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Evaluation of the Cost of a High-Dose Intravenous Iron Protocol in a Regional Hemodialysis Program: Research Letter

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Abstract

Background: Intravenous (IV) iron and erythropoietin stimulating agents (ESAs) are standard treatments for anemia in patients receiving maintenance hemodialysis. These medications are associated with significant costs to hemodialysis programs and patients. Recent trial evidence demonstrated that a high-dose IV iron protocol reduces ESA usage and improves cardiovascular outcomes. The cost of implementing a high-dose iron protocol within the Canadian public healthcare context remains unknown.

Objective: Our primary aim was to estimate the costs of a high-dose IV iron protocol in a large Canadian hemodialysis program that currently uses a low-dose and reactive IV iron strategy. Our secondary aim was to estimate the reduction in ESA use required to maintain cost neutrality with a high-dose IV iron protocol.

Design: In this modeling study of IV iron and ESA utilization from a regional hemodialysis program, changes in medication utilization were calculated based on observed effects from published trial data. Using data from a quality improvement audit of regional anemia management and medication utilization, we estimated potential cost differences under various modeling conditions.

Setting: Four adult hospital-based and 9 community in-center hemodialysis units in the Alberta Kidney Care—South renal program during the observation period of September 1, 2018, to November 30, 2018.

Patients: In total, data from 826 patients were included.

Measurements: Mean monthly IV iron and ESA doses were obtained from routine audit data captured within an electronic medical record. Costs were determined from provincially negotiated medication prices.

Methods: Current IV iron and erythropoietin dosages were aggregated at the hemodialysis unit level. We used the results from the PIVOTAL trial to estimate the expected increase in IV iron dose and reduction in ESA dose with a high-dose IV iron protocol. We assumed the split between various manufactures of IV iron and ESA were maintained in our cost model. Total medication costs were aggregated by hemodialysis unit, and the mean costs in each unit were used to estimate per-patient costs. Sensitivity analyses included models that assumed 100% IV iron sucrose usage, as well as models where community hemodialysis units and hospital-based hemodialysis units were examined separately. Finally, we calculated a break-even point for ESA dose reduction required to maintain cost neutrality.

Results: Actual baseline IV iron and ESA dose utilization across 13 adult HD units were 118 mg/patient/month (95% confidence interval [CI]: 102-134 mg) and 20,764 IU/pt./mo. (95% CI: 18,104-23,424 IU), respectively. The mean combined cost of ESA and IV iron was $315/pt./mo. (95% CI: $274-$355). In comparison, using the results of the PIVOTAL trial and assuming a high-dose IV iron scenario, we estimated mean IV iron use of 215 mg/pt./mo. (95% CI: 187-243 mg/pt./mo.) and a reduction in mean ESA use to 15,923 IU/pt./mo. (95% CI: 13,883-17,962 IU/pt./mo.). This resulted in an estimated cost savings of $38/pt./mo. (95% CI: $33–$42/pt./mo.) and a total program savings of $370,000 per year (95% CI: $325,000-$420,000). Sensitivity analyses under various alternate conditions also showed potential cost savings. We estimated that a dose reduction of ESA of 10% would be required for cost neutrality with a high-dose IV iron protocol.

Limitations: Our study is limited in its use of data from a single randomized controlled trial (RCT) to estimate cost savings rather than actualized utilization. Our models do not take into consideration anticipated reductions in transfusions and hospitalizations that could be realized from a high-dose IV iron protocol.

Conclusions: Based on cost modeling, a high-dose IV iron protocol could be integrated in large Canadian regional hemodialysis program in a cost saving manner. Programs implementing such a protocol should monitor IV iron and EPO use prospectively to determine if the trial protocol as applied in a real-world setting translates into cost savings.

Abrégé

Contexte: Le traitement habituel pour soigner l'anémie chez les patients sous hémodialyse d'entretien consiste en l'administration d'un supplément de fer par voie intraveineuse (IV) et d'agents de stimulation de l'érythropoïétine (ASE); des médicaments coûteux pour les programs d'hémodialyse et les patients. Des études récentes ont démontré qu'un protocole de fer IV à dose élevée réduisait l'utilization des ASE et améliorait les résultats cardiovasculaires. On ignore toutefois les coûts associés à la mise en œuvre d'un tel protocole dans le système public canadien.

Objectifs: Notre principal objectif était d'estimer les coûts d'un protocole de fer IV à dose élevée dans un program majeur d'hémodialyse canadien utilisant une stratégie d'administration de fer IV à faible dose et réactive. Nous souhaitions également estimer le taux de réduction de l'utilization des ASE permettant de maintenir la neutralité des coûts avec un protocole de fer IV à dose élevée.

