Pharmacist Integration into the Hemophilia Treatment Centre: A Canadian Pilot Project to Optimize Treatment and Improve Cost-savings

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Abstract

Coagulation factors used in prophylactic treatment of patients with clotting disorders are associated with significant costs to health care systems. These products have complex pharmacokinetic profiles subject to large inter-individual variation making their efficient use challenging. Prior to this project, pharmacists were not involved as part of the Hemophilia care teams across Canada. The purpose of this pilot project was to determine whether employment of a pharmacist with expertise and a focus on plasma protein and related products including hemophilia treatments, would be an effective strategy to reduce costs associated with clotting factor prophylaxis regimens and identify the pharmacist's activities associated with this new role. A cost-minimization analysis was conducted to compare the addition of a pharmacist to the care team of the Hemophilia Treatment Centre (HTC) at a pediatric hospital serving 500,000 children and youth. The analysis was performed from the perspective of the formulary manager, Canadian Blood Services, over a 1-year period including 9 months of interventions. The pharmacist performed 18 therapeutic optimizations on 14 patients with moderate to severe hemophilia A or B, and 1 von Willebrand patient, aged 3 to 18 years old. As a result of the pharmacist's intervention, clotting factor treatment costs extrapolated over one year were reduced by 20.5% for these patients. This represents a net savings of $225K CAD/year, or $12.5K CAD/optimization/year. The addition of a pharmacist to the HTC to manage recombinant and plasma-derived coagulation factors can optimise the treatment plan and significantly reduce the costs of managing patients with hemophilia.

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Key Points

The substitution of clotting factor products and the reduction of administered doses undertaken by the pharmacist have resulted in significant savings.

The current intervention demonstrated pharmacists can reduce clotting factor treatment costs by 20.5% (net savings of $12,000 for each treatment optimization).

Keywords: Hemophilia; Pharmacist; Prophylactic Treatment; Recombinant; Cost-Minimization

Abstract

Coagulation factors used in prophylactic treatment of patients with clotting disorders are associated with significant costs to health care systems. These products have complex pharmacokinetic profiles subject to large inter-individual variation making their efficient use challenging. Prior to this project, pharmacists were not involved as part of the Hemophilia care teams across Canada. The purpose of this pilot project was to determine whether employment of a pharmacist with expertise and a focus on plasma protein and related products including hemophilia treatments, would be an effective strategy to reduce costs associated with clotting factor prophylaxis regimens and identify the pharmacist's activities associated with this new role. A cost-minimization analysis was conducted to compare the addition of a pharmacist to the care team of the Hemophilia Treatment Centre (HTC) at a pediatric hospital serving 500,000 children and youth. The analysis was performed from the perspective of the formulary manager, Canadian Blood Services, over a 1-year period including 9 months of interventions. The pharmacist performed 18 therapeutic optimizations on 14 patients with moderate to severe hemophilia A or B, and 1 von Willebrand patient, aged 3 to 18 years old. As a result of the pharmacist's intervention, clotting factor treatment costs extrapolated over one year were reduced by 20.5% for these patients. This represents a net savings of $225K CAD/year, or $12.5K CAD/optimization/year. The addition of a pharmacist to the HTC to manage recombinant and plasma-derived coagulation factors can optimise the treatment plan and significantly reduce the costs of managing patients with hemophilia.

1. Introduction

Prophylactic treatment with coagulation factors in patients with hemophilia A and B reduces the number of bleeds and their consequences on joints and organs, thus increasing the length and quality of life of patients.[1,2] Nevertheless, it is associated with significant costs to the health care system. In Canada, coagulation factors are purchased and distributed by Hema-Québec, for the Province of Québec, and by Canadian Blood Services for all the other Provinces and Territories. Funding is provided entirely by the Provincial and Territorial governments. Whether recombinant or plasma-derived therapies, factors are expensive drugs that follow complicated pharmacokinetic (PK) trajectories making it a challenge to use them in an optimal way.[3]

