Erythropoietin Use in a Hemodialysis Population

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ABSTRACT

The purpose of this project was to assess how well erythropoietin improves anemia in a hemodialysis population, and if anemia was not resolved, to determine the contributing factors, and to assess the frequency and severity of complications of erythropoietin therapy.

DUE criteria were developed based on published literature. Hemodialysis patients initiating erythropoietin therapy were entered in a retrospective chart review. Data were collected from the one month prior to erythropoietin therapy to six months after initiation of erythropoietin.

During the six-month period, 54.3% of patients reached the target hemoglobin range of 105-115 g/L, however, at the conclusion of the period, only 32.6% were in the target range. Six months after the initiation of erythropoietin therapy, 78.6% of patients required fewer blood transfusions compared to a six-month baseline period. Seventy eight percent of patients with ferritin concentrations <100 ng/mL received iron supplementation. Eighty-three percent of erythropoietin dose changes were appropriate. Hemoglobin and hematocrit were monitored on average once every two weeks. An elevated diastolic blood pressure was detected in 63% of patients. No seizures or allergic reactions were noted.

Our dialysis patients did not receive maximum benefit from erythropoietin. Contributing factors include low initial and maintenance doses, inadequate monitoring of hemoglobin and iron therapy, and inaccurate dose modifications. It is recommended that an algorithm be developed for dosing and monitoring of erythropoietin.

Key Words: Drug Use Evaluation, erythropoietin

RÉSUMÉ

L'objet de ce projet était d'évaluer dans quelle mesure l'érythropoïétine corrige l'anémie chez les hémodialysés.

Si l'anémie n'était pas corrigée, on déterminait les facteurs qui ont contribué à cet état et on évaluait la fréquence et la gravité des complications du traitement à l'érythropoïétine.

Des critères ÉUM ont été élaborés à partir de la documentation existante. Une analyse rétrospective des dossiers médicaux des patients hémodialysés qui amorçaient un traitement à l'érythropoïétine a été menée. Les données ont été recueillies dans le mois précédent le début du traitement à l'érythropoïétine et durant les six mois suivants.

Au cours de la période thérapeutique de six mois, 54,3 % des patients ont atteint des taux d'hémoglobine cibles variant entre 105 et 115 g/L.; cependant ce taux a chuté à seulement 32,6 % au terme du projet. Six mois après le début du traitement à l'érythropoïétine, 78,6 % des patients ont eu besoin d'un moins grand nombre de transfusions, comparativement à la période initiale. De plus, 78 % des patients dont les concentrations de ferritine étaient inférieures à 100 ng/mL ont reçu un supplément de fer. Les modifications posologiques de l'érythropoïétine étaient appropriées dans 83 % des cas. Les taux d'hémoglobine et d'hématocrites étaient mesurés en moyenne à toutes les deux semaines. On a observé une tension diastolique élevée chez 63 % des patients, mais aucune crise ni réaction allergique.

Les patients hémodialysés n'ont pas tiré un avantage maximum de l'érythropoïétine. Les facteurs ayant contribué à ce phénomène comprennent des doses initiales et d'entretien faibles, une surveillance inadéquate des taux d'hémoglobine et du traitement supplétif en fer, et une modification posologique inadéquate. On recommande de mettre au point un algorithme des modalités posologiques et de surveillance du traitement à l'érythropoïétine.

Mots clés : érythropoïétine, évaluation de l'utilisation des médicaments.

