

Utilization of recombinant activated factor VII in southern Ontario in 85 patients with and without haemophilia

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Summary. Recombinant activated factor VII (rFVIIa) is licensed for the treatment of bleeding in individuals with haemophilia and inhibitors. The use of rFVIIa appears to be increasing, and an increase in unlicensed use is suspected. There are currently few data about the specific indications for its use. The aim of this study was to describe the patterns of utilization of rFVIIa. We performed a retrospective cohort study using rFVIIa infusion data collected prospectively and clinical data collected retrospectively. Patients were identified using a tracking system designed to account for use of all coagulation factor concentrates issued in southern Ontario. Between 1 January 2001 and 31 December 2005, 85 patients received rFVIIa. 1164 infusions were given (8246.4 mg). Haemophilia patients with inhibitors accounted for 82.9% of rFVIIa infused and represented 8.2% of patients. The total amount of rFVIIa used increased each year from 2001 to 2004 and then

decreased in 2005. The total number of infusions of rFVIIa administered annually increased. Both on-label and off-label use of rFVIIa increased. The number of patients with haemophilia receiving rFVIIa remained small and constant. The number of patients receiving rFVIIa for off-label indications increased markedly. Most rFVIIa infusions were given for licensed indications; however, these infusions represented <10% of patients treated. Overall, the utilization of rFVIIa is increasing, mostly for approved indications; however, the number of patients being prescribed rFVIIa for off-label indications has increased. The tracking system used in this study is a valuable tool to describe ongoing utilization patterns of rFVIIa.

Keywords: blood products, coagulation, haemostasis, NiaStase[®], NovoSeven[®], transfusion

Introduction

Recombinant activated factor VII (rFVIIa; NiaStase[®], NovoSeven[®]) has been licensed in Canada for the treatment of bleeding in individuals with haemophilia A or B having inhibitors [1]. Recombinant FVIIa has also been used for unlicensed or 'off-label' indications including: bleeding in patients with acquired inhibitors; patients with FVII deficiency [2,3] and patients with coagulopathies other than haemophilia, such as thrombocytopenia, disseminated intravascular coagulopathy and liver

dysfunction [4]. In addition to patients with identified bleeding disorders, rFVIIa has been administered 'off-label' for control of haemorrhage in the absence of coagulation defects, in the context of trauma [5–8], surgery and obstetrical complications; and for the rapid reversal of oral anticoagulation [9–11]. In general, the evidence supporting these indications is weak, consisting mainly of case reports, case series and few small randomized-controlled trials [8,12–16].

The safety of rFVIIa has not been systematically evaluated in patients with or without coagulation disorders [17]. Although rFVIIa appears to be safe in patients with haemophilia, recognized adverse effects in other patient populations include arterial and venous thrombotic complications and disseminated intravascular coagulation [16–21]. Furthermore, rFVIIa is expensive. In 2005, a single injection (80 kg person receiving 7.2 mg or 90 µg kg⁻¹) cost

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between \$6622.56 and \$8240.04 Canadian dollars (data provided by Canadian Blood Services). The total cost of rFVIIa used in Canada (excluding Québec) in 2002/2003 was \$26.3 million, which represents an increase of 30% over the preceding year (data provided by Canadian Blood Services). It is generally agreed that its use is increasing and an increase in its use for unlicensed indications is suspected [12,13,18]. However, there are currently few data about the specific indications for use of rFVIIa.

An opportunity to gather such data was provided by the development of a validated system that tracks the use of factor concentrates in the region in southern Ontario serviced by the Hamilton-Niagara Regional Hemophilia Program (HNRHP) and Canadian Blood Services (CBS) Hamilton Centre [22]. This region includes 26 hospitals. The tracking system, which incorporates purpose-specific software, may be a valuable tool to describe ongoing utilization patterns of the various factor concentrates, including rFVIIa.

Materials and methods

We performed a retrospective cohort study including all patients who received rFVIIa in this region of southern Ontario. Data on rFVIIa infusions, including indications, dose and frequency of administration were collected prospectively and clinical data were obtained by retrospective chart review. The objectives of the study were to describe the patterns of utilization and the clinical indications for rFVIIa administration.

Study population

All patients who received rFVIIa from 1 January 2001 until 31 December 2005 within southern Ontario were prospectively registered into the tracking system database. Patients with a diagnosis of an inherited bleeding disorder were identified by the HNRHP. Other patients were identified through the Transfusion Medicine service at each hospital and reported to the HNRHP soon after the rFVIIa was issued.

The factor tracking system of southern Ontario

The HNRHP has developed a database to track and monitor the distribution and use of factor concentrates, including rFVIIa, in the region [22]. This system tracks the use of factor concentrates in hospitals, in the haemophilia clinic and at home by individuals on home infusion therapy. Data from

three independent sources were entered prospectively into the database at regular intervals: (i) CBS Hamilton Centre (CBS is the only distributor of blood products in Canada) provided information regarding the amount of rFVIIa distributed to 26 hospitals; (ii) the hospital transfusion services provided information about the amount of rFVIIa received from CBS and the amount of rFVIIa issued to inpatient facilities or to outpatients for home infusion therapy and (iii) patients on home infusion therapy provided information about personal rFVIIa utilization including the indications for infusion, date of infusion and the amount infused. The flow of this information has previously been described [22]. Demographic and infusion data were prospectively entered into the database using a specialized software program called the Canadian Hemophilia Assessment and Resource Management System (CHARMS) [22] by a trained data manager. Data from medical charts were abstracted using standardized data collection forms. All data were entered into a Microsoft Office Access database (Microsoft Corporation, 2003).

