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The incidence of delirium in patients pretreated with statins who remain in an intensive care unit after cardiac surgery

Incidência de delirium durante a internação em unidade de terapia intensiva em pacientes pré-tratados com estatinas no pós-operatório de cirurgia cardíaca

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“Something is impossible only until someone doubts and proves the opposite”.
Albert Einstein

Dear Editor,

I read, with great interest, the article “The incidence of delirium in patients pretreated with statins who remain in an intensive care unit after cardiac surgery,” published by Cruz et al. in the Brazilian Journal of Intensive Therapy (Revista Brasileira de Terapia Intensiva) volume 24, number 1, pages 52 to 57.⁽¹⁾ The subject is highly relevant.

In 1970, Akira Endo synthesized inhibitors of hydroxymethylglutaryl coenzyme A (HMG-CoA) reductase (statins) from fungal metabolites that inhibit cholesterol synthesis to counteract parasites. The compound was called compactin.

In animal models (except rats), the new inhibitors were effective in diminishing total cholesterol by approximately 30%. After the reduction of medication levels due to the occurrence of lymphomas and with the development of lovastatin, broader use in humans was able to begin in 1987.^(2,3)

Statins have demonstrated powerful effects on the overall reduction of cholesterol (by the inhibition of hepatic cholesterol synthesis) and on the subsequent increase in the number of hepatic LDL receptors. Hypercholesterolemia causes endothelial dysfunction, and the statins can even result in the removal cholesterol from arterial walls.⁽⁴⁾

Pleiotropic effects are so named because they encompass effects unrelated to those involving LDL production as a result of therapy with statins and are perhaps related to actions in the vascular wall.

Among the pleiotropic effects, we can list effects on sepsis, deep vein thrombosis, endometriosis, and chronic obstructive pulmonary disease (COPD) as well as neuroprotective effects. These effects have not yet been fully explained but remain much discussed. In addition, included here are studies related to delirium in the immediate postoperative (IPO) period after cardiac surgery.

I would like to ask the author about the patients who used alcohol or psychiatric drugs or who were elderly (over 65 years) during the preoperative period. Was there a greater presence of delirium in the IPO period? Mariscalco et al. observed that these groups presented greater risks.⁽⁵⁾ The other question would be regarding the patients who underwent aneurysm correction or aortic dissection: do they present a greater number of delirium cases?

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In light of today's knowledge and despite the anti-inflammatory, immunomodulator, and antithrombotic effects of statins, the "Holy Grail" (the statins) has not yet been discovered or unveiled. Additionally, because "happiness, health,

and eternal youth" are facing the collateral effects to be considered in treatment.⁽⁶⁾

Sincerely,
Hélcio Giffhorn

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AUTHOR RESPONSE

Dear Dr. Giffhorn,

We appreciate your interest and your attentive reading of our manuscript. Your questions are extremely pertinent. Unfortunately, the relationships among the use of alcohol, the use of psychiatric medications, and aneurism correction surgery cannot be adequately evaluated in our database due to the small sample size. However, as cited in your comments, the literature does illustrate a greater incidence of delirium in these populations. As for age, the literature shows that an elevation in the incidence of delirium generally occurs with increased age. In our patients, when dichotomized by age (≥ 65 years *versus* < 65 years), we do find that age is a risk factor for developing delirium during the postoperative period (OR=1.17 [1.03-1.33]).

We hope that in the near future, we can better understand the mechanisms associated with delirium and the effects of statins on the dysfunction of the central nervous system in attempts to improve our patients' care.

Sincerely,

Felipe Dal-Pizzol and Cristiane Ritter

In the name of the authors
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