

# A hypercoagulable state associated with intravenous pulse methylprednisolone therapy in patients with Graves' Orbitopathy

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## INTRODUCTION

Chronic exposure to glucocorticoid (GCS) excess, either endogenous or exogenous, is associated with a hypercoagulable state and a high risk of thromboembolic complications like deep vein thrombosis and pulmonary embolism. The underlying mechanism of this phenomenon is still unclear. Chronic exposure of excess of GCS can cause disorders of all components of the Virchow triad, namely: i) abnormalities of hemostatic parameters, ii) vascular and endothelial damage secondary to obesity, insulin resistance, hypertension or dyslipidemia and iii) disturbed blood flow secondary to polycythemia, obesity or decreased mobility. However, there is a lack of studies dealing with the problem of influence of high dose intravenous (iv) GCS pulse therapy on coagulation system. This treatment is commonly used for a wide range of inflammatory, neoplastic and autoimmune diseases, including Graves' Orbitopathy (GO). In literature, there are some reported cases of even fatal side effects related to this therapy, including pulmonary embolism. Moreover, some of those diseases necessitating iv GCS treatment can cause a hypercoagulable state by itself. Taking the foregoing into account, it is important to determine whether the use of GCS enhances this process and whether thromboprophylaxis for patients receiving this kind of treatment should be recommended.

## AIM

The aim of the study was to examine the influence of iv methylprednisolone (MP) on hemostasis in patients with active, moderate to severe GO. Patients were treated according to European Group on Graves' Orbitopathy (EUGOGO) recommendation with MP pulse given once a week for 12 consecutive weeks (cumulative dose 4.5 g).

## DESCRIPTION OF METHODS

	Mean (±SD) or n (%)
Patients	20
Age	54 (± 11,4)
Female	14 (70%)
Smoking	11 (55%)
Hypertension	7 (35%)
Diabetes mellitus	none
Low-density lipoprotein (LDL) (<130 mg/dL)	111,5 (± 26,6)
Body Mass Index (BMI) (kg/m <sup>2</sup> )	24,5 (± 4,1)
Thyroid-stimulating hormone (TSH) (0.4 - 4.0 mIU/L)	1,5 (± 1,2)
History of venous thromboembolism events	none
Use of medications that affect hemostasis	none

Table 1. Characteristic of patients

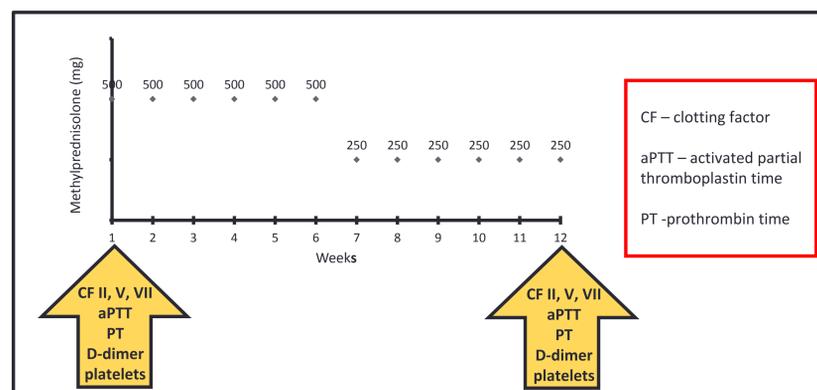


Figure 1. Schedule of treatment and interventions

## RESULTS

- Statistically significant increase of clotting factor (CF) II, CF V, CF VII and platelets was observed. The increase was noted respectively in 90%, 75%, 70% and 63% of patients.
- Prothrombin time (PT) and activated partial thromboplastin time (aPTT) tended to decrease - in 65% and 50% of patients respectively, this change did not demonstrate statistical significance.
- The increase of D-dimer in 55% of patients was observed, in 50% the increase was over 20%.
- There were no episodes of clinically overt venous thromboembolism.

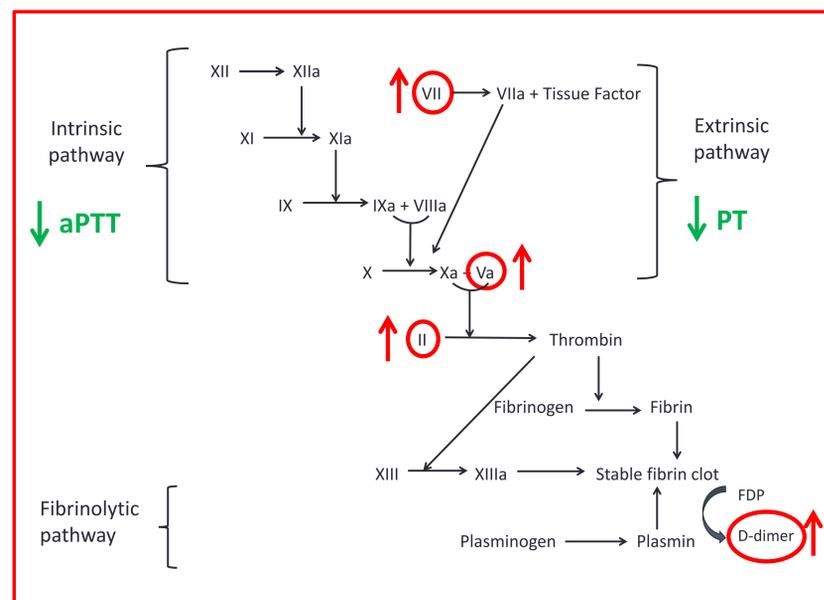
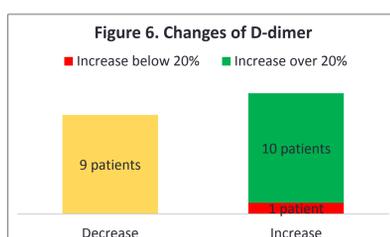
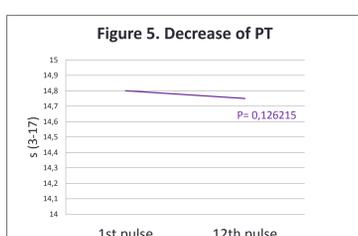
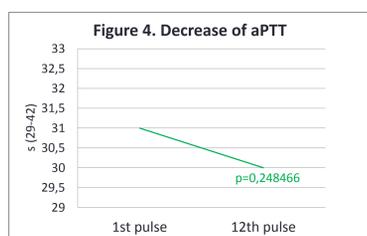
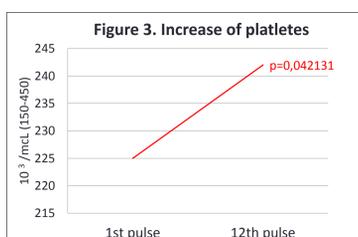
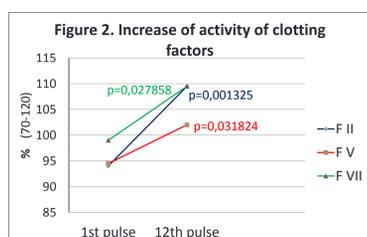


Figure 7. Coagulation cascade and alterations after iv MP therapy

## CONCLUSIONS

High dose iv MP pulse therapy in patients with GO may be associated with a hypercoagulable state which can be a cause of fatal adverse effects (e.g. pulmonary embolism). This study indicates the increase of activity of CF II, CF V and CF VII with subsequent shortening of aPTT and PT. However, the casual relationship of those changes with the onset of clinically overt thrombosis remains to be confirmed. In patients with additional risk, prophylactic treatment may be required.