Journal of Neurology (2019) 266:3160–3161
https://doi.org/10.1007/s00415-019-09515-6

LETTER TO THE EDITORS

High-dose steroid therapy for CNS inflammatory diseases increases INR in patients taking oral vitamin K antagonist

Stefano Gelibter[1] · Mario Orrico[1] · Tommaso Croese[1] · Luca Bosco[1] · Vittorio Martinelli[1] · Francesca Sangalli[1] · Massimo Filippi[1,2,3]

Received: 12 August 2019 / Accepted: 16 August 2019 / Published online: 21 August 2019

Dear Sirs,

Many patients with central nervous system (CNS) inflammatory diseases are young, without significant comorbidities. Nevertheless, some of those patients can be affected by other medical conditions that may require anticoagulant treatment.

We recently faced CNS inflammatory relapses in two patients chronically treated with vitamin K antagonist (VKA) anticoagulant therapy for more than 5 years and international normalized ratio (INR) was generally within the target therapeutic range (2.0–3.0). In both cases, intravenous (iv) administration of methylprednisolone (MP) led to significant increase in INR. None of the patients were taking concomitant drugs known to potentiate oral anticoagulant effect.

Patient 1 was a 46-year-old man, admitted to our department for MS diagnosis, with history of pulmonary embolism (PE) in the context of hereditary thrombophilia (homozygosis for prothrombin A20210 gene variant). In the days before steroid treatment, mean INR value was 2.36. Because of mild clinical and radiological disease activity, he was treated with MP 500 mg iv for 3 days, monitoring INR values daily. The second day of steroid therapy INR increased to 3.29, requiring an adjustment of warfarin dose; the third day it further increased to 3.92 and anticoagulant treatment was temporarily suspended until INR returned within therapeutic range during the following days.

Patient 2 was a 66-year-old woman with an idiopathic CNS inflammatory disease and history of PE chronically treated with warfarin. While she was hospitalized, she experienced an important clinical and radiological inflammatory relapse. She was treated with 1000 mg of MP iv for 7 days, monitoring INR daily. Mean INR before steroid treatment was 2.28 and it was 2.37 the day the therapy was started. After 1 day, INR reached 7.92 and anticoagulant therapy was suspended. The third day it decreased to 6.88. In the following day, INR decreased to 1.97 and then low molecular weight heparin was administered for the remaining period of steroid treatment.

A potentiation of VKA by a high dose of iv MP has been reported in two MS patients by Kaufman [1], and in ten patients not affected by CNS diseases by Costedoat-Chalumeau et al. [2], but there is still a lack of relevant published data. The aim of our report is to draw the MS community's attention to the possible interactions between high-dose steroid treatment and VKA, since it could lead to serious and potentially life-threatening side effects. When administering high-dose iv steroid in patients chronically treated with VKA, INR monitoring should be performed daily during treatment and in the next following days with an adjustment of dose or a suspension of VKA when needed.

Author contributions Stefano Gelibter: acquisition and analysis of data, drafting the manuscript; Mario Orrico, Tommaso Croese, Luca Bosco, Vittorio Martinelli, Francesca Sangalli: acquisition and analysis of data, revising the manuscript; Massimo Filippi: revising the manuscript; study supervision.

Compliance with ethical standards

Conflicts of interest Stefano Gelibter, Mario Orrico, Tommaso Croese, Luca Bosco, Vittorio Martinelli, and Francesca Sangalli have nothing to disclose. Massimo Filippi is Editor-in-Chief of the *Journal of Neurology*; received compensation for consulting services and/or speaking activities from Biogen Idec, Merck-Serono, Novartis, and Teva Pharmaceutical Industries; and receives research support from

✉ Massimo Filippi
filippi.massimo@hsr.it

[1] Neurology Unit, IRCCS San Raffaele Scientific Institute, Milan, Italy

[2] Neuroimaging Research Unit, Institute of Experimental Neurology, Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy

[3] Vita-Salute San Raffaele University, Milan, Italy

Biogen Idec, Merck-Serono, Novartis, Teva Pharmaceutical Industries, Roche, Italian Ministry of Health, Fondazione Italiana Sclerosi Multipla, and ARiSLA (Fondazione Italiana di Ricerca per la SLA).

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional committee and the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards.

References

1. Kaufman M (1997) Treatment of multiple sclerosis with high-dose corticosteroids may prolong the prothrombin time to dangerous levels in patients taking warfarin. Mult Scler 3:248–249
2. Costedoat-Chalumeau N, Amoura Z, Aymard G et al (2000) Potentiation of Vitamin K antagonists by high-dose intravenous methylprednisolone. Ann Intern Med 132:631–635