HIGHER THAN RECOMMENDED DOSES OF COLISTIMETHATE SODIUM IN PATIENTS WITH MULTI-DRUG RESISTANT GRAM-NEGATIVE BACTERIAL INFECTIONS: A BENEFIT OR AN INCREASED RISK OF TOXICITY?

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BACKGROUND

Recent pharmacokinetic studies suggest the administration of higher colistimethate sodium (CMS) doses for treating multidrug resistant Gram-negative (MDR-GNB) infections.

OBJECTIVES

The aim was to compare the efficacy, pharmacokinetics and toxicity of the manufacturer's recommended CMS doses (RD) versus higher doses (HD).

METHODS

Pharmacokinetic study performed at a university hospital in patients with MDR-GNB infections treated with CMS. Data: demographics, severity (APACHE-II), CMS dose, type of infection, colistin plasma concentration (Cminss before next CMS dose and at steady state), nephrotoxicity at day 7 (RIFLE criteria), clinical cure and crude mortality. CMS doses were selected by the clinicians' criteria. All patients treated with higher doses than those recommended by the national manufacturer were considered HD group.

RESULTS

Total number of included patients: 102 (70 (68.6% with RD and 32 (31.4%) with HD).

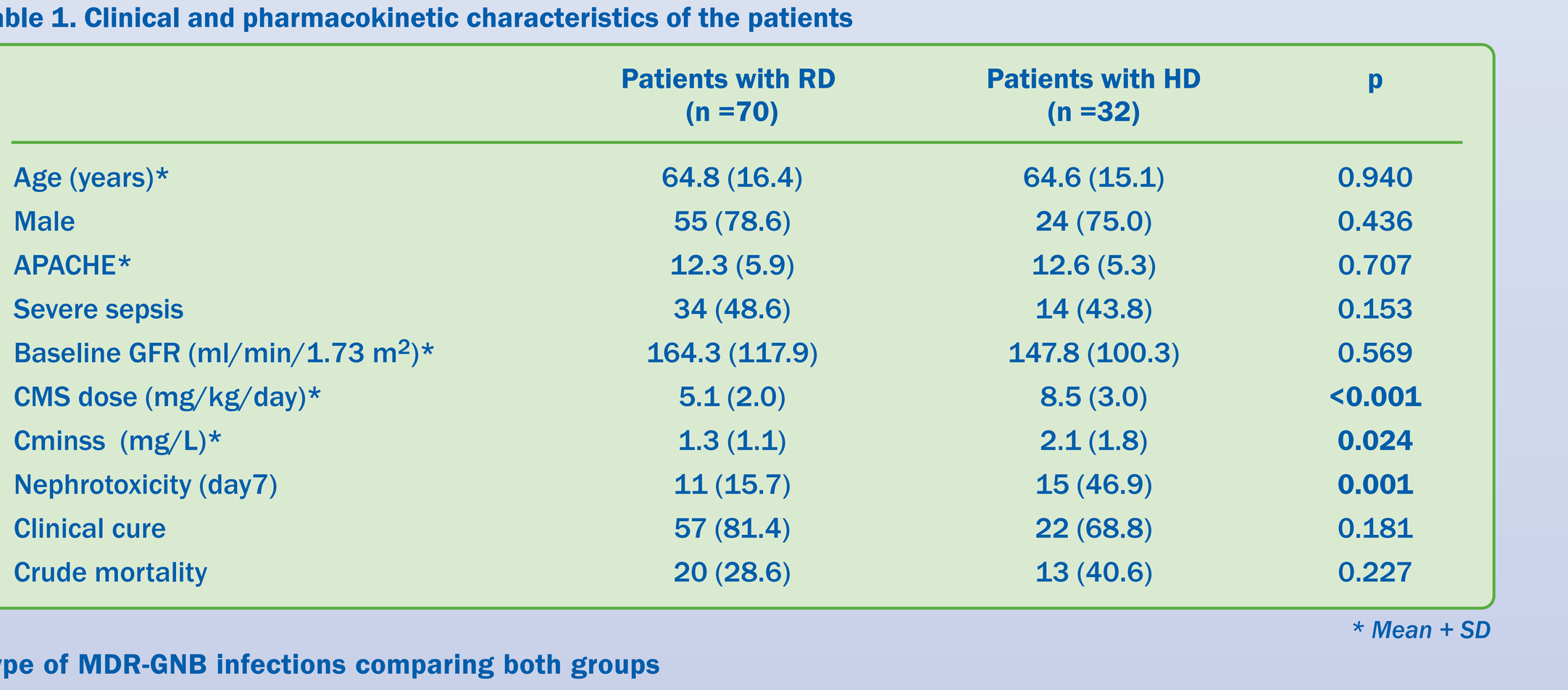
Clinical and pharmacokinetic characteristics are detailed in table 1

Table 1. Clinical and pharmacokinetic characteristics of the patients

	Patients with RD (n =70)	Patients with HD (n =32)	p
Age (years)*	64.8 (16.4)	64.6 (15.1)	0.940
Male	55 (78.6)	24 (75.0)	0.436
APACHE*	12.3 (5.9)	12.6 (5.3)	0.707
Severe sepsis	34 (48.6)	14 (43.8)	0.153
Baseline GFR (ml/min/1.73 m^2)*	164.3 (117.9)	147.8 (100.3)	0.569
CMS dose (mg/kg/day)*	5.1 (2.0)	8.5 (3.0)	**<0.001**
Cminss (mg/L)*	1.3 (1.1)	2.1 (1.8)	**0.024**
Nephrotoxicity (day7)	11 (15.7)	15 (46.9)	**0.001**
Clinical cure	57 (81.4)	22 (68.8)	0.181
Crude mortality	20 (28.6)	13 (40.6)	0.227

** Mean + SD*

Type of MDR-GNB infections comparing both groups



**p value = 0.838 after comparing the distribution in both groups*

CONCLUSIONS

More than 30% of the patients received a higher than recommended CMS dose, but they didn't achieve better clinical outcomes in terms of clinical cure and mortality and they developed nephrotoxicity more frequently, a fact probably related to the higher colistin plasma levels.

These findings suggest the need to carefully select which patient's profile can benefit from these higher than recommended doses of colistin.

REFERENCES

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