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INTRODUCTION

Erythropoietin, a naturally occurring hormone produced by the kidney, regulates production of red blood cells in humans. Once released by the kidney, it stimulates division and differentiation of erythroid progenitor cells in the bone marrow resulting in red blood cell production. In chronic renal failure patients, production of erythropoietin is impaired causing anemia. The signs and symptoms of this anemia include

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fatigue, increasing angina, shortness of breath, generalized coldness, Raynaud's syndrome, anorexia, insomnia, depression, sexual disinterest and dysfunction, neurobehavioral changes, and cardiomegaly.[1]

Human erythropoietin, manufactured by recombinant DNA technology, contains the identical amino acid sequence of isolated natural erythropoietin. Subcutaneous or intravenous injections of erythropoietin given one to three times weekly can decrease the severity of the anemia of chronic renal failure.[2-4] Erythropoietin was approved for use in Canada in March 1990. The average annual cost of erythropoietin therapy for one patient is estimated to be $5,000-10,000 CDN. From fiscal year 1991 to 1994, our hemodialysis unit, which provides care to approximately 95 patients, purchased between $450,000 and $488,000 of erythropoietin annually.

It is important to assess the impact a new drug has on three types of outcomes; humanistic, clinical, and economic. Erythropoietin has demonstrated a positive effect of humanistic outcomes, such as improved quality of life and patient satisfaction.[4-7] The clinical effects of erythropoietin on improvement of anemia in patients with end stage renal disease are well documented in the literature.[2-4] Pharmacoeconomic studies have demonstrated that erythropoietin therapy can be cost effective.[8,9] However, clinical studies can only assess drug use in well controlled situations and limited populations according to the study design. It is important to review the use of erythropoietin in actual practice to ensure that the positive outcomes observed in clinical trials are realized.

The purpose of this study was to determine how effectively erythropoietin was being used in our hemodialysis unit. Our objectives were to assess whether erythropoietin therapy resolves anemia in our hemodialysis population, to determine the contributing factors in those patients not reaching target hemoglobin, and to assess the frequency and severity of complications of erythropoietin.

METHODS

The erythropoietin use criteria (modified from published criteria[10]) were developed by the nephrology pharmacist and the physician responsible for the hemodialysis unit and subsequently approved by the Pharmacy and Therapeutics Committee (Table I). All chronic hemodialysis patients who had erythropoietin therapy initiated between April 1990 and June 1992 were eligible for participation in the retrospective chart review. Patients were excluded if they had participated in a prior erythropoietin research study, had hemodialysis discontinued or were switched to alternate renal replacement therapy during the six-month study period.

Data collection and analysis forms were developed using the criteria as a template. Baseline patient data were collected for one month prior to initiation of erythropoietin. After initiating erythropoietin, data about erythropoietin usage were collected for six months. The number of blood transfusions was determined for six months baseline and six months post initiation. Demographic information collected included age, gender, dry body weight, and length of time on hemodialysis. Several clinical pharmacists were recruited and trained to complete the initial data collection and analysis forms.

Data were summarized and analyzed using FoxPro (Microsoft, Redmond, Washington). Descriptive statistics were stated as mean ± standard deviation. Comparative data were analyzed using t-tests with statistical significance defined as $p<0.05$.

RESULTS

Demographics

Forty-nine patients were evaluated for entry into the study, three patients were excluded because sections of the patient's chart with information on bloodwork and medication were not available.

Forty-six patients, 48% female, with a mean age of 50.2 ± 15 years (range 18-82 years) and a dry weight of 65.8 ± 14.8 kg (range 37-112 kg) were entered into the study. All patients received in-centre hemodialysis two or three times a week and had been on dialysis for a mean duration of 11.8 ± 16.7 months (range 0.25-79 months) prior to starting erythropoietin.

Drug Utilization Criteria

Table I summarizes the percentage of individuals or lab values meeting the drug utilization criteria.

Erythropoietin Dosing and Iron Supplementation

Figure 1 summarizes the initial and final erythropoietin doses. The average initial dose of erythropoietin was 119.9 ± 34.9 U/kg/week (range 53-197) and the average final dose of erythropoietin was 112.5 ± 53.3 U/kg/week (range 44-287). All erythropoietin doses were administered subcutaneously two or three times a week post-dialysis.

During the study period, 30 patients (65.2%) were initiated or maintained on oral iron therapy for a mean duration of 19.8 ± 7.6 weeks of the 26-week study period. Six patients received iron therapy despite ferritin levels >200 ng/mL. Seven patients with ferritin <100 ng/mL were not prescribed iron supplementation. In four patients, iron therapy could not be evaluated since a complete list of prescribed medications was not available.

