

THE EFFECT OF ALBUMIN ON SERUM CONCENTRATION OF DIRECT ORAL ANTICOAGULANTS: A CROSS-SECTIONAL STUDY

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Introduction. One of the main advantages of direct oral anticoagulants (DOACs) in the management of venous thromboembolism (VTE) is the possibility of administering at fixed doses without routine laboratory monitoring. However, concerns emerged regarding their use in obesity, severe chronic kidney disease, and concomitant drug therapy. In these situations, measurement of DOACs plasma concentrations had been proposed as a potential strategy to optimize therapeutic management and improve patient outcomes. DOACs display a relevant degree of binding to plasma proteins, predominantly to serum albumin, which represents the most abundant protein component in plasma. Hypoalbuminemia has been associated with an increased risk of bleeding among patients receiving DOAC therapy. However, few studies evaluated DOACs plasma concentrations. Therefore, the aim of the study was to evaluate the variation in peak and trough DOACs plasma concentrations according to serum albumin levels in a cohort of patients with VTE. Patients attending the study center were eligible if they had age ≥18 years; diagnosis of VTE with DOACs treatment; signed a written informed consent.

Results. The overall population consisted of 88 patients with 56.8% of male patients and a mean age of 67±14 years. 58% of patients presented with hypoalbuminemia. Patients with hypoalbuminemia were significantly older than those with normal albumin levels and showed a higher prevalence of male sex. Regarding risk factors, the prevalence family history of VTE, personal history of VTE, smoking habit, and active malignancy was similar between the two groups. The proportion of patients with a VTE provoked by a persistent or transient risk factor and that of unprovoked VTE were similar between groups. No significant difference was observed in renal function as assessed by eGFR. Correlation analysis did not demonstrate a significant relationship between serum albumin levels and standardized DOACs trough (p =0.78) and peak concentrations (p=0.40). No significant association between serum albumin levels and DOACs trough and peak concentrations has been found.

Discussion. The rationale for investigating the role of serum albumin stems from recent evidence suggesting an association between hypoalbuminemia and adverse outcomes in patients receiving DOACs. We sought to determine whether the increased clinical risk observed in hypoalbuminemic patients could be mediated by alterations in DOAC plasma concentrations. In our cohort, analyses of DOAC plasma concentrations did not demonstrate a significant association with serum albumin levels. Age was the only independent determinant (p = 0.027). One possible explanation for the lack of association between albumin levels and total plasma DOAC concentrations may lie in the mechanisms of fractional drug clearance. In hypoalbuminemia, the reduction in available binding sites leads to an increase in the unbound fraction of drug. Since the free fraction undergoes glomerular filtration, an increase in unbound drug may result in a proportional acceleration of kidney elimination. This mechanism may counterbalance the increase in pharmacologically active drug, leading to stabilization of total plasma concentrations. In conclusion, the present study suggests that serum albumin levels do not represent an independent determinant of total DOAC plasma concentrations.