With the introduction of new extended half-life products (EHL), efficient management of coagulation factors has become even more challenging. Indeed, many of these newer products have considerable inter-individual variation in half-life,[4,5] such as the new factor VIII EHL product, Adynovate. Adynovate has been shown in clinical trials to have a half-life that ranges from 6 to 30 hours, depending on the patient. Thus, initiating therapy using the standard dosing regimen, as prescribed in the product monograph, rather than optimising the individual treatment plan is very cost inefficient. Effective management of these products therefore requires tailoring treatment to the patient. To do so, it is essential to assess and interpret the PK profiles of patients. Recently, the Web-Accessible Population Pharmacokinetic Service-Hemophilia (WAPPS-Hemo) web-based platform based at McMaster University, which allows individual PK assessments on a limited number of plasma samples, has become readily available for clinicians to use[7]. At Children's Hospital of Eastern Ontario (CHEO), we have started to routinely perform PK assessments for hemophilia patients, particularly when the type of product is changed, but not systematically due to ressource limitations, including time constraints.

To be performed systematically, PK assessment and interpretation requires sufficient time to make extensive arrangements, ensure patient availability and coordinate a time to review the data and results with the care team. A dedicated pharmacist could greatly assist this process by standardizing the approach and assisting with the interpretation of the PK results. Since the therapy for patients with moderate to severe hemophilia costs $50,000-500,000 CAD/year/patient, small changes could result in significant cost savings. For instance, two US studies have shown that involvement of a pharmacist in the management of recombinant and plasma derived factor therapies for hemophilia improves patient management and reduces associated costs.[8,9]

As in Canada, in the US pharmacists are not typically part of the comprehensive care team for the hemophilia population. The Hemophilia Management Program[8] and The Factor Stewardship Program[9] were conducted to evaluate the impact of including a pharmacist in the management of hemophilia patients. This gave the pharmacist the opportunity to participate in rounds, multidisciplinary meetings and regular patient assessments. Due to this close contact with patients and collaboration with the team, the pharmacist was able to identify and propose therapeutic optimizations, including dose/frequency adjustments, to improve drug dispensing, drug administration and also reduce wastage. One of the pharmacist's roles was to provide guidelines and training to the care team in order to increase and update the knowledge of each staff member involved in the management of patients with hemophilia. The pharmacist was also involved in coordinating the transition of care to the community by facilitating the flow of information with the pharmacy service. The combination of these activities allowed the pharmacist to improve the management of coagulation factors in patients with clotting disorders, which led to a reduction in the quantity of factor being used and significantly reduced the cost associated with therapy. Thus, the implementation of a pharmacist working as part of the transfusion medicine team in our institution could maximize patient outcomes while minimizing the cost of these expensive therapies.

The purpose of this pilot project was to determine whether a pharmacist working as part of the Hemophilia Treatment Centre (HTC) would render the management of coagulation factors more cost effective and to identify the pharmacist's activities associated with this new role. The intent of incorporating a pharmacist as part of the care team was to optimise protocols and maximize cost savings through reduced wastage while

maintaining patient outcomes.

2.Materials and Methods

This project occurred at the Children's Hospital of Eastern Ontario (CHEO), Canada, which specializes in pediatric care, with over 6,700 annual admissions, serving a population of 500,000 children and youth. CHEO patients with moderate to severe hemophilia A or B or von Willebrand disease (vWD) receiving prophylactic treatment with recombinant or plasma-derived clotting factor were eligible for a pharmacist assessment.

2.1 Model design

We conducted a cost-minimization design study to determine the most cost-effective clotting factor management strategy for patients receiving prophylactic treatment. We compared the pre-intervention strategy, current model of care without pharmacist involvement, to the post- intervention strategy, model of care that included pharmacist interventions and support. We assumed that the effectiveness of both strategies was the same. The study was conducted from the perspective of the formulary manager, Canadian Blood Services, with a one-year time horizon.

