Functional Ability of Patients on Dialysis: The Critical Role of Anemia

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Maintaining hemoglobin (Hb) levels in the range (11 to 12 g/dL) recommended by the National Kidney Foundation's Kidney Disease Quality Initiative (NKF/KDOQI™) has been shown to significantly improve functional ability in patients on dialysis. The combination of partial anemia correction and an individualized exercise program yields additional incremental benefits. Nurses fulfill a crucial role in ensuring that appropriate Hb levels are maintained while at the same time encouraging patients to improve their physical conditioning and functional status.

Functional ability describes the extent to which people are able to live their lives, provide for their own needs, and fulfill their expected roles as active members of society. When medical professionals, hear the term "functional ability", they typically think of activities of daily living (ADL), including both basic and instrumental functions of life. Basic ADL comprise fundamental tasks such as eating, walking, dressing, and using the bathroom. Instrumental ADL encompass more advanced skills such as driving, shopping, paying bills, exercising lightly, doing housework, volunteering, and working. While ADL are the basis of assessments of functional ability, other factors may also have to be evaluated depending on the patient population (Hays, Steffens, Flint, Bosworth, & George, 2001; Raina, Wong, & Massfeller, 2004).

Anemia negatively influences a broad range of parameters that can significantly decrease functional ability in patients on dialysis (Table 1). Conversely, partial correction of anemia to maintain hemoglobin (Hb) levels at 11 to 12 g/dL, as recommended by the National Kidney Foundation's' Kidney Disease Outcomes Quality Initiative (NKF-K/DOQI™), has been shown to improve functional status (Eschbach, et al., 1989; Evans, Rader, Manninen, & the Cooperative Multicenter EPO Clinical Trial Group, 1990; National Kidney Foundation, 2001). This article reviews clinical data on the effects of partial anemia correction on patients' functional ability.

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Table 1: Symptoms Associated with Anemia in Patients on Dialysis

↓ Energy and activity levels
↓ Sleep and eating behaviors
↓ Health status
↓ Sex life
↓ Psychological effects
↓ Exercise capacity (VO_2 max)
↓ Strength
↓ Energy
↑ Muscle weakness
↑ Leg cramps
↑ Shortness of breath

Effect of Anemia Correction on Overall Functional Ability

Severe anemia is one of the primary factors limiting functional ability and rehabilitation in patients on dialysis (Beusterien & Nissenson, 1996). The potential for ameliorating the functional limitations observed in patients with anemia was first reported in a study of 130 patients on dialysis whose hematocrit (Hct) was increased from a mean baseline level of 23.7% to 33.9% and maintained after initiation of Epoetin alfa therapy. An assessment of the effects of this intervention revealed consistent, significant improvements in functional limitations, energy, and activity levels at the higher level (Figure 1). Overall, there was almost a two-fold increase in the percentage of patients who had no complaints and could accomplish normal activities ($P \leq 0.01$) (Eschbach, et al., 1989).

In a more complete evaluation, Evans, Rader, Manninen, and the Cooperative Multicenter EPO Clinical Trial Group (1990) assessed quality of life in a study of 333 patients on hemodialysis whose Hct increased from 22.3% to 34.0% after treatment with Epoetin alfa. Functional ability was assessed by analyzing questionnaires completed by both the patients and the staff at each dialysis center. Results showed significant improvements in many objective and subjective parameters related to functional ability, including an increase in the percentage of patients who were free of physical limitations and full of energy, and a decrease in the percentage of patients who tired easily or experienced general weakness, shortness of breath, and muscle weakness ($P < 0.001$) (Figure 2).

Effect of Anemia Correction on Exercise Capacity and Oxygen Consumption

Exercise capacity, a key driver of functional ability, has been the focus of many investigations into the effects of partial anemia correction in patients on dialysis. Exercise capacity has frequently been determined by analyzing respired gases during graded exercise to determine whether therapeutic interventions alter the maximum rate at which oxygen can be taken up and consumed (VO_2 max) (Sietsema, et al., 2002). The VO_2 levels required to perform sample basic and instrumental functions are listed in Table 2. (In general, people can sustain an activity level that is about 40% to 50% of their maximum level.)

