

## REVIEW

from

Prof. Dr. Raina Teodosieva Robeva

Head of the Clinic of nephrology

MMA, Sofia

under the procedure for obtaining the educational and scientific degree "Doctor" in the scientific specialty "Nephrology" of Dr. Miroslava Stancheva Benkova-Petrova, according to the order of the Rector of MU - Varna №109-580 / 17.12.2021. and Protocol from Faculty Council № 56 / 07.12.2021 with dissertation on the topic: "Relationship between erythropoietin resistance and secondary hyperparathyroidism in patients undergoing dialysis"

Dr. Miroslava Stancheva Benkova graduated from high school in 2004 at the Mathematical High School "Baba Tonka" in Ruse. In 2010 she obtained the educational qualification degree "Master", specialty "Medicine" at the Medical University "Prof. Dr. Paraskev Stoyanov" Varna. Since 2011 she has been working at the University Hospital "St. Marina" in Varna, and since 2016 - at the Medical University "Prof. Dr. Paraskev Stoyanov" Varna as an assistant. In 2016 acquires a specialty in nephrology. Fluent in English.

The dissertation of Dr. Miroslava Benkova examines a topical and underappreciated problem of great practical importance - it examines the relationship between erythropoietin resistance and secondary hyperparathyroidism in patients undergoing dialysis. The incidence of chronic kidney disease (CKD) has increased rapidly in recent years. Anemia is one of the most common complications. It reduces the quality of life and increases the risk of cardiovascular disease and mortality, especially in the group of patients with end-stage CKD. Many of the reasons for its occurrence are specified - decreased production or resistance to endogenous erythropoietin, reduced half-life of red blood cells and bone marrow fibrosis. Secondary hyperparathyroidism is a lesser known but potentially significant cause of anemia in these patients. Parathyroid hormone (PTH) is considered a uremic toxin that inhibits erythropoietin synthesis, shortens red blood cell survival and causes myelofibrosis.



Erythropoietin resistance is directly related to the incidence of comorbidity in dialysis patients and is one of the most potent predictors of the risk of cardiovascular events and mortality. Clarifying the reasons for its occurrence and its properly treatment can help prevent potential complications.

The dissertation is written on 145 pages. It is illustrated with 59 figures, 12 tables and one appendix using 390 literature sources - 3 in Cyrillic and 387 in Latin.

The review made by Dr. Benkova is detailed and purposeful. It shows in-depth knowledge of the issue, the ability to systematize information and bring out the most important issues.

The aim of the dissertation is well formulated. The PhD student sets six tasks that allow for its implementation. 80 patients with chronic kidney disease were studied, divided into two groups - 30 pre-dialysis and 50 patients on hemodialysis treatment. The inclusion and exclusion criteria as well as the laboratory tests are adequately selected. The results are processed with modern statistical methods. Well-founded, clear conclusions are formulated. The work has theoretical and practical contributions. Non-invasive biomarkers in patients in the risk groups of CKD - pre-dialysis and dialysis stages, which can be implemented in practice regarding the diagnostic and treatment process, have been studied and followed. For the first time in Bulgaria, the level of erythropoietin resistance was monitored with a direct study of the titer of antibodies to erythropoietin, as well as determining their interdependence with other biomarkers.

The association between secondary hyperparathyroidism and erythropoietin resistance in patients with CKD has been demonstrated. The adequacy of the therapy in relation to the anemia and the secondary hyperparathyroidism was assessed. The individual quality of life of the patients with erythropoietin resistance and secondary hyperparathyroidism was assessed. Antibodies to erythropoietin and a soluble erythropoietin receptor, were tested for the first time. A developed algorithm for the diagnosis of erythropoietin resistance in patients with CKD is very valuable for practice.

The results of the dissertation confirm the hypothesis that the developed constellation of diagnostic and therapeutic methods contributes to elucidating the

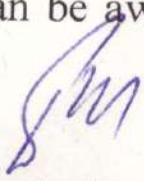
causes of erythropoietin resistance and their relationship with secondary hyperparathyroidism in patients with chronic kidney disease.

The PhD student encloses a list of 3 publications related to the dissertation. The attached list meets the requirements for acquiring the educational and scientific degree "Doctor"

The abstract is well-formed, sufficiently illustrated and reflects the essence of the dissertation.

**In conclusion**, the dissertation of Dr. Benkova is a current scientific work of theoretical and practical significance. Based on the presentation, I believe that the presented work meets the requirements of the law for the development of the scientific staff and Dr. Miroslava Stancheva Benkova-Petrova can be awarded the educational and scientific degree "Doctor".

23.12.2021

  
Prof. Raina Teodosieva Robeva