2.2 Model inputs

Only drug prices were considered since it has been shown that more than 97% of the cost is due to clotting factor replacement[10]. Other sources of costs, such as drug administration and storage costs, do not substantially impact on the overall cost. Due to the confidential nature of the cost of coagulation factors, the financial calculation was done by Canadian Blood Services. The unit cost of each product was used and then multiplied by the units projected to be consumed annually for each patient. Since the unit costs are proprietary information, the doses and unit costs will not be disclosed, only the annual cost savings per patient will be reported. We assumed that the annual salary of a pharmacist is $130K CAD.

2.3 Scenario

A pharmacist was assigned for the period of 1 year. This pharmacist began with a 3-month phase-in period during which no interventions were done by the pharmacist, followed by 9 months of specific action on optimization protocols with the goal of achieving cost savings while maintaining best patient care. Training material for the pharmacist was developed and provided by the Canadian Blood Services Plasma Protein and Related Product Formulary Program team. The pharmacist worked in collaboration with CHEO staff on patient level data pertaining to the pharmacokinetics of individual treatment responses in an effort to optimise the dose and the treatment. McMaster's WAPPS-Hemo served as the basis for therapeutic optimization. WAPPS-Hemo generates PK profiles that allow the pharmacist to tailor the treatment to the clotting factor's actual profile, the targets of treatment, and the needs of the patient.[7]

2.4 Sensitivity analysis

Since the parameters used are subject to variation, we performed one-way and two-way sensitivity analyses to assess the robustness of our model. We varied the cost of drugs and the pharmacist's salary and observed the impact it would have on the project savings. Drug costs were varied by +/-30%. The pharmacist's salary was varied within +/-30% of its baseline value.

3.Results

3.1 Cost-savings

Fourteen (14) patients aged 3 to 18 years old, with severe (12) or moderate (2) hemophilia A (12) or B (2), and one patient with severe vWD had their treatment optimised during the 1-year period of the projet. The pharmacist made a total of 18 interventions to optimise therapy.

As a result of the pharmacist's interventions (*Table 1*), the costs of coagulation factors for 15 patients with coagulation disorders extrapolated over 1 year would be reduced by 20.5%, representing savings of $355K CAD/year. After accounting for the $130K CAD investment for the employment of the pharmacist, this

represents a total saving of $225K CAD/year, or an average savings of $12.5K CAD per optimization per year.

The largest projected savings were seen in patients initially treated with plasma-derived factors. The seven therapeutic optimizations with Wilate as the initial therapy resulted in savings of $409K CAD, or $58K CAD/year per patient. Substitution of Wilate with Adynovate generated savings of $101K CAD/year per patient, compared with $26K CAD/year per patient for dose optimization of Wilate alone. Among the eight hemophilia A patients who underwent product substitution, seven were switched to Adynovate for a total projected savings of approximately $281K CAD/year. In total, product substitutions saved $24K CAD/year per patient while keeping the same treatment and optimising doses saved about $15.5K CAD/year per patient.

Insert Table 1. About Here

3.2 Sensitivity analysis

A sensitivity analysis was conducted to analyze the effect of a +/- 30% variation in both drug costs and pharmacist salary (Table 2). In the worst-case scenario where there is a combination of a 30% decrease in drug cost and a 30% increase in the pharmacist's salary, there is still a net savings of $79.5K CAD/year. There would have to be a 63% reduction in drug costs or a 173% increase in pharmacist salary for the cost-effectiveness of adding a pharmacist as part of the transfusion medicine team to be lost. These drastic changes in drug cost and pharmacist salaries are highly unlikely; therefore, the strategy of adding a pharmacist to manage coagulation factors remains beneficial.