Exercise tolerance in patients on dialysis who are anemic but have not received Epoetin alfa is extremely low

compared with age-predicted values. In several classic evaluations, for example, patients on dialysis with a Hct below 25% were shown to have VO_2 max levels that were 50% to 60% lower than the levels predicted for healthy, sedentary, age-matched individuals (Guthrie, et al., 1993; Robertson, et al., 1990). The decrease in VO_2 max observed in patients on dialysis with lower Hct levels is significant, and can adversely affect their ability to walk independently, perform self-care, do housework, or pursue other ADL (Painter, 1994).

Increases in Hb or Hct following initiation of Epoetin alfa therapy have been shown to improve VO_2 max in patients on dialysis. In a study of 19 hemodialysis patients with anemia, for example, an increase in Hct from 21.2% to 35.0% led to an increase of 166 ± 157 mL/kg/min (or 17.8 ± 5.4 mL/kg/min) in the VO_2 max ($P < 0.0005$). The increase in Hct was also accompanied by a significant decrease in maximum heart rate (from 138.5 ± 23.9 to 132.4 ± 24.7 beats per minute) ($P = 0.043$) (Robertson, et al., 1990). A similar study of 11 patients on hemodialysis assessed the effect on VO_2 max of increasing Hct levels from 21.6% to 33.5%. At the higher level, VO_2 max increased by approximately 50%—from 1,045 mL/min to 1,566 mL/min (Delano, 1989). A more recent examination of 193 patients on hemodialysis characterized VO_2 max during symptom-limited graded ergometry. At a mean Hb of 11.2 g/dL, Hb levels correlated positively with peak VO_2 levels in both univariate ($P = 0.0004$) and multiple regression ($P = 0.01$) analyses (Sietsema, et al., 2002).

Similar results have been observed among pediatric patients. In an evaluation of 10 pediatric patients on hemodialysis, for example, an increase in Hb levels from 6.4 ± 0.9 g/dL to 11.5 ± 1.0 g/dL yielded an increase in VO_2 max from 24.1 ± 7.1 to 32.6 ± 12.7. These results were accompanied by a greater tolerance for physical effort that was denoted by a doubling of the maximum work during exercise tolerance testing (Montini, et al., 1990).

Effect of Anemia Correction on Muscle Weakness and Exercise Duration

Muscle weakness and exercise duration have also been shown to improve after partial correction of anemia. Guthrie and colleagues (1993), for example, reported significant improvement in isometric and isokinetic strength performance in 15 patients on hemodialysis whose Hct increased from 21.2% ± 4.6% to 35.4% ± 2.3% ($P < 0.01$). Overall, 63.6% reported muscle weakness at baseline, compared with only 36.4% at the higher level. Similarly, 81.8% reported weakness or lack of strength at baseline, compared with 45.4% at follow-up. Patients also reported improvements in endurance and functional status as determined by the Nottingham Health Profile, the Karnofsky Index, and a symptom checklist. These improvements resulted in comparative decreases in weakness and shortness of breath, and an increase in energy level. (Guthrie, et al., 1993).

Similar results were reported in a study of 19 patients on hemodialysis by Robertson, et al., (1990). In this investigation, an increase in Hct from 21.2% to 35.0% was associated with significant improvements in exercise duration ($P < 0.0005$), isometric strength ($P = 0.003$), and isokinetic strength ($P = 0.018$) and a decrease in maximal heart rate during exercise ($P = 0.043$). There were also significant decreases in mid-exercise heart rate ($P < 0.001$), minute ventilation, ($P = 0.011$), and respiratory ratio ($P = 0.003$).

In addition, exercise duration has been shown to improve after partial correction of anemia. Wizemann, Kaufmann, and Kramer (1992) studied the effects of higher Hct levels in 7 patients with confirmed coronary artery disease and observed an increase in exercise duration and a decrease in exercise-induced ischemia. When the Hct increased from 25% ± 2% to 34% ± 0.5%, ST segment depression during maximal exercise decreased from 2.1 mm to 0.4 mm ($P < 0.01$). These results were mirrored in a study in which Hct levels in 11 patients on hemodialysis were increased from 21.6% to 33.5%. At the higher level, exercise duration (the mean amount of time patients could remain on a treadmill until they were exhausted) increased from 5.8 minutes to 10.5 minutes (Delano, 1989).