Table I. Drug Utilization Criteria and Results

Criteria[a]	Percentage Meeting Criteria (N)
A. Prior to Initiation of Erythropoietin	
Anemia due to chronic renal failure as defined by Hgb<95 g/L	76.1 (46)[b]
A Ministry of Health form completed by a staff nephrologist	97.8 (46)[b]
No history of allergy to mammalian cell-derived products, human albumin or erythropoietin	100 (46)
Ferritin > 200 ng/ml	32.6 (46)[b]
Iron supplementation provided if ferritin < 100 ng/ml (ferrous gluconate or sulphate 300 mg tid)	77.8 (9)
Normal B_{12} levels (140 - 700 pg/ml)	2.2 (46)[b]
Normal folate levels (2 - 12 ng/ml)	0 (46)[b]
Negative Coombs test	0 (46)[b]
Stool occult blood negative	6.5 (46)[b]
Pretreatment control of blood pressure achieved (diastolic blood pressure not controlled if more than two readings of > 100 mmHg in the baseline month)	84.8 (46)[b]
Aluminum concentration of < 370 nmol/L	32.6 (46)[b]
Pretreatment control of potassium levels (not controlled if potassium > 6 mmol/L on two or more occasions in the baseline month)	89.1 (46)[b]
No evidence of infection within the two weeks baseline (no antibiotic usage during this period)	91.5
B. Erythropoietin Dosing and Iron Supplementation	
Appropriate initial dose of 150 U/kg/week subcutaneously in two to three divided doses (rounded to nearest 1000 U)	15.2 (46)
Iron supplementation provided if ferritin is < 200 ng/ml	69.3 (90)
If ferritin is < 50 ng/ml then erythropoietin held until ferritin > 100 ng/ml	2.4 (41)
If diastolic BP > 110 mm Hg erythropoietin held	10.2 (127)
When diastolic BP > 110 mm Hg, erythropoietin held until diastolic < 110 mmHg	53.8 (13)
When Hgb reaches target (105-115 g/L) dose reduced by 25 U/kg	0 (25)
If Hct increased by > 6% in any four-week period then dose reduced by 25 U/kg	0 (5)
After eight weeks of therapy, dose increased by 25 U/kg if Hgb did not increase by 10-20 g/L and remains below target range	83.8 (6)
If Hgb > 115 g/L then erythropoietin held	37.3 (51)
When Hgb > 115 g/L, erythropoietin held until Hgb < 115 g/L	52.6 (19)
Maximum dose of 600 U/kg/week not exceeded	100 (46)
C. Monitoring	
Hgb/Hct measured weekly for eight weeks after initiation of erythropoietin	4.3 (46)
Hgb/Hct measured weekly for eight weeks after dosage adjustment	14.1 (64)
Complete blood count measured monthly	82.6 (46)
Platelet count measured monthly	80.4 (46)
Urea nitrogen/creatinine measured monthly	76.1 (46)
Phosphate measured monthly	76.1 (46)
Potassium measured monthly	78.3 (46)
Uric acid measured monthly	0 (46)
Ferritin measured monthly for first three months	8.7 (46)
Ferritin measured at least once in months four to six if ferritin had been < 200	88.9 (27)
Blood pressure measured weekly	97.8 (46)
D. Outcomes	
Resolution of chronic anemia (Hgb = 105-115 g/L)	32.6 (46)
Decreases need for transfusions	78.6 (14)
No evidence of hypertension	93.5 (46)
Iron stores remain normal (ferritin > 200 ng/ml)	28.3 (46)
No thrombolic events	84.8 (46)
No allergic reactions	100 (46)
No seizures	100 (46)

a-Criteria adapted from reference 10.
b-Includes patients in which data were not available in the baseline month (counted as not meeting the criteria)

