ABSTRACT #113139

Epidemiology and Clinical Management of Patients with Methotrexate Toxicity in Spain Using the Delphi Technique

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INTRODUCTION

High-dose methotrexate (**HDMTX**) is administered for the treatment of malignancies such as lymphoma, acute lymphoblastic leukaemia (ALL) and osteosarcoma[1,2,3]. Although HDMTX is usually well tolerated, some patients develop **acute kidney injury (AKI)**, a life-threatening complication[4,5,6]. No studies have been published about the impact of methotrexate (MTX) toxicity in Spain.

OBJECTIVES

To estimate the incidence and clinical management of patients receiving HDMTX as part of their chemotherapy treatment who develop MTX toxicity due to delayed MTX elimination in Spain using the **Delphi technique**[7].

METHODOLOGY

A two-round Delphi study was performed to reach consensus between medical experts on haemato-oncology and paediatric oncology with experience in the management of HDMTX treated patients from leading Spanish hospitals. An online questionnaire was developed based on national and international guidelines and previous evidence regarding HDMTX-related toxicity. Consensus was established at 80% agreement. Median and interquartile range (IQR) were calculated, and incidence data were extrapolated to the Spanish general population.

Table 1. Estimated epidemiology and clinical implications of MTX delayed elimination.

	General population		Adults		Paediatrics (<18 years)	
	n	%	n	%	n	%
Patients treated with HDMTX	1475	-	912	-	563	-
MTX delayed elimination	406	**27.5%**	274	**30.1%**	132	**23.4%**
HDMTX-induced AKI	171	**11.6%**	118	**12.9%**	53	**9.5%**
Developing severe systemic toxicities (≥grade 3)	68	**39.6%**	52	**43.9%**	16	**30.0%**
Chronic kidney disease	32	**18.8%**	30	**25.8%**	2	**3.3%**
Mortality	7	**4.2%**	4	**3.0%**	4	**6.7%**

Table 2. Treatment availability in Spanish hospitals in case of persistent MTX toxicity.

	Hospitals with availability	Patients with HDMTX-induced AKI receiving the treatment if available	
Treatment	**%**	**Median(%)**	**IQR* [Q1-Q3]**
Haemodialysis	90%	5%	[0-20]
Glucarpidase	60%	63%	[5-100]
Hemofiltration	60%	5%	[0-14]
Exchange transfusion	50%	0%	[0-5]
High-flux haemodialysis	30%	0%	[0-20]
Enterohepatic circulation	20%	35%	-
Charcoal hemoperfusion	20%	5%	-
Thymidine	10%	0%	-

*IQR was calculated when a minimum of 3 data were available.

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RESULTS

- Ten medical experts participated in the study. 40% of the experts were paediatricians, and their expertise covered lymphoma (3/10), ALL (2/10), ALL and lymphoma (1/10) and osteosarcoma (4/10).
- According to the experts, 1475 patients were estimated to be treated annually with HDMTX in Spain. Out of this, 11.6% were estimated to develop HDMTX-induced AKI (12.9% adults; 9.5% paediatric) **(table 1)**
- Immuno-enzymatic assay was the common method used in the hospitals to monitor MTX serum levels (9/10). HPLC was not available in most of the hospitals.
- All experts would use high leucovorin doses and increased supportive care as first line of treatment in case MTX-delayed elimination.
- If MTX toxicity persists, haemodialysis, glucarpidase, hemofiltration and exchange transfusion/plasma exchange are most common alternative treatment options. **(table 2).**
- 63% [5-100] of patients were treated with glucarpidase in case of persistent MTX toxicity at the hospitals where glucarpidase is available **(table 2).**
- Most prevalent non-renal systemic toxicities of grade 3 or above were haematologic toxicity and mucositis (21-40% of patients).
- Approximately, 5% [1-13] of patients with HDMTX-induced AKI would require intensive care.
- Mortality due to complications related to MTX toxicity was estimated in 4.2% (**table 1**)

CONCLUSIONS

These results are one of the few evidence on epidemiology and management of MTX toxicity due to delayed MTX elimination. Incidence of HDMTX-induced AKI and mortality obtained in this study are in line with previous studies from other countries (incidence between 2-12%, mortality 4-6%)[4,8,9,10]. Although HPLC is a more accurate method, immuno-enzymatic assay is the most used in Spanish hospitals to monitor MTX serum levels due of the lack of availability of HPLC. Further studies based on Real-World Data would be necessary to validate these results.

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