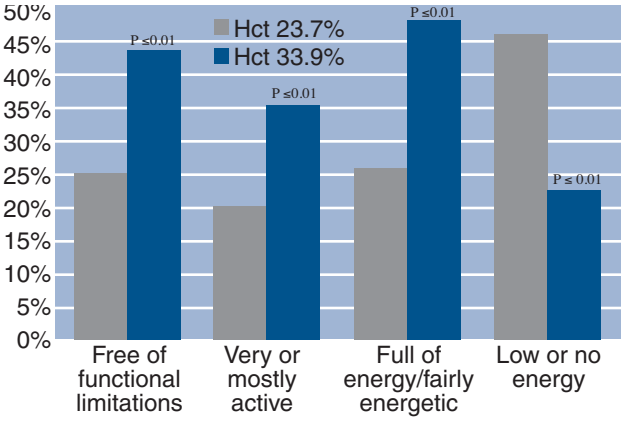
Similarly, in a study of 11 patients on hemodialysis, exercise workload rose from a median of 100 W to 120 W ($P < 0.05$) after Epoetin alfa was used to increase Hb from 6.0 to 11.1 g/dL. At the same time mean exercise duration increased from 13.0 to 15.5 minutes ($P < 0.05$), resting blood lactate concentration decreased from 0.8 to

Table 2:
VO_2 Requirements for Sample Basic and Instrumental Functions

Function	VO_2 Requirements
Resting, awake	3.5 mL/min/kg
Walking on level ground	11 mL/min/kg
Self-care activities Nominal housekeeping Bathing Shopping Cooking Vacuuming	7 to 14 mL/min/kg
More vigorous activities Carrying groceries upstairs Mowing a lawn General gardening	20 to 25 mL/min/kg

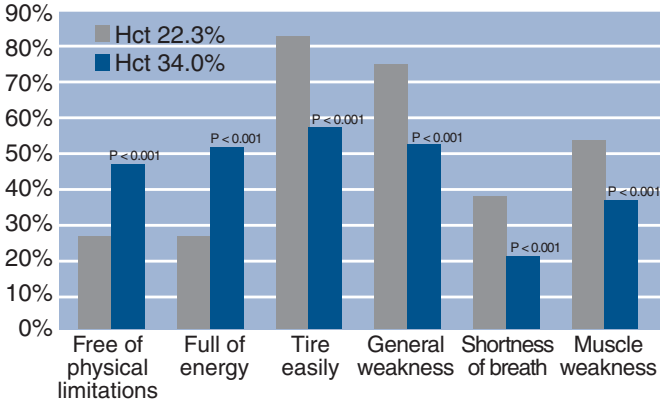
Note: VO_2 max = the maximum rate at which oxygen can be taken up and consumed.

Figure 1:
Effect of Epoetin alfa on Functional Impairment, Energy, and Activity



Adapted from Eschbach, et al. 1989.

Figure 2:
Improvements in Functional Activities Following Hct Correction



Adapted from Evans, Rader & Manninen. 1990.

0.3 mmol/L ($P < 0.05$), and median arterial oxygen content increased from 79 to 150 mL. The authors suggest that the improvement in muscle function was probably due to an increase in tissue oxygen delivery (Davenport, Will, Khanna, & Davison, 1992).

Combining Partial Anemia Correction and Exercise Training: Implications for Nurses

By the time patients reach end-stage renal disease (ESRD), many have experienced a downward spiral in functional ability caused by a combination of disease, deconditioning, and disability. While maintaining Hb in the NKF-K/DOQI™ target range is vital to partially reversing this deterioration, there are physiological limits to the benefits of anemia correction alone (Painter, 1994; Painter, et al., 2002). Indeed, in addition to anemia, other factors such as age, deconditioning, gender, body mass, cardiac dysfunction and other comorbid conditions, metabolic disturbances, impairment of cardiac autonomic control, defects in muscle oxidative metabolism, and skeletal muscle atrophy can also affect functional capacity in patients on dialysis (Sietsema, et al. 2002).

