

Neurological toxicity caused by ifosfamide in children

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Background

Ifosfamide is used in the treatment of sarcomas, lymphomas and germ-cell tumors. This anti-cancer drug may induce a neurological toxicity known for adults not for children.

Purpose

Describing the neurological toxicity of ifosfamide from our experience, in Pediatric Hematology, and the implications on patients.

Materials and Methods

We performed a retrospective study of reported cases at the regional pharmacovigilance centre for children who presented neurological toxicity due to ifosfamide, from January 2011 to September 2013. Data recorded were: indication, ifosfamide dose, neurotoxicity events, toxicity management and patients' outcomes.

Results

	Child #1 (12 years old)	Child #2 (8 years old)	Child #3 (15 years old)	Child #4 (2 years old)	Child #5 (1 year old)
Medical history	Tubulopathy				
Pathologies	Osteosarcoma	Ewing sarcoma	Metastatic ewing sarcoma	Nephroblastoma	Neuroblastoma
Ifosfamide dose (associated to appropriate anti-cancer drugs)	3g/m ² /course				
Neurological toxicity	• Encephalopathy • Coma	• Convulsions • Generalized convulsions	• Convulsions • Encephalopathy • Coma	• 2 Generalized convulsions	• Convulsions • Encephalopathy
Toxicity occurrence	2 nd day of the 1st course	Begining of the 6th course	2 nd day of the 1st course	2 nd day of the 1st course	2 nd day of the 1st course
1 st treatment Intensive care unit	Methylthioninium chloride (to reduce the risk of neurological toxicity)				
2 nd treatment	No need for 2 nd treatment due to clinical amelioration	• Diazepam	• Diazepam *	• Diazepam • Clonazepam • Phenytoin replaced by Phenobarbital due to its inefficiency	• Diazepam • Clonazepam • Phenytoin
Leaving treatment	No need for treatment	No need for treatment	• Clonazepam • Levetiracetam	• Clonazepam • Valproate	Deceased

* One month after a first encephalopathy and because only ifosfamide can cure metastatic ewing sarcoma, child #2 received a second course associated to methylthioninium chloride. He had a second encephalopathy and received clonazepam and levetiracetum to be continued after leaving the hospital.

Conclusions

Neurological toxicity involved in the use of ifosfamide have been identified and confirmed.

Ifosfamide must be used with caution because even associated to methylthioninium chloride the risk of leading to neurological disorders remains.

Indeed, two children out of five are treated with an antiepileptic treatment on a long term basis.