Conception: Dans cette étude de modélisation, où l'administration de fer IV et d'ASE a été examinée dans le cadre d'un program régional d'hémodialyse, les changements dans l'utilization des médicaments ont été calculés en fonction des effets observés à partir des données publiées. Les potentielles différences de coûts ont été estimées dans diverses conditions de modélisation à l'aide des données d'un audit mesurant l'amélioration de la qualité de la gestion de l'anémie et l'utilization des médicaments au niveau régional.

Cadre: Quatre unités d'hémodialyse pour adultes en milieu hospitalier et neuf centers d'hémodialyse communautaires du program Alberta Kidney Care — South Renal entre le 1er septembre 2018 et le 30 novembre 2018.

Sujets: Les données de 826 patients ont été incluses.

Mesures: Les doses moyennes mensuelles de fer IV et d'ASE ont été obtenues avec les données d'un audit courant tirées d'un dossier médical électronique. Les coûts ont été évalués avec les prix négociés par la province pour ces médicaments.

Méthodologie: Les posologies actuelles de fer IV et d'érythropoïétine ont été agrégées au niveau de l'unité d'hémodialyse. Les résultats de l'essai PIVOTAL ont servi à estimer l'augmentation prévue de la dose de fer IV et la réduction prévue de la dose d'ASE avec un protocole de fer IV à dose élevée. Nous avons supposé que la division entre les divers fabricants de fer IV et d'ASE était maintenue dans notre modèle de coûts. Les coûts totaux des médicaments ont été agrégés par unité d'hémodialyse, et les coûts moyens pour chaque unité ont été employés pour estimer les coûts par patient. Les analyses de sensibilité ont inclus des modèles qui supposaient une utilization à 100 % du fer saccharose IV et des modèles où les unités d'hémodialyse communautaires et hospitalières ont été examinées séparément. Enfin, nous avons calculé un seuil de rentabilité pour la réduction d'ASE nécessaire au maintien de la neutralité des coûts.

Résultats: L'utilization réelle initiale de fer IV et d'ASE dans les 13 unités d'HD pour adultes était respectivement de 118 mg/patient/mois (IC 95 %: 102 mg à 134 mg) et de 20 764 UI/pt/mois (IC 95 %: 18 104 à 23 424 UI). Le coût combiné moyen du fer IV et des ASE était de 315 $/pt/mois (IC 95 %: 274 à 355 $). En comparaison, en utilisant les résultats de l'essai PIVOTAL et en supposant un scénario de fer IV à dose élevée, nous avons estimé une utilization moyenne de fer IV à 215 mg/pt/mois (IC 95 %: 187 à 243 mg/pt/mois) et une réduction de l'utilization moyenne d'ASE de 15 923 UI/pt/mois (IC 95 %: 13 883 à 17 962 UI/pt/mois); ce qui entraînerait une possible économie de 38 $/pt/mois (IC 95 %: 33 à 42 $/pt/mois) et une économie totale de 370 000 $ par année pour le program (IC 95 %: 325 000 à 420 000 $). Les analyses de sensibilité dans diverses conditions ont également montré des économies potentielles. Nous avons estimé qu'une réduction de 10 % de la dose d'ASE serait nécessaire pour maintenir la neutralité des coûts avec un protocole de fer IV à dose élevée.

Limites: Notre étude utilize les données d'un seul essai clinique randomisé pour estimer les économies de coûts plutôt que l'utilization actualisée. Nos modèles ne prennent pas en compte les réductions dans les nombres de transfusions et d'hospitalisations qui pourraient découler d'un protocole de fer IV à dose élevée.

Conclusion: Selon la modélisation des coûts, un protocole de fer IV à dose élevée pourrait être intégré à un program majeur d'hémodialyse régional canadien et réduire les coûts. Les programs qui mettent en œuvre un tel protocole devraient surveiller l'administration de fer IV et d'EPO de façon prospective pour déterminer si le protocole de l'essai, lorsqu'il est appliqué dans un contexte réel, se traduit par une réduction des coûts.

Keywords

anemia, dialysis, health economics, quality improvement

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Introduction

Intravenous iron and erythropoietin stimulating agents (ESAs) are standard treatments for end-stage kidney disease (ESKD)-related anemia. Most patients treated with maintenance hemodialysis will require one or both medications to maintain a hemoglobin level within the target range specified by their dialysis program.[1] However, these medications are associated with significant costs to hemodialysis programs and patients.[2] Furthermore, high doses of ESA have been linked to poor cardiovascular outcomes.[3]

The recently published Proactive IV Iron Therapy in Hemodialysis Patients (PIVOTAL) trial is the largest randomized study of IV iron dosing in hemodialysis patients. In the high-dose iron arm of this trial, ESA doses were reduced by 19.4% and red cell transfusions reduced by 21%.[4] The IV iron protocol from this trial offers an opportunity to simplify IV iron management in hemodialysis programs and possibly improve outcomes; however, the cost implications of adopting a similar protocol in Canadian hemodialysis programs remain unknown.