While some of these factors may not be correctable, considerable attention has been focused on reversing physical deconditioning by means of a consistent exercise program. The mechanisms by which an exercise program and Epoetin alfa therapy affect exercise capacity are different. Epoetin alfa raises Hb levels, thereby leading to improvement in the oxygen-carrying capacity of the blood. Partial correction of anemia with Epoetin alfa therapy may make patients more willing to participate in an exercise program and enable them to perform higher- intensity exercise. By contrast, exercise leads to improvement in oxygen uptake or the ability of cells to use the oxygen they receive. Studies indicate that adding an exercise training program to a patient's regimen can increase exercise tolerance by up to 25%. Further, the combination of exercise and Epoetin alfa is synergistic, thereby facilitating even greater improvements in functional capacity (Guthrie, et al., 1993; Painter, 1994; Painter, et al., 2002).

Care plans at many dialysis facilities include anemia management to maintain Hb levels at 11 to 12 g/dL, in conjunction with an exercise training program, referrals for physical therapy, and/or in-center exercise. Nurses are typically responsible for monitoring and managing the anemia management protocol to ensure that Hb levels remain in the target range. However, nurses should also be aware that improvements in functional capacity often depend on encouragement from the nephrology team—with nurses being the ones who have the most frequently contact with patients. Therefore, improvements in functional ability can be greatly enhanced when nurses regularly tell patients that they are expected to adhere to both the anemia management prescription and the exercise program (Painter, 1994; Painter, et al., 2002). The importance of anemia management in conjunction with an individualized exercise program is illustrated in the following case study.

Case Study

AZ is a 67-year-old female who is new to dialysis. ESRD resulted from hypertension, currently controlled by antihypertensives. She also has mild rheumatoid arthritis. Pertinent laboratory values at presentation include a Hb of 9.4 g/dL, a transferrin saturation of 34%, and a ferritin of 495 ng/mL. The patient complains of general weakness and shortness-of-breath on exertion. She states that she dreads climbing the stairs to her home because "it drains all of my strength." Her physical limitations make it difficult for her to perform housework, do her grocery shopping, or go out with her friends. She has not participated in a regular exercise program for many years.

Epoetin alfa therapy is initiated on the first day of dialysis at a dose of 5,000 Units three times a week (approximately 80 Units/kg). Hb levels increased steadily over the next 8 weeks, stabilizing at about 11.7 g/dL. The patient reported gradual improvement in functional capacity as Hb levels increased, including higher energy levels and the feeling that she is stronger than she has been in many years. She also reported that she is no longer short-of-breath, that she can do her housework and grocery shopping without problems, and that she now spends occasional evenings with her friends. Her muscle strength has improved, and she is no longer exhausted when she climbs stairs, although she still finds it difficult.

In consultation with the physical therapist, the nurse helps design an initially light exercise conditioning program, consisting of bicycle ergometery and a home-based weight lifting program (repetitions using canned goods) to improve arm strength, and educates the patient on its benefits. Initially, AZ's adherence to the regimen is sporadic. However, as her Hb and energy levels increase, she becomes more willing to participate. Ongoing reminders and encouragement from the nurse stress the importance of physical conditioning to further improve functional ability, and adherence gradually improves. After several months of therapy, the patient expresses pride over her arm strength.

Discussion

Partial correction of anemia to maintain Hb levels in the range recommended by the NKF-K/DOQI™- (11 to 12 g/dL) can have a significant and positive impact on functional ability. However, data indicate that even with the combination of partial anemia correction and exercise, functional capacity for most patients remains below expected values for healthy, age-matched individuals (Painter, et al., 2002). While the improvements in functional ability associated with partial correction of anemia may occur relatively quickly, the additional incremental improvements associated with exercise training may take longer. Nurses should recognize that incremental improvements in exercise duration and functional ability that might seem inconsequential to a healthy individual can be extremely important and even life changing for a someone who is on dialysis. Ongoing encouragement by the nursing staff can help motivate patients to adhere to these vital therapies and help them improve their functional ability.

Conclusions

Anemia is a devastating consequence of ESRD that can contribute to deterioration in functional ability. Clinical data indicate that patients who maintain Hb levels in the target range of 11 to 12 g/dL recommended by the NKF-K/DOQI™ typically experience significant improvements in many facets of functional ability. Nurses are influential in ensuring that target Hb levels are achieved and maintained, while at the same time encouraging patients to participate regularly in activities that improve physical conditioning and functional ability.

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