Insert Table 2. About Here

3.3 Pharmacist activities

PK analyses conducted by the pharmacist consisted of entering and analyzing factor levels, and identifying and performing therapeutic optimizations. These activities consumed 30% of the pharmacist's working time. Given these PK assessments, two types of optimizations were proposed: product substitution or dose optimization with the same drug. Once identified, possible optimizations were discussed with the physician and then proposed to the patient's family. The pharmacist's role was not restricted to PK analyses. The most time-consuming activity conducted by the pharmacist involved clinic attendance which represented 40% of the pharmacist's working time. Clinic attendance activities included discussions with families, education on new product administration, and discussions with the multidisciplinary team. Furthermore, 20% of the pharmacist's time was dedicated to administrative activities such as organization of appropriate switch days, coordinating laboratory tests and timing of PK assessments, ensuring entire supply consumption, adverse event reporting and inventory management support. Finally, the pharmacist developed practice improvement policies and trained staff 10% of the time.

4. Discussion

The current intervention was made possible with a novel clinical tool (WAPPS-HEMO) that pharmacists can now use that allows individual PK assessments to help the transfusion team optomize coagulation factors. Findings from the current pilot study demonstrated a successful cost-minimization model of adding a trained pharmacist as part of personalized treatment of patients living with hemophilia receiving prophylaxis with coagulation factors. We showed that the substitution of clotting factor products and the reduction of administered doses undertaken by the pharmacist have resulted in savings that were 2.7 times greater than the investment in the pharmacist's salary, savings that were realized by only the 7th patiet optimization. Indeed, the current intervention demonstrated pharmacists can reduce clotting factor treatment costs by 20.5% (net savings of $12,000 for each treatment optimization).

Product substitution can particularly result in significant cost savings, but a strong understanding of PK profiles is required to make these interventions effective. Additionally, increased support to counsel patients and avoid product wastage is important when switching products.[5]

Slocum et al[8] had previously demonstrated that the involvement of a pharmacist in the care team for the hemophilia population resulted in significant cost savings. Implementation of their hemophilia management program resulted in an ROI of 20:1. This is higher than ours, but this difference can be explained by the larger number of patients they treat and by the higher pricing of factors in the US. In support of our findings, this study highlighted the fact that the new role given to the pharmacist should not be limited to therapeutic optimization and treatment management alone. The support and counseling of patients and families in treatment management is also important; optimization of treatment on its own is insufficient. This is especially true when dealing with a pediatric population. The pharmacist's involvement as a member of the care team is crucial to improve practices and deepen the team's knowledge of medications, thus improving the patient's clinical outcome and reducing costs.

Due to the one-year time horizon, we were unable to measure long-term outcomes and therefore assumed that patients with and without pharmacist intervention achieved the same outcomes. It is possible that these interventions could lead to improved outcomes such as decreased hospitalizations, in which case more savings would be possible. Although the pharmacist performed therapeutic optimizations for only 9 months, given the initial 3-month phase-in period, savings were calculated on an annual basis to obtain savings over the entire project duration. On a longer time scale, therefore, greater annual savings could be expected. The validity of the costs was difficult to confirm, although this was compensated for by performing a sensitivity analysis. The small population size could be responsible for important cost variations between each of the optimizations made. This limitation challenged whether it is appropriate to extrapolate the results on a larger scale. As the study population was exclusively pediatric, the effect of implementing such a project on adults remains unknown. However, because the doses of clotting factor products consumed in adults are higher, implementation of the project in the adult population could result in significant cost savings. Following the success of this pilot project, it will be continued in children and expanded to adults, bringing more information to a larger number of patients and a broader age group. If the findings in this project continue to be demonstrated, this will be used as a case study to expand to HTCs across Canada.

Our pilot project demonstrated that involvement of a pharmacist in the hemophilia care team allowed for significant reduction in the costs of coagulation factor therapy in Canada. Thorough analyses of PK data, relationships with patients and families, involvement in the care team and development of protocols are activities that can be performed by a pharmacist in a HTC to help improve the management of prophylactic therapy with coagulation factors.

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