Chapter 7 Hemoglobin Level Analysis In Hemodialysis Patients Treated with Erythropoiesis Stimulating Agents: A Neural Network Approach

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ABSTRACT

This work proposes the use of two neural models for data analysis of hemodialysis patients with end-stage renal disease. There are two main goals: firstly, the knowledge extraction from a database using Self-Organizing Maps (SOMs); and secondly, to provide an accurate prediction of Hb levels next month. The achieved results show the ability of SOM to profile different behaviors present in the database. Regarding the prediction task, the obtained neural models are equivalent (p<0.05) to the linear ones in the case of EPO beta but they differ in the case of Darbepoietin. In terms of the committed error, the prediction is relatively accurate; Mean Absolute Errors are lower than 0.5 g/dl for both kinds of EPO, thus ensuring that the obtained prediction models can be used to get the goal of maintaining patients stable, within a target range of Hemoglobin (Hb) (usually, between 10 and 12 g/dl). The accurate prediction provides sufficient knowledge to be even more demanding in the target range, being able to work with narrower, more demanding ranges; e.g., 10-11 g/dl for female patients and 11-12 g/dl for male patients.

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INTRODUCTION

Secondary anemia due to end-stage renal disease (ESRD) is a clinical situation that is present in more than 90% of patients undergoing periodic hemodialysis. This situation increases the rate of hospitalization as well as patient mortality, and it decreases the patient's quality of life (QoL). The latter can be attributed to clinical consequences of the chronic anemia. From this point of view, the accurate diagnosis and treatment of this pathology are of vital importance. Patients are considered to undergo anemia when the blood Hemoglobin (Hb) concentration is lower than 13.5 g/dl in adult male patients, 12 g/dl in male patients older than 70 years, and 11.5 g/dl in female patients. Anemia is commonly attributed to CKD (Chronic Kidney Disease) when the glomerular filtration rate is lower than 60 ml/min, and other causes of anemia are excluded. In the framework of CKD, anemia is mostly due to the lack of Erythropoietin (EPO) production, whose synthesis is mainly produced in the peritubular fibroblasts of the external part of the kidney. As renal function performs worse in the ESRD, there is a decrease in the EPO production. It finally leads to the anemia.

The symptoms due to anemia are quite variable, and they usually appear when Hb concentration is lower than 11 g/dl. The patients' quality-of-life decreases, and changes in the cardiac function may also involve an increase in the ratio of morbidity and mortality.

In these circumstances the parenteral or subcutaneous administration of erythropoiesis stimulating agents (ESAs) like recombinant human erythropoietin (rhuepo) or darbepoetin is the treatment of choice) trying to maintain the Hb levels between 11 and 12 g/dl (National Kidney Foundation, 2007). Several studies have demonstrated a relationship between lower Hb levels and poorer outcomes in managing the anemia of CKD patients and those included in dialysis (Ma, 1999; Mohanram, 2004). Also, some studies have shown an association between anemia treatment and reduction of left ventricular mass index (London, 1989; Martínez Vea, 1992). As an altered ventricular geometry is a predictor of poor outcome among dialysis patients, treatment of anemia in these patients could be followed by an improvement in cardiovascular events and mortality (Foley, 1995). The clinical investigation performed in recent years regarding the administration of different rHu-EPO (ESAs) has allowed the optimization of treatment and, consequently, the improvement in the QoL in patients undergoing chronic dialysis. However, ESAs are an expensive treatment that increases the high costs of the renal replacement therapy through dialysis and transplantation, and it is not without risks. The main secondary effects of ESAs are arterial hypertension, and thromboembolic complications including thrombosis of vascular access (Lynne Peterson, 2004; Phrommintikul, 2007). Several recent randomized trials have addressed whether targeting a higher Hb level in non-dialyzed CKD patients (Singh, 2006; Drueke, 2006) and dialysed patients (Besarab, 1998) was associated with an increased rate of cardiovascular complications and death. In these three studies patients assigned to the arm with a target of Hb level around 13 g/dl, compared to those with Hb levels around 11 g/dl, showed an increased risk or no benefit with regard to cardiovascular outcomes. These findings indicate that there is a need to increase the scientific knowledge on the effects of ESAs, in order to provide further confirmation of the risk-benefit ratio of these agents. Consequently, dosage optimization is critical to ensure adequate pharmacotherapy as well as patient's safety.

Although the guidelines for the administration of ESAs are followed in daily clinical routine (NKF-K/DOQI, 2006; KDOQI, 2007), the response is not always the expected one since many complex and non-linear relationships tend to appear in the assimilation of the drug by the patient, and usual protocols take into account the average population response to the treatment (Gaweda, 2005). Therefore, in spite of the general 18 more pages are available in the full version of this document, which may be purchased using the "Add to Cart" button on the publisher's webpage: www.igi-global.com/chapter/hemoglobin-level-analysis-hemodialysispatients/43253

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