

Improving Management of Anemia Using CQI Techniques

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Introduction

During the last two years, the National Kidney Foundation's Dialysis Outcomes Quality Initiative (NKF-DOQI) Anemia Work Group has been developing clinical practice guidelines for the management of anemia in patients with chronic renal failure. After an in-depth critical analysis of the scientific literature, with a consensus of "expert opinion" used to support recommendations in areas with inadequate published data, evidence-based guidelines were developed. These clinical practice guidelines, regardless of how well-founded in scientific evidence, are likely to be disregarded if they are not applicable in the day-to-day care of patients. Thus, they must be practical, clearly stated, and usable, given available resources and constraints. The purpose of this article is to describe our experiences' in implementing some of these guidelines over the last two years, as they were being developed, for the care of patients in our hemodialysis unit.

Our dialysis unit is a privately-owned, urban hemodialysis unit with about 125 patients (mean age 63 yrs., 44% with diabetes mellitus), cared for by one group of three nephrologists. Patients are seen three-times weekly at each dialysis treatment. Dialyzers are not reused. Ninety percent of patients have a Kt/V>1.2 (single pool). In 1995, when we began revising our anemia management policies and procedures to coincide with the evolving NKF-DOQI guidelines, patients were receiving recombinant human erythropoietin (EPO) by intravenous (IV) injection. The median HCT was 32%, 79% of patients had a transferrin saturation (TSAT) \geq 20% (median TSAT 25%), and 89% of patients had a serum ferritin \geq 100 ng/ml.

Our first step was to identify the main goals for anemia management that we wanted to accomplish. Next, we needed to make the changes in our existing policies which we thought would be necessary to accomplish these goals. Third, these changes needed to be implemented with appropriate staff and patient education. Finally, we needed to monitor the effects of our efforts, and make appropriate revisions in our policies and protocols when needed.

Believing that the NKF-DOQI Anemia guidelines were developed to improve anemia management in a broad sense, rather than specifically "EPO management" or "iron management," we set as our primary goal the achievement and maintenance of HCTs in the 33-36% range in all of our hemodialysis patients. We wanted to exercise efficient use of EPO and judicious use of iron dextran, but these were secondary issues. In order to accomplish this target we: 1) changed to administration of EPO subcutaneously, and 2) began a program of administration of intravenous iron dextran on a maintenance basis to prevent iron deficiency (we were already giving iron dextran periodically in doses of 100 mg for a total of 600-1,000 mg to treat iron deficiency), by maintaining TSAT of 25-50% and ferritin of 200-800 ng/ml.

Improving HCTs

Administering EPO Subcutaneously

Having heard comments that the subcutaneous injection of EPO was painful and would not be well accepted by patients or staff, we anticipated some resistance in changing from IV to subcutaneous administration. However, since published data rather convincingly shows that on average patients require less EPO for a given target HCT level when it is given subcutaneously rather than IV, we felt that the change in route of administration was reasonable to try. We also hoped that some of the HCT "see-sawing" would be reduced because of the difference in the pharmacodynamic profile of subcutaneous vs. IV EPO.

Once the nephrologists agreed to convert to subcutaneous EPO, the staff and then the patients were informed of the plan and the rationale behind it. Many patients had previously received EPO subcutaneously in the office before starting dialysis or had been treated with insulin, so subcutaneous drug administration was not entirely a foreign concept. **Table 1** shows the components of our conversion to subcutaneous EPO.

TABLE 1: STRATEGIES FOR CONVERSION FROM IV TO SUBCUTANEOUS EPO ADMINISTRATION

- 1) Review new policies and rationale with staff
- 2) Patient education regarding reasons for use of subcutaneous EPO
- 3) Unit-wide implementation
 - ◆ 28 g needle (ultra-fine insulin needle)
 - ◆ multi-dose preparation containing benzyl alcohol
 - ◆ reduce number of weekly doses if possible

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Anemia Management

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From a nursing perspective, the conversion progressed smoothly, with active patient teaching during the first several weeks of the conversion. There was some grumbling initially (among patients and staff), but this was short-lived. Obviously, the nursing staff needs to be supportive of the use of subcutaneous EPO and provide ongoing reinforcement to patients in order for a change from IV to subcutaneous dosing. The fact that we are maintaining higher HCTs than previously in many patients, which could result in enhanced well-being (we hope!), may also help.

We use ultra-fine needles and the 10,000 unit/ml multi-dose preparation containing benzyl alcohol to minimize pain

receive two doses/wk., and 3% receive only one dose/wk. (4% receive no EPO). Only one patient has refused subcutaneous EPO; patients receive > 10,000 units/dose and most of those on chronic oral anticoagulation receive IV EPO.

Using Maintenance Iron Dextran

The second significant change in our anemia management protocol was the use of maintenance iron dextran. We wanted to provide sufficient iron on a regular basis to maintain HCTs in the target range while avoiding the development of iron deficiency. We hoped that by avoiding repeated administration of large doses of iron dextran in response to iron deficiency, wide HCT swings, as patients went from periods of iron-deficient to iron-replete erythropoiesis, and the need to make frequent changes in EPO doses would be minimized.

