Quantitative analysis on the development of musculoskeletal adverse effects of corticosteroids using common data model

Sun Geu Chae, Sang-Heon Kim, Yoon-Kyoung Sung, Yeesuk Kim

Background

Since their discovery in the 1940s, corticosteroids have become one of the most widely used and effective treatments for various inflammatory and autoimmune disorders. Despite their beneficial effects, long-term systemic (oral or parenteral) use of these agents is associated with well-known musculoskeletal adverse events (AEs) such as osteoporosis, bone fractures and osteonecrosis.[1,2] Although the AE of corticosteroid usage is well known, the relationship between dosage and AE has not been determined thoroughly. The purpose of this study was to perform the quantitative analysis about the adverse events of the corticosteroid using common data model

Methods

Data for this study were collected between 2001 and 2018 from OMOP Common Data Model of Hanyang University Seoul Hospital.

The patients aged between 25 and 64, who used systemic corticosteroids for the treatment of autoimmune diseases were included in the cohort, and we excluded the patients with previous history of hip fracture and caisson disease which are the predisposing factor occuring the osteonecrosis that is one of the outcomes of interest. The outcomes of interest are osteoporosis, bone fracture, and osteonecrosis which are considered as musculoskeletal AEs of corticosteroids.

The crude incidence rates of outcomes were investigated. To evaluate the dose related factor associated with the outcome of interest of this study, we developed a R package “SteroidDoseStudy” that analyzed the corticosteroid dosage occurring the osteoporosis, bone fracture and osteonecrosis. (https://github.com/estone96/SteroidDoseStudy.git) Using logistic regression modeling to determine the probability of outcomes in accordance with the cumulative dosage and daily average dosage of prednisolone equivalent, as well as the period of corticosteroid usage resulting in musculoskeletal AEs. The separate logistic regression models were constructed with the log-transformed input parameters and the model output is the probability of AEs, and optimal cutoff points for prediction of outcomes were chosen to maximize sensitivity and specificity.

Results

15,127 patients were included in this study. There were 1342 osteoporosis, 278 fracture, and 118 osteonecrosis patients. The crude incidence rates were 8.9%, 1.8%, and 0.8% respectively. The optimal cutoff value of cumulative dosage was 1882mg in osteoporosis, 1425mg in fracture, and 2312.5mg in osteonecrosis. In terms of daily dosage, the optimal cutoff values were 4.7mg per day in osteoporosis, 5.4mg per day in fracture, and 6.8mg per day in osteonecrosis. The optimal cutoff points of the corticosteroid period were 255 days for osteoporosis, 339 days for fracture, and 439 days for osteonecrosis.

Conclusion

The incidence rate of muscular adverse effects were relatively low in our study, and a possible dose-response relationship was observed for bone related adverse effects. Therefore, our results support the need for developing new treatment strategies with a better safety profile than that of systemic corticosteroids.

References/Citations

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