The aims of this study were to estimate the cost of implementing a high-dose IV iron protocol in a large regional hemodialysis center under various model conditions and to estimate the ESA reduction required to realize cost savings.

Methods

We conducted a modeling study using baseline data on IV iron and ESA use from an ongoing audit of the anemia protocol within 13 hospital-based and community adult, in-center hemodialysis units in a regional hemodialysis program, Alberta Kidney Care—South (AKC-S). Data on historical IV iron and ESA dosages during hemodialysis were collected from an electronic health record audit of actual delivered medications between September 1, 2018 and November 30, 2018 as part of a quality assurance process to understand baseline medication utilization trends. During the observation period, the AKC anemia management protocol (Supplement 1) followed a reactive iron strategy, similar though not identical to the PIVOTAL trial whereby loading iron doses would be administered if transferrin saturation fell below 20% and maintenance doses if transferrin saturation was between 20% and 40%.

We used local baseline data and the results from the PIVOTAL trial to estimate the expected increase in IV iron use and the expected reduction in ESA usage in our hemodialysis program. To achieve this, we calculated the mean differences realized in the trial and applied them to actual program usage to create the model estimates. Whereas the PIVOTAL trial used exclusively IV iron sucrose, our hemodialysis program used a combination of IV iron sucrose and IV sodium ferric gluconate. Therefore, multiple cost scenarios were analyzed. Our primary model assumed the same IV iron formulation distribution used in the AKC-S program. We assumed equal potency of IV iron formulations and a conversion ratio of darbepoetin alfa to epoetin alfa of 1 mcg:200 IU.[5] The cost of IV iron was derived from the drug cost paid by AKC-S in 2018 of $0.375/mg for IV iron sucrose and $0.274/mg for IV sodium ferric gluconate. The cost of ESA was based on Alberta Blue Cross retail drug formulary, with an estimated cost of $27.60 per 10 mcg darbepoetin alpha and $15.68 per 1000 IU epoetin alfa.

Sensitivity analyses included models with an assumption of 100% usage of each formulation of IV iron and ESA to reflect practices at other Canadian centers. Further analyses included models for hospital and community units separately. Finally, we modeled the costs in the PIVOTAL trial under each intervention arm using Alberta drug prices to estimate costs of replicating the trial protocol. Given that the reduction in ESA use from the trial may not be observed in clinical practice, we also estimated the ESA dose reduction required to achieve cost neutrality.

Results

To inform our modeling, we used data from 826 patients across 13 hemodialysis units in the AKC-S regional program. Overall, 96.1% of the study population was receiving IV iron and 80.5% was receiving ESA. Of those that required IV iron, 86% used IV sodium ferric gluconate (remainder used iron sucrose), and 85% of those that required ESA used darbepoetin alfa (remainder used epoetin alfa). The total yearly medication cost for ESA and IV iron across the AKC-S program ranged from $2.6 to $3.3 million dollars per year. The bulk of these costs were driven by ESA usage, which made up 89% of the medication costs, on average. Mean actual IV iron and ESA doses were 118 mg/patient/month (95% confidence interval [CI]: 102-134 mg) and 20,764 IU/patient/month (95% CI: 18,104-23,424 IU), respectively. The mean cost of ESA and IV iron was $315/patient/month (95% CI: $275-$355), of which $289/patient/month was attributed to ESA and $34/patient/month was attributed to IV iron.

In a high-dose IV iron scenario that maintained our program's current iron sucrose/sodium ferric gluconate split, we estimated a mean IV iron use of 215 mg/patient/month (95% CI: 187-243 mg) and a mean ESA use of 15,923 IU/patient/month (95% CI: 13,883-17,962 IU). This resulted in estimated cost savings of $38/patient/month (95% CI: $34-$42) and total program savings of $370,000 per year (95% CI: $320,000-$420,000) (Table 1).

Modeling of medication usage as reported in the PIVOTAL trial with Alberta medication costs showed cost savings of $75/month with a high-dose IV iron protocol assuming AKC-S split of ESA (85% darbepoetin alfa and 15% epoetin alfa). Sensitivity analysis using various combinations of IV iron and ESA formulations all resulted in savings between 10% and 14%. Finally, analyses examining costs according to outpatient hemodialysis unit location showed estimated cost savings

Table 1. Comparison of Baseline Medication Usage to Predicted Usage Under Each Model Condition With Associated Savings (Values Represent Monthly Cost Per Patient).

