LETTER TO THE EDITOR
(RESEARCH LETTER)

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Improved cytoreductive potential of plateletapheresis in the treatment of thrombocythemia: a single center study

Poboljšani citoreduktivni potencijal trombocitafereze u lečenju trombocitemije

To the Editor:

Extreme thrombocytosis (ETC; cell-count ≥ 1500 × 10^9/L) in the essential thrombocythemia (ET) patients – with altered platelet (Plt) morphology/aggregability (Plt-dysfunction) and immature reticulated Plts – increases the risk of both thromboembolic and/or hemorrhagic events (up to 50%). The evidence-based clinical guideline for therapy of asymptomatic-ET (e.g., exact cytapheresis-threshold, target Plt-count, etc.) is not yet established. In the treatment of symptomatic-ET (when low-dose aspirin or other anti-Plt and the highest doses of chemotherapy are without rapid response or contraindicated, as in pregnancy), cytoreduction by plateletapheresis is useful or essential [1–4]. The first cytapheresis in our Apheresis Center was performed in 1971 for treatment of pregnant women with hyperleukocyte-leukostasis [1, 2].

The aim of this study was to evaluate cytoreductive potential of the Spectra-Optia/IDL-System, based upon the *ex vivo* Plt-removal and the *in vivo* Plt-depletion (Plt-removal/depletion) efficacy (using our modifications of manufacturer's original protocol). The Plt-removal/depletion efficacy of this study was compared to our earlier results (historical database) and the latest literature data for different devices. To the best of our knowledge, this is the second published clinical evaluation of the efficacy and safety of therapeutic plateletapheresis using the Spectra-Optia.

In the treatment of a 68-year-old female patient suffering from symptomatic-ET (with headaches, vertigo, visual-disturbances and paresthesia) the Plt-removal/depletion procedure was performed by the Spectra-Optia/IDL-System (Terumo BCT; USA). Our modifications of apheresis protocol included the collection-preference and inlet flow corrections (altered collection speed) as well as an increase of the target cell suspension volume to improve the Plt-removal/depletion efficacy. As previously described, the Plt morphology (shape-ratio) and ultrastructural properties by the phase-contrast microscope (Polyvar, Austria) and electron-microscope (Philips-201-C; The Netherlands) were examined, respectively [5, 6]. The Plt-function by the Multiplate Analyzer (Dynabyte GmbH, Germany) was evaluated. Statistical analysis was performed by the Student's *t*–test, using the "Origin-PC-Program". The results were considered to be significant at $p < 0.05$. The apheresis therapy was approved by the Military Medical Academy (MMA) Ethics Committee.

In the treatment of this patient with ETC associated clinical emergency, using an intensive "single-plateletapheresis" (by Spectra-Optia/IDL-System) 7.5 × 10^{12} Plts were removed from circulation (cell suspension = 1150 mL). A significant Plt-depletion (from 2330 × 10^9/L to 633 × 10^9/L; $p < 0.05$) and *in vivo* Plt-fall = 72.8% (the circulating Plt ratio before and after plateletapheresis expressed in percentage; $p < 0.05$) was realized and followed by the clinical advances and prevention of thromboembolic (e.g., stroke) and/or hemorrhagic events. As replacement fluid, albumin in saline was used. There were no side effects due to intensive plateletapheresis.

The baseline aggregability of Plts in the patient′s venous blood sample was 918 aggregation units (AU)*min (normal = 923–1509 AU*min) by the Thrombin Receptor Activating Peptide (TRAP)-test [10 AU*min is equal to one Area Under the Curve (AUC) value]. The ultrastructural features of various Plt-shapes are visualized in Figure 1.

As shown, the discoid Plt-shapes had the typical ultrastructural properties without the membrane integrity destructions, intact microtubules and open canalicular system. There were also several dendritic Plt-shapes with the extensive cell membrane damages and pseudopods, reduced electron density, peripheral dislocation of granules and/or cytoplasm organelles with the resultant Plt-dysfunction.

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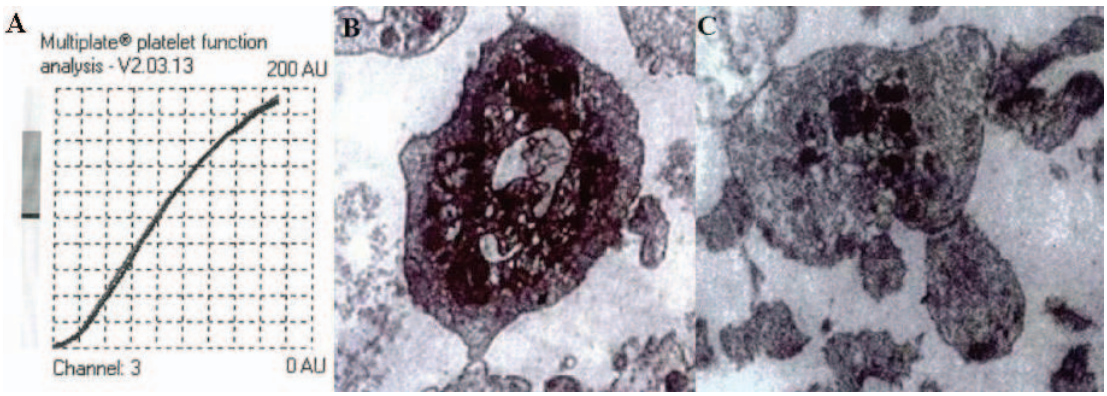

Fig. 1 – Platelet (Plt) functional and ultrastructural analysis: (A) Reduced Plt-aggregability – TRAP-test = 918 AU*min); (B) Discoid Plt-shape (prevalent incidence); (C) Dendritic Plt-shape (sporadic occurence).

As previously described [2], in the treatment of our comparable ET-patients (n = 20; procedures = 126; historical database), using the Cobe-Spectra by "single-plateletapheresis" 2.8±2.1 × 10^{12}/L, Plts (cell suspension = 800–1300 mL; $p < 0.05$) were removed. The *in vivo* Plt-depletion was approximately threefold smaller/lower. Only the use of whole "plateletapheresis-cure" (typically 5 "single-plateletapheresis"; range = 3–11) resulted with a comparable *in vivo* Plt-fall (68 ± 14%) [2].

The Plt-removal/depletion efficacy in our current study was significantly ($p < 0.05$) superior when compared to the most recent literature data [4, 7]. Precisely, after a "single-plateletapheresis" by the CS-3000-Plus (Baxter, USA) or Cobe-Spectra (Terumo BCT, USA) in the therapy of six hemato-oncological patients [4] and the treatment of one ET-patient by the Spectra-Optia/Apheresis-System (Terumo BCT, USA; version 11.3; manufacturer's protocol used), [7] the levels of *in vivo* Plt-depletions were only 38% and 56%, respectively.

In conclusion, intensive therapeutic plateletapheresis by the Spectra Optia/IDL-System is a safe and effective treatment for the patients with life-threatening ETC. The use of a "single-plateletapheresis" – with some protocol modifications – resulted in the undoubtedly superior Plt-removal/depletion efficacy (for both normal and altered cells) when compared to our earlier study (Cobe-Spectra) and literature data for the CS-3000-Plus or Cobe-Spectra, even for the Spectra-Optia setting (using original protocol).

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