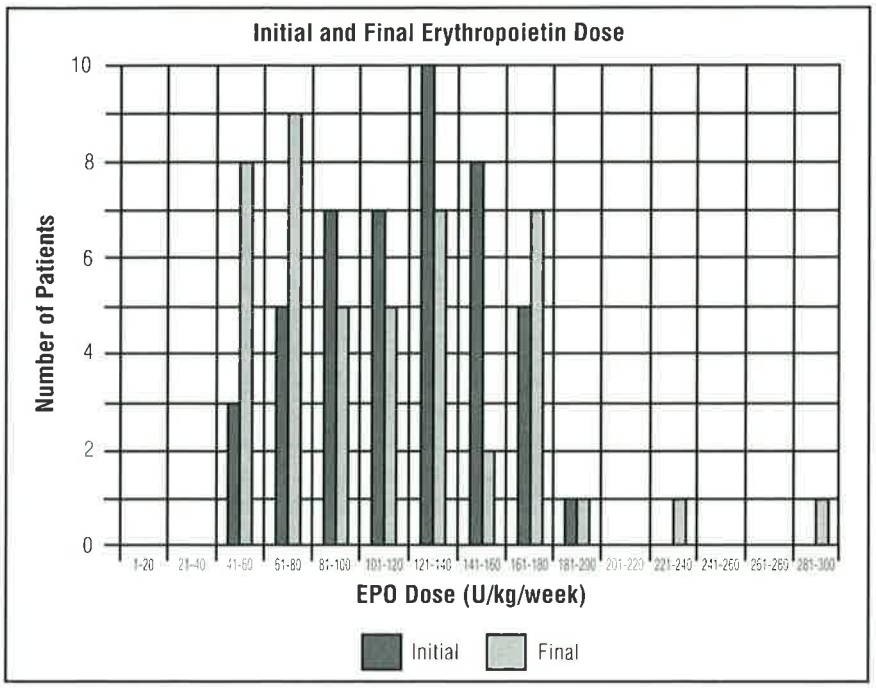

Figure 1. Initial and Final Erythropoietin Dose

During the six-month period, 25 (54%) of the patients achieved a hemoglobin within the target range of 105-115 g/L. However, at the conclusion of the six-month study, only 15 (32%) patients had resolved their chronic anemia (hemoglobin=105-115 g/L). (This includes one patient who had a hemoglobin of 124 g/L).

During the six-month study period, 36 patients underwent 64 erythropoietin dose modifications. Further erythropoietin dose changes are summarized in Figure 2.

Monitoring

The average baseline values for hemoglobin and ferritin are summarized in Table II. Average baseline aluminium was 475.8 ± 527.7 nmol/L (range 130-2705). During the first eight weeks after erythropoietin initiation, hemoglobin and hematocrit were monitored an average of 3.8 ± 1.9 times. After erythropoietin dose changes, the hemoglobin and hematocrit were monitored on average every two weeks rather than weekly. Six (9.4%) of the erythropoietin dose changes occurred in the last few weeks of the study period and the subsequent hemoglobin and hematocrit monitoring did not fall into the six-month data collection period.

During the first three months of erythropoietin therapy, 27 (58.7%) patients had ferritin <200 ng/mL and 20 of these patients had ferritin <100 ng/mL. Twenty four (89.9%) of these patients subsequently had ferritin monitored at least once during the next three months. A total of 146 ferritin measurements were made during the study period and there were 90 incidents of ferritin <200 ng/mL, average value 79.6 ± 50.7 ng/mL (range 16-199), detected in 30 patients. Only two patients had transferrin measured and in these two patients, the transferrin value was >20%.

In 127 of 3122 blood pressure measurements, a mean elevated diastolic blood pressure of 113 ± 7.2 mmHg (110-160) was detected in 29 patients.

Complications

No neurological symptoms such as aura or seizures were noted. Thrombotic events such as clots in the arterial line or venous chamber occurred in seven patients. Blood pressure changes have been summarized in the previous section.