	IV iron usage (mg/month)	ESA usage (IU/month)	Baseline cost ($CAD/month)	Predicted cost ($CAD/month)	Savings from baseline ($CAD/patient/month) (% savings)
Actual utilization	118	20,764	315	N/A	N/A
Primary model[a]	215	15,923	315	277	38 (12%)
Sensitivity analyses					
Hospital-based units	212	16,820	330	288	42 (13%)
Community units	217	15,309	304	270	34 (11%)
100% iron sucrose and darbepoetin alfa	215	15,923	331	299	32 (10%)
100% iron sucrose and epoetin alfa	215	15,923	370	329	41 (11%)
100% sodium ferric gluconate and darbepoetin alfa	215	15,923	319	278	41 (13%)
100% sodium ferric gluconate and epoetin alfa	215	15,923	358	308	50 (14%)

[a]Model of usage assuming AKC-S split of IV iron (86% sodium ferric gluconate, 14% iron sucrose) and ESA formulations (85% darbepoetin, 15% epoetin) under high-dose iron conditions. IV = Intravenous; ESA = erythropoietin stimulating agents; AKC-S = Alberta Kidney Care—South; $CAD = values represent monthly cost per patient in Canadian dollars.

of $42/patient/month in hospital-based units and $34/patient/month in community units with a high-dose IV iron protocol (Table 1). We estimated a 10% reduction in ESA dose was required to active cost neutrality with high-dose IV iron.

Discussion

To our knowledge, this is the first study to report the potential cost impact of a high-dose IV iron protocol in a large hemodialysis program. This work shows that high-dose IV iron might reduce costs through its impact on lowering the use of ESAs, as was observed in the PIVOTAL trial. Challenges with the implementation of a program such as this include the multiple payers involved in medication coverage in Canada. Specifically, in Alberta, the budget for IV medications (including IV iron) is often covered by the AKC-S renal program, whereas ESAs are covered by provincial drug plans or private insurance as an outpatient medication. Therefore, hemodialysis programs with similar medication funding models to ours may be disincentivized to implement a high-dose IV iron protocol as they may not realize the cost savings directly. We found this to be a limitation in implementation within our regional setting — administrators within Alberta Health Pharmacy Services were hesitant to approve a protocol that would increase direct costs to the program without proven costs savings that could be derived elsewhere. Given the reduced rates of cardiovascular events in the high-dose IV iron group in PIVOTAL, this protocol may be considered standard of care in the future. However, currently these recommendations have not yet been incorporated into international or Canadian practice guidelines and would likely require confirmation of findings in additional trials to ensure robust results.[6] This barrier could be overcome with more research on the direct cost savings health care systems might realize if reductions in cardiovascular disease-related hospitalizations or transfusions are seen in real-world settings. Furthermore, there may be local hesitation related to implementing a protocol that delivers significantly more IV iron without long-term safety data. Longitudinal safety studies on populations that have implemented a high-dose iron protocol would be beneficial in overcoming this.

Future directions of this work including implementing and testing a high-dose IV iron protocol on prevalent dialysis patients in the Canadian dialysis context. Metrics of interest, including hospitalizations, blood transfusions, actual medication usage, and rates of iron toxicity, should be collected to better appreciate the economic consequences of a high-dose iron protocol. Further study is also needed regarding the potential impact of a high-dose IV iron protocol on patient-relevant outcomes, such as symptoms, quality of life, and care experiences.

Our study is limited by its use of data from a single trial to estimate cost savings rather than actualized utilization. Furthermore, estimates are based on Alberta drug costs and may change with different provincial pricing elsewhere. Our models do not take into consideration likely reductions in transfusions and hospitalizations that could be realized from a high-dose IV iron protocol, nor do they consider potential costs from iron overload, which are challenging to classify clinically in a dialysis population and therefore measure.[7]

Conclusions

In this modeling study, we estimated that a high-dose IV iron protocol may be cost saving among adults receiving in-center hemodialysis in Southern Alberta. Important next

steps will be to adapt and implement a similar protocol in practice, track iron and ESA usage prospectively, and determine whether trial results are mirrored in the real world through actual cost savings.

Ethics Approval and Consent to Participate

An REB exemption was provided by the Conjoint Health Research Ethics Board at the University of Calgary due to the focus of this project being quality improvement.

Consent for Publication

All authors read and approved the final version of this manuscript.

Availability of Data and Materials

This study is based in part on data provided by Alberta Health Services. We are not able to make our dataset available due to restrictions on sharing confidential patient-level data in the setting of waived consent of participants, and patients could be identifiable with our sample size. Questions about the data can be directed to the authors directly.

Declaration of Conflicting Interests

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Supplemental Material

Supplemental material for this article is available online.

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