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DETECTION OF ADVERSE DRUG REACTIONS TO ANTIMICROBIAL DRUGS IN HOSPITALIZED PATIENTS

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ABSTRACT

PURPOSE of this study was to detect and analyze adverse drug reactions (ADR) to antimicrobial drugs in hospitalized patients. METHODS: An observational prospective study was carried out in two departments of University hospital, Pleven. Patients were included in order to their hospitalization in Gastroenterology and Nephrology Departments. Demographic data, diagnosis, drug treatment, co-morbidity and ADR to antibiotics were registered in a patient chart. Type, causality, severity and incidence of ADR were assessed according to accepted criteria. RESULTS: Of all 485 inpatients evaluated (58,7% male and 41,3% female), 133 received an antibiotic. In 22 patients (4,54%) antibiotics were responsible for ADR (63,64% determined as type A; 31,82% as type B). CONCLUSIONS: ADR to antibiotics in inpatients are frequent, often predictable and with a moderate severity. Surveillance and risk factor considered treatment could improve the outcomes and reduce the incidence of ADR in hospitalized patients.

Keywords: antibiotics, adverse drug reactions, hospitalized patients.

INTRODUCTION

Over half of all hospitalized patients are treated with antimicrobial agents and their use account for 20% to 50% of drug expenditures in hospitals (1, 2) The total costs associated with antibiotics are not only related to antibiotic use itself, but also to co-medication and adverse drug events (3). At least one ADR has been reported to occur in 10 to 20% of hospitalised patients (4). The incidence of ADR varies greatly (1,5-30%) depending on the method used to detect them (chart review, computer monitoring or spontaneous reporting) (5,6). In a meta-analysis, incidence of adverse drug reactions, including non-serious and serious events was 10.9% (CI 7,9-13,9%) of hospitalized patients. Factors possibly influencing the incidence have been identified: average length of stay, age, gender, renal function, hepatic function and drug exposure (7). In Darchy's report, antibiotics accounted for 11% of iatrogenic disease (8). Classen states that, although adverse events seem to occur in a small proportion of antibiotic courses, the frequency of antibiotic use makes them account for 23% of all adverse events recorded (2,9). In Switzerland, an epidemiological study of drug exposure and adverse drug reactions reported an incidence rate of clinically relevant ADR for antibiotics of 2,8% (2,0-3.5), in internal medicine units (10).

AIM of this study was to detect and analyze adverse drug reactions (ADR) to antimicrobial drugs in hospitalized patients.

METHODS

An observational prospective study was carried out in two departments of University hospital, Pleven. Patients were included in order to their hospitalization in Gastroenterology and Nephrology Departments. Demographic data, diagnosis, drug treatment, co-morbidity and ADR to antibiotics were registered after a personal patient interview by two clinical pharmacologists and a specialist, according to

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the patient hospital charts. Detected ADR were assessed according to the following criteria: for type – Edwards&Aronson, 2000 (as A, B, C, D, E and F); for causality – Naranjo et al., 1981 (as sure, probable, possible and unlike); for severity – WHO-UMC (as mild, moderate and severe). Statgraphics Plus for Windows was used for statistical analysis of collected data-base.

RESULTS

All 485 patients admitted to Gastroenterology and Nephrology departments for a three-month period were included in the study. For patient characteristics see Table 1.

Table 1: *Characteristics of patients*

	All patients	Patients on antibiotics	Patients with ADR to antibiotics
Number	485	133	22
Age n (%)			
<30	26 (5,34%)	14 (10,52%)	3 (13,64%)
30-70	370 (76,26%)	100 (75,19%)	16 (72,72%)
>70	89 (18,42%)	19 (14,29%)	3 (13,64%)
Gender			
Female	58,7%	54,9%	63,6%*
Male	41,3%	41,9%	36,4%
Hospital stay (days)	8,87±0,76	8 (2-51)	8 (3-51)

*t=3,33; p<0,001

Thirteen antibiotics were used by 133 patients during the hospital stay: amikacin (0,72%), ampicillin (2,06%), amoxicillin and clavulanic acid (1,44%), azatril (0,4%), cefazolin (2,89%), cefepime (0,21%), ceftriaxone (14,23%), cefuroxime (1,24%), ciprofloxacin (2,89%), gentamicin (5,15%), piperacillin (0,41%), imipenem (1,03%) and vancomycin (0,24%).

ADR were documented in 22 (4,54%) inpatients on antibiotics, with a history of ADR in 13 (9,77%) of them. The frequency of ADR was 21,43% with cefazolin, 20% with gentamicin, 14,29% with amoxicillin and clavulanic acid, 13,04% with ceftriaxone and 10% with ampicillin. One reaction was observed in a patient, received azithromycin, and no ADR were detected with amikacin, cefuroxim, ciprofloxacin, cefepime, piperacillin and vancomycin.

Median length of hospital stay was 8 (2-51) for patients on antibiotics and 8 (3-51) for patients on antibiotics with ADR, with no significant difference between the groups.

Of all patients with ADR, 63,6% were female and 36,4% were male. Gender was found as a risk factor for development of ADR (t=3,33; p<0,001), but not the age (F=0,06; p=0,8).

According to Edwards&Aronson classification, 63,64% of ADR were determined as type A, 31,82% as type B and one reaction to gentamicin was assessed as type C.

Seven ADR (31,8%) were estimated as possible, with Naranjo index from 1 to 4 and fifteen ADR (68,2%) as probable, with Naranjo index 5-8.

Almost all detected reactions were moderate, followed by change of therapy, additional drug treatment and increased length of hospital stay at least for one day.

ADR to antibiotics were manifested with dysbacteriosis (36,36%), allergic reactions (27,27%) and gastrointestinal disturbances (27,27%), with 2 cases of cholestasis and impaired renal functions.

CONCLUSIONS

Antibiotic treatment is associated with high frequency of ADR in hospitalized patients. ADR to antibiotics in inpatients are presented mainly as type A and type B, with a prevalence of dose-dependent and predictable reactions. They are mild to moderate, dominantly manifested by dysbacteriosis and allergic reactions. Female gender, but not the age is significantly associated with higher risk for ADR to antibiotics in hospitalized patients.

Detected ADR do not increase significantly the length of hospital stay, but could interfere with the clinical outcomes and costs of hospital treatment regimens. Detailed surveillance and risk factor consideration could be helpful in prediction, early detection and limitation of ADR to antibiotics in hospitalized patients.

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