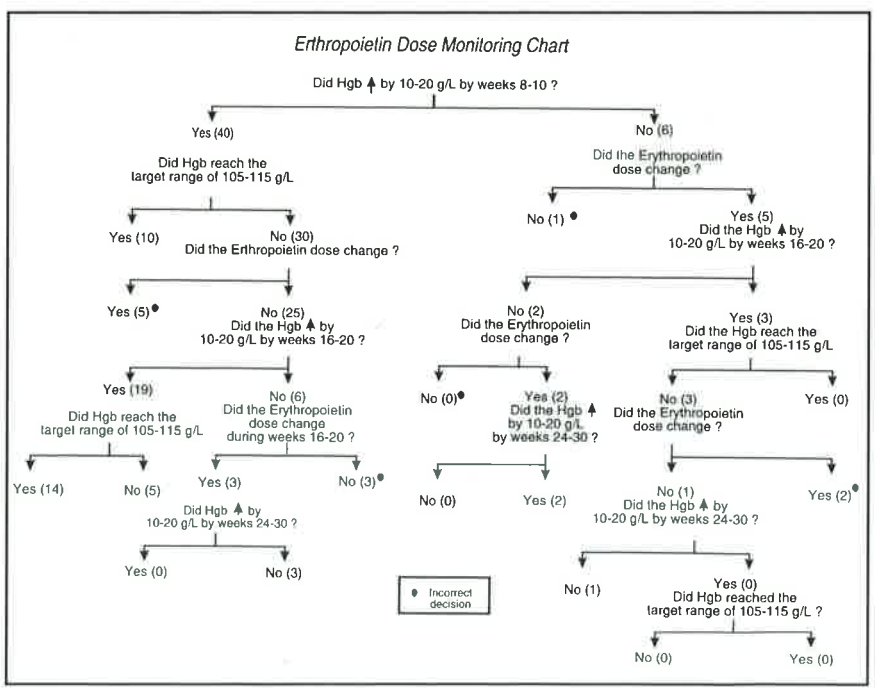

Figure 2. Erythropoietin Dose Monitoring Chart

Table II. Average Hemoglobin and Ferritin Values and Transfusion Rates

Variable	Baseline		After 6 Months Erythropoietin	
	Mean ± SD (N)	Range	Mean ± SD (N)	Range
Hemoglobin	63.8 ± 11.9 g/L (38)	52-99	93.8 ± 13.4 g/L (46)[a]	71-115
Transfusions	2.6 ± 3.4 units/6 months (22)	0-13	0.6 ± 1.2 units/6 months (22)[ab]	0-5
Ferritin	436.6 ± 535.7 ng/ml (37)	17-2500	423.0 ± 713.4 ng/ml (25)	29-2500

a-p <0.05

b-Two patients were excluded from the transfusion analysis as there were other confounding variables (one patient received chemotherapy for myeloma and one patient experienced an enteric cutaneous fistula), 22 patients were excluded because data for the time period were incomplete.

Outcomes

Table III outlines the differences between the group of patients who attained a target hemoglobin and the group which did not. Further analysis of the erythropoietin dose modifications in the patients who did not reach target hemoglobin (N=21) indicate that five patients did

Table III. Comparison of Parameters for Patients Who Did and Did Not Achieve Target Hemoglobin

Parameter (Hgb<105)	Anemia not resolved some time in the 6 month data collection period	Anemia resolved (Hgb≥105) at
Number of Patients	21	25
Age	53.1 ± 12.1 years	47.7 ± 17.4 years
Gender: Male	10	14
Female	11	11
Initial erythropoietin dose	106.6 ± 35.8 units/kg/week	131.2 ± 35.8 units/kg/week[a]
Average weekly erythropoietin dose before Hgb≥105 g/L	122.7 ± 42.4 units/kg/week	131.2 ± 35.3 units/kg/week
Average weekly erythropoietin dose after Hgb≥105 g/L	not applicable	90.2 ± 32.4 units/kg/week
Initial ferritin	363.1 ± 356.0 ng/mL (n=17)	477.3 ± 645.4 ng/mL (n=21)
Initial ferritin < 200 ng/mL	7 patients (n=17)	14 patients (n=24)
Iron supplement given?	7 patients (n=7)	10 patients (n=14)
At any time ferritin <100 ng/mL	9 patients (43%)	14 patients (56%)
At any time ferritin <50 ng/mL	6 patients (29%)	12 patients (48%)

