	0.05 (0.27)	<0.001
Thiazide diuretics	0.95 (1.32)	0.13 (0.55)	<0.001
Statin	0.07 (0.27)	0.03 (0.17)	<0.001
NTG	0.71 (1.39)	0.61 (1.60)	<0.001
Long-acting nitrates	0.21 (0.91)	0.003 (0.050)	<0.001
Metformin	0.32 (0.85)	0.20 (0.53)	<0.001
α-AA	0.26 (0.81)	0.21 (0.69)	<0.001
Antibiotics	0.03 (0.19)	0.003 (0.050)	0.001
ARB	0.11 (0.43)	0.06 (0.27)	<0.001
Sulfonylurea	0.23 (0.84)	0.06 (0.34)	<0.001
Cholecalciferol	0.04 (0.22)	0.009 (0.092)	<0.001
Antiastmatics	0.30 (1.39)	0.09 (0.58)	<0.001
Digoxin	0.13 (0.58)	0.10 (0.47)	0.002
Antiarrhytmic	0.10 (0.59)	0.08 (0.48)	0.019
Levothyroxin	0.03 (0.17)	0.02 (0.13)	0.025
AChEI	0.05 (0.33)	0.02 (0.18)	0.018
Pentoxifylline	0.14 (0.70)	0.003 (0.053)	<0.001
Antipsychotics	0.24 (1.40)	0.17 (1.00)	0.033
Insulin	0.08 (0.52)	0.05 (0.34)	0.016
Alpha-lipoic acid	0.04 (0.25)	0.003 (0.05)	0.010
Allopurinol	0.04 (0.25)	0.02 (0.17)	0.008
NSAID	0.05 (0.33)	0.02 (0.18)	0.041

Conclusion and relevance. Careful choice of drugs can reduce, but not eliminate pDDIs in hypertensive patients. Close monitoring for hypotension, renal failure, hypoglycemia, bradycardia and lactic acidosis is necessary.