Our policies now call for the regular administration of 50-100 mg iron dextran, typically weekly or every other week,

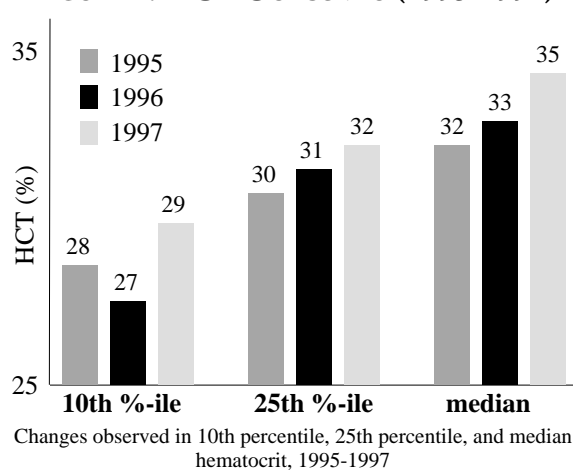
TABLE 2: IRON INDICES

	median TSAT	percent with TSAT<20%	median serum ferritin	percent with ferritin<100ng/ml
1995	25%	20.8	481 ng/ml	11.1
1997	26%	9.5	577 ng/ml	7.4

TABLE 3: PROTOCOL FOR EPO DOSE ADJUSTMENTS

- A. If HCT is increasing and $\geq 35\%$, reduce dose by 10%, do not hold dose, repeat HCT in 1 week.
- B. Increase dose by 50% every 2-6 weeks if HCT is not increasing by 1-2 % per week.
- C. If HCT exceeds 36%, hold dose and repeat HCT weekly until HCT $\leq 36\%$, then resume EPO with 10% dose reduction.
- D. Reduce dose by 25% if HCT rises by > 4% in a 2 week period or > 8% in a 4 week period.
- E. Changes in EPO dose may be made in amount per dose and/or dose frequency (subcutaneously).

FIGURE 1: HCT OUTCOMES (1995-1997)



with injection. There have not been any injection-related complications aside from minor ecchymosis in some chronically anticoagulated patients. All new patients are now started on subcutaneous EPO.

One mistake we made initially was that we converted patients on an equal dose basis (i.e., 4,000 units IV three times/wk. was changed to 4,000 units subcutaneously three times/wk.). As a result, quite a few patients ended up with HCTs in the high 30s and low 40s. A reduction to about two-thirds of the IV dose if the HCT was already in the target range would have been better.

Currently, 63% of patients receive three doses/wk., 30%

after an initial 6-10 doses of 100 mg, if needed, to correct any existing iron deficiency and maintain a TSAT of 25-50% and serum ferritin of 200-800 ng/ml. Some patients receive more or less frequent doses. Oral iron is stopped once the decision is made to use iron dextran. Iron dextran is also routinely held for two weeks prior to testing of iron studies, which is done every three months in most patients. Maintenance iron dextran is therefore typically given during a 10-week period, with two weeks off before testing. Iron dextran is discontinued if the TSAT is greater than 50% or the ferritin is over 800 ng/ml; iron studies are reevaluated in three months.

One problem we identified was that when EPO was being

held for a HCT > 36%, iron dextran was still administered. Since some patients, when fully iron replete, may go weeks and even months without EPO and still maintain HCT > 36%, elevated TSAT and serum ferritin levels were observed in some instances because of the continued administration of iron dextran. Now, iron dextran and EPO are held at the same time, unless the TSAT is < 20% and ferritin is < 200 ng/ml. **Table 2** shows observed changes in TSAT and ferritin following implementation of this iron dextran treatment protocol. We have recently seen mild reactions to iron dextran in three patients, two of whom subsequently tolerated another iron dextran preparation. One patient experienced an anaphylactic-like reaction, which did not require hospitalization.

Results

Figure 1 shows the changes in HCT we have observed over the last two years. Monitoring and adjustment of EPO and iron dextran dosing requires regular attention by the hemodialysis unit nursing staff and nephrologists. Hematocrits are measured every two weeks by automated laboratory methods. Since patients are seen at each hemodialysis session, the physicians tend to be very actively involved in anemia management.

Monitoring of iron indices and adjustment of iron dextran dosing are primarily the responsibility of the nephrologists. EPO dosing adjustments are more regularly handled by the dialysis nursing staff, based upon approved protocols (see **Table 3**), which continue to

evolve. Dose adjustments, the holding of doses, and the subsequent restarting of doses, are made for the most part by the dialysis nurses with review by the nephrologist, exemplifying the "team approach" to anemia management.

Conclusion

Clinical practice guidelines, such as the soon to be unveiled NKF-DOQI guidelines, can be useful tools to help drive improved patient care in the outpatient hemodialysis unit. Hopefully, others can learn from (and improve upon) our experiences with anemia management guidelines. Each facility and its medical and nursing staffs will need to determine how best to apply these guidelines to their particular circumstances. ...NN&I

Authors' Note: The anemia management protocols used by the authors and described in this report may differ from the final NKF-DOQI Clinical Practice Guidelines for the Treatment of Anemia of Chronic Renal Failure, expected to be published in the American Journal of Kidney Diseases in October 1997.

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EPO Wars?

Improved anemia management is putting a crunch on Amgen Inc. Company chairman and CEO Gordon Binder said in an Aug. 13 article in the *Wall Street Journal* that sales of Epogen have been on a rollercoaster this year. The drops may be in response to the Health Care Financing Administration's new hematocrit audit, expected to go into effect Sept. 1. The new audit will mean closer scrutiny of hematocrits for patients and will likely lead to reduced dosages.

The forthcoming Dialysis Outcome Quality Initiative on anemia management may also result in reduced dosages of Epogen, based on its emphasis on improving iron management.

Company stock was trading at \$48^{9/16} on Aug. 18 after a 12% slide. The stock was up to \$63 in March. Amgen has also been facing legal challenges with
(see **EPO**, page 16)