a-p<0.05

Hgb = hemoglobin

not have their erythropoietin dose increased at any time, and 10 patients were inappropriately dosed in that the erythropoietin dose increase was less than 20 units/kg/dose and/or the dose increase was delayed. Three patients had decreases in their erythropoietin dose; one patient had a slight elevation in blood pressure and no reason was documented for the dose decrease in the other two patients. Three patients, who did not reach target hemoglobin, had their erythropoietin dose increased in the 20-30 unit/kg/dose range, however, these patients also had low iron stores during the six-month period (ferritin <200ng/mL); one patient did not receive iron supplementation, and the other two patients continued to have low ferritin levels despite oral iron therapy.

Table IV outlines the differences between those patients who maintained a target hemoglobin versus those who achieved a target range hemoglobin but did not sustain it. Ten patients reached the target hemoglobin range, but ended the six-month period below the target range. One of these 10 had their erythropoietin dose decreased when they experienced uncontrolled hypertension (repeat diastolic blood pressure >110 mmHg). This patient's erythropoietin dose remained low for the remainder of the six-month data collection period. Another patient's erythropoietin was stopped completely when the hemoglobin exceeded the target range, and was not restarted as the hemoglobin fell. There was no significant difference in ferritin levels or iron supplementation between the two groups. The group of patients who did not maintain target hemoglobin had a significantly lower average erythropoietin dose compared to the patients who remained in the target hemoglobin range.

DISCUSSION

Erythropoietin therapy has been a major advance in the management of anemia in end stage renal disease. It has been shown to improve the quality of life and functional capacity of anemic hemodialysis patients.[4-7] In Canada, erythropoietin use in hemodialysis patients has increased from 38.0% of patients in 1990 to 54.1% in 1993.[11]

Clinical trials are conducted in controlled settings and can have findings different than those found in routine clinical practice. A drug use evaluation assesses how and with what degree of safety and effectiveness a drug is used in actual practice. Two studies have examined erythropoietin utilization. In the first study, Mason et al[12] studied erythropoietin use in a hospital setting and their

Table IV. Comparison of Parameters for Patients Who Maintained or Did Not Maintain Target Hemoglobin

Parameter	Anemia resolved (Hgb≥105)	
	Hgb≥105 maintained	Hgb≥105 not maintained
Number of Patients	15	10
Age	53.8 ± 14.4 years	38.6 ± 18.2 years[a]
Gender: Male Female	8 7	6 4
Initial erythropoietin dose	130.7 ± 27.7 units/kg/week	131.9 ± 47.0 units/kg/week
Average weekly erythropoietin dose prior to Hgb≥105 g/L	131.3 + 27.8 units/kg/week	131.1 ± 46.1 units/kg/week
Average weekly erythropoietin dose after Hgb≥105 g/L	99.6 ± 33.9 units/kg/week	76.2 ± 25.3 units/kg/week[a]
Initial ferritin (ng/mL)	535.6 ± 752.3 (n=14)	344.4 ± 327.1 (n=10)
Initial ferritin <200 ng/mL	8 patients (n-14)	6 patients (n=10)
Iron supplement given?	5 patients (n=8)	5 patients (n=6)
At any time ferritin <100 ng/mL	7 patients (47%)	7 patients (70%)
At any time ferritin <50 ng/mL	6 patients (40%0	6 patients (60%)

a-p<0.05
Hgb = hemoglobin

criteria were similar to those used in our study. However, a more varied patient population, both adult and pediatric patients receiving peritoneal dialysis or hemodialysis, were evaluated resulting in small numbers in the individual groups (e.g., 27 adult hemodialysis patients). As well, this was a US study with different erythropoietin funding mechanisms. In the second study, conducted by Powe et al, Medicare claims data for erythropoietin (59,462 end stage renal disease patients) provided a very broad perspective of US erythropoietin prescribing practices. However, access to limited patient data resulted in difficulty explaining their results.[13] Due to these differences in patient population and in setting, results from these two studies could not necessarily be extrapolated to a Canadian, adult, hemodialysis population. Therefore, our study was done to conduct a detailed analysis of erythropoietin utilization in our institution.

