DI-056

DYSPNEA INVOLVING DIMETHYL FUMARATE: FIRST CASE REPORT

Picard A[1], Leroy B[1], Casulli C[2], Grandvuillemin A[3], Renzullo C[1], Coutet J[1], Penaud JF[1]
[1]Central Pharmacy– William Morey Hospital Center – Chalon sur Saône (France)
[2]Neurology Department – William Morey Hospital Center – Chalon sur Saône (France)
[3]Regional Pharmacovigilance Center – Universitary Hospital Center – Dijon (France)
alexandre.picard@ch-chalon71.fr

Introduction :

Dimethyl fumarate (DMF, TECFIDERA®) has been recently approved for multiple sclerosis. The most common DMF adverse reactions are flushing and gastro intestinal events. Indeed, a dose escalation is necessary after 7 days from 120 mg to 240 mg bid to minimize the occurrence of adverse effects at the treatment beginning.

Purpose :

We report a patient treated by DMF who experienced dyspnea after increasing the dosage.

Methods :

- An adverse effect declaration was reported from the Department of Neurology
- Naranjo algorithm was used to evaluate the probability of adverse drug reaction

Results :

A 48 year old woman without medical or surgical history received DMF for multiple sclerosis started at a dose of 120 mg bid. Dosage was increased on day 7 at a dose of 240mg bid. 24 hours later, she experienced dyspnea that required hospitalization on day 20.

DMF was reduced to 120 mg bid and complete resolution appeared 24 hours later. Two months later, pulmonary function tests were normal.

New dose escalation led in the next 24 hours to a recurrence of dyspnea with breathlessness. DMF was finally stopped. The Naranjo score was 9 so this ADR was considered as definite.

Clinical Data :

- Dyspnea was classified stage III by NYHA classification.
- A 93% oxygen saturation, 68 mmHg pO2, 48 mmHg pCO2 were observed during hospitalization while electrocardiogram was normal.
- Biological assessment with negative troponin, D-dimer, CRP and a normal pulmonary radiography excluded pulmonary embolism.

Naranjo Adverse Drug Reaction Probability Scale

Question	Yes	No	Do Not Know	Score
1. Are there previous *conclusive* reports on this reaction?	+1	0	(0)	
2. Did the adverse event appear after the suspected drug was administered?	(+2)	-1	0	
3. Did the adverse reaction improve when the drug was discontinued or a *specific* antagonist was administered?	(+1)	0	0	
4. Did the adverse event reappear when the drug was re-administered?	(+2)	-1	0	
5. Are there alternative causes (other than the drug) that could on their own have caused the reaction?	-1	(+2)	0	
6. Did the reaction reappear when a placebo was given?	-1	+1	(0)	
7. Was the drug detected in blood (or other fluids) in concentrations known to be toxic?	+1	0	(0)	
8. Was the reaction more severe when the dose was increased or less severe when the dose was decreased?	(+1)	0	0	
9. Did the patient have a similar reaction to the same or similar drugs in *any* previous exposure?	(+1)	0	0	
10. Was the adverse event confirmed by any objective evidence?	+1	0	(0)	
TOTAL SCORE:				+9

Discussion-Conclusions :

- This is the first dyspnea case reported to the French Pharmacovigilance system.
- Since this event, another case of dyspnea involving DMF was reported in our hospital. It seems important to monitor the tolerance of DMF treatment particularly after the dose escalation, whatever the symptoms.
- The management of some adverse reactions by dose reducing may be necessary.
- Adverse drug reactions discovered during post-marketing authorization should systematically be reported to the Pharmacovigilance System.

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