One of the primary outcomes of erythropoietin therapy is to achieve target hemoglobin. In our study, only 32.6% of patients had attained the target hemoglobin of 105-115 g/L at the end of the six-month study period. However, hemoglobin significantly increased after six months of erythropoietin therapy. Powe et al[13], who also examined the hematological response to erythropoietin in clinical practice, found that target hematocrit was met in 60% of patients. This is in contrast to a controlled, prospective trial completed by the Canadian Erythropoietin Study Group which demonstrated that a target hemoglobin of 95-110 g/L and 115-130 g/L could be achieved in all patients in an average of six weeks and 11 weeks, respectively.[4] The other erythropoietin outcome was to decrease transfusion requirements. In our study, transfusion requirements significantly decreased during the study period, however, transfusions were not completely eliminated. Mason et al[12] and Powe et al[13] found 16% and 5.3% of the patients, respectively, still requiring transfusions. This is in contrast to a clinical trial that achieved the ultimate goal of elimination of transfusion, within two to three months of initiation of erythropoietin.[3] The following discussion will attempt to explain the poor response to erythropoietin therapy seen in our study.

Since our study was conducted shortly after erythropoietin was marketed in Canada, the average baseline hemoglobin (63.8 g/L) was low (as compared to a new patient population in 1995). It may be postulated that these patients required a large percentage increase in their hemoglobin and, therefore, it may have been difficult to achieve target levels during the six-month study period. Currently most anemic hemodialysis patients would be considered for erythropoietin therapy before the hemoglobin had decreased to levels seen at the initiation of our study. However, a previous Canadian study with an average baseline hemoglobin that was slightly higher than ours (71.9 g/L) was successful in achieving target hemoglobin within a shorter time period.[4]

Nutritional deficiencies (iron, B12, folate), hemolysis, blood loss, hyperparathyroidism, aluminium overload and infection/inflammation[16] all contribute to anemia and may result in failure of erythropoietin to achieve target hemoglobin. Baseline assessment of these parameters in our study was quite variable. In particular, B12, folate, and aluminum levels, Coombs test and stool occult blood were rarely monitored. Stool occult blood results may be in several places in the patient's chart, making it difficult to access and possibly accounting for the low frequency of monitoring. Erythropoietin deficiency remains the primary contributor to anemia in this population,[1] and nutritional deficiencies and aluminum toxicity are relatively uncommon. This may then lead to decreased diligence in assessing for these contributing but potentially reversible factors. Since factors such as low folate and B12 serum concentration and high aluminum serum concentration are potentially correctable, more frequent monitoring of these parameters should be assured. Furthermore, correction of these parameters may improve response to erythropoietin. For future drug use evaluations, it would be more appropriate to monitor specific patients (i.e., checking the aluminum concentration in those who have received or are currently receiving therapy with aluminum containing medications, or checking serum folate and B12 in patients with increased mean corpuscular red blood cell volume).

Iron deficiency is also a common cause of diminished or delayed response to erythropoietin therapy.[16] It is crucial to have adequate iron stores to support erythropoiesis. It has been shown that as many as 74% of patients will require iron supplementation during erythropoietin therapy.[17] In our study, a large percentage of patients (43.5%) had low iron stores (ferritin <100 ng/mL). In patients with ferritin <50 ng/mL, iron supplementation was continued or initiated in 88%. There was no significant difference in serum ferritin values or iron supplementation between patients who responded to erythropoietin and those who did not (Table III). However, due to the importance of iron status, improvement in this area is required. Current practice is to initiate iron therapy before or at the beginning of erythropoietin therapy, including patients with adequate iron stores, to prevent iron deficiency.

The initial dose of erythropoietin (119.9 U/kg/wk) in our study was less than that recommended by the product monograph of 150-300 U/kg/wk. Our study reflects the importance of selecting an appropriate initial dose since there was a significant difference between the initial erythropoietin doses of those who achieved the target hemoglobin range compared to those who did not reach

target hemoglobin. Powe et al[13] found a similar low dosing trend (initial dose = 115.3 U/kg/week) in clinical practice. They suggested that inadequate education of medical personnel regarding dosing and hematologic targets, and concern regarding side effects such as hypertension may explain why lower initial doses were selected.

We also found that patients had inappropriate dosage modifications which resulted in patients not reaching or maintaining target hemoglobin. Specifically, there were 11 inappropriate erythropoietin dose modifications; seven errors were due to early erythropoietin dose modification prior to allowing adequate time for hemoglobin response, and four errors were due to not increasing the erythropoietin dose adequately. Development of a protocol and algorithm to ensure appropriate erythropoietin dose modification and intensive monitoring by the health care team would assist in avoiding these types of error.

Upon erythropoietin initiation and after dosage adjustment, hemoglobin/hematocrit monitoring was inadequate in the majority of patients. This parameter identifies those at risk of adverse events (e.g., hypertension, seizures) secondary to a rapid increase. For example, initial recommendations suggested that an increase in hematocrit of more than six percentage points over a four-week period has been associated with development or exacerbation of hypertension.[18] In our study, one of the five patients who experienced a greater than 6% increase in hematocrit, also experienced uncontrolled hypertension. As well, hemoglobin/hematocrit monitoring assesses poor progress towards target goals. Close monitoring of hemoglobin/hematocrit may have lead to more patients having erythropoietin doses modified and attaining the target hemoglobin range.

Other parameters such as CBC, platelet count, serum urea/creatinine, phosphate and potassium were monitored adequately in the majority of patients. Discrepancies probably reflect current policy at our institution to complete bloodwork on a six-week cycle rather than monthly.

Adverse events were generally lower than reported in the literature. For example, there was a low incidence of hypertension (6.5%) versus an approximate 20-25% incidence reported in the literature.[19] This is likely due to the retrospective nature of the study and different definitions of adverse events. Only thrombotic events were reported at a higher incidence than the literature (15.2% compared to 7%).[18] As data in this study were collected on all episodes of thrombotic events, including any notation of clots (e.g., clots in arterial line, clots aspirated, small clots in line), this is probably responsible for the relatively high incidence. Furthermore, the relationship between erythropoietin and clotted access had been debated in the literature,[14,20] and it is not clear whether these thrombotic events are directly related to erythropoietin therapy.

Limitations to this study include the retrospective nature of data collection, the time period in which the study was conducted (just after release of erythropoietin and therefore, may not reflect current use) and as patients were not interviewed, no assessment of compliance with iron therapy was completed. Conducting the study immediately after erythropoietin was marketed, however, allowed us to gather the most patient data as this was the time period when the largest number of patients had erythropoietin initiated.

In conclusion, the dialysis patients in this study did not receive maximum benefit from erythropoietin. There were a number of factors which contributed to this:

1. low initial and maintenance doses;
2. inadequate monitoring of hemoglobin/hematocrit, iron therapy; and
3. inappropriate erythropoietin dose modifications.

In order, to improve the benefit of our patients receiving erythropoietin, we recommended that:

a) an algorithm be developed for dosing and monitoring of erythropoietin with input and clearly defined responsibilities from multiple disciplines;
b) patient monitoring forms charts be developed;
c) education regarding the above algorithm be provided to all team members;
d) consideration be given to integration of algorithm on erythropoietin dosing and monitoring with technologies such as the hospital laboratory computer system; and
e) after implementation of the above recommendations a repeat criteria assessment with a small group of new patients.

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