Data monitoring

Details of the flow of information, data validation and data monitoring have been previously reported [22]. Data entry was subjected to regular integrity checks according to standard operating procedures. Any discrepancies were addressed and resolved prior to data analysis.

Analysis

Infusions were classified by the following indications: haemophilia A or B with inhibitors; FVII deficiency; acquired coagulation factor inhibitor; other congenital bleeding disorder and other indication. Infusions were considered to be for 'on-label' indications if they were given to patients with haemophilia A or B and inhibitors [1]. Infusions were considered to be 'off-label' if they were given for any other indication, bearing in mind that licensed indications vary internationally. Mean values, standard deviations (SD), medians and interquartile ranges (IQR) were computed as descriptive summary statistics.

Ethics

Procedures used to maintain and operate the database were approved by the Research Ethics Board (REB) of Hamilton Health Sciences and McMaster University. The REBs at participating institutions approved the study and waived the need for individual patient

consent as all data were anonymized and no intervention was performed.

Results

Between 1 January 2001 and 31 December 2005, 85 patients received rFVIIa at 10 different hospitals (four tertiary care teaching hospitals and six community hospitals). A total of 1164 infusions were given amounting to 8246.4 mg of rFVIIa. Patients ranged in age from newborn to 85 years old (mean 58.5, SD 21.5 years), and 62 patients (72.9%) were male. Overall, 79.5% of rFVIIa was infused in the hospital or in the clinic and 20.5% was infused at home. The proportion of rFVIIa infused in the hospital/clinic and at home per year is illustrated in Fig. 1.

Overall rFVIIa indications

Most (82.9%) of rFVIIa infused during the 5-year study period was administered to seven patients with

haemophilia A (Fig. 2); 3.4% was administered to patients with congenital FVII deficiency; 4.3% was given to patients with acquired FVIII inhibitors; 0.9% was given to patients with other bleeding disorders (including α_2 -antiplasmin deficiency, Factor X deficiency and von Willebrand's disease with FVIII inhibitor); and 8.5% was given for bleeding associated with a variety of medical or surgical diagnoses. Therefore, 82.9% of the rFVIIa utilization over the 5-year period was for approved indication of treatment or prevention of bleeding in haemophilia patients with inhibitors.

Table 1 describes the medical and surgical patients who received rFVIIa. Twenty-six patients were medical patients with the following diagnoses: haematological/oncological (*n* = 11); liver dysfunction (*n* = 4); renal failure (*n* = 3); sepsis (*n* = 2); use of anticoagulant therapy (*n* = 2); pancreatitis (*n* = 1), blunt trauma (*n* = 1) and penetrating trauma (*n* = 1). Three patients had more than one underlying diagnosis and four patients had none recorded. One

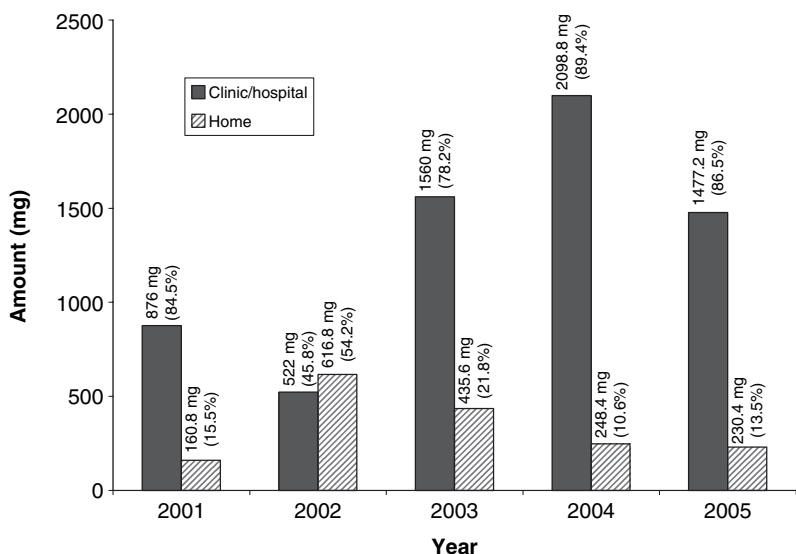


Fig. 1. Location of recombinant activated factor VIIa infusion for the years 2001–05.

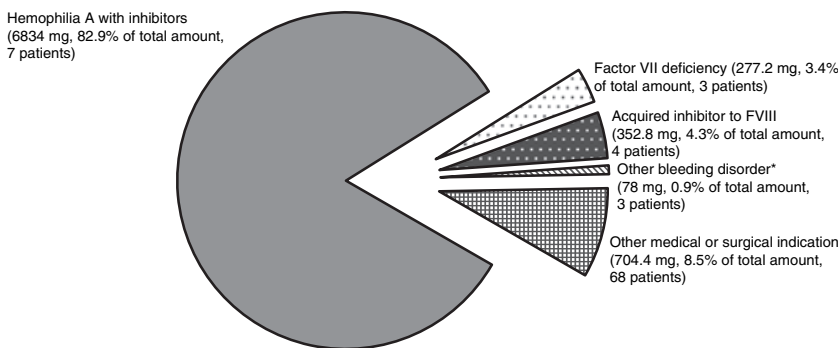


Fig. 2. Total utilization of recombinant activated factor VIIa by indication for the years 2001–05. Patients were classified as having: (i) haemophilia A with inhibitors; (ii) factor VII deficiency; (iii) acquired inhibitors to factor VIII; (iv) other congenital bleeding disorder and (v) other medical or surgical indication. *Patients included in the 'Other bleeding disorder' category were diagnosed with α_2 -antiplasmin deficiency, factor X deficiency and von Willebrand's disease with acquired inhibitor to FVIII.

Table 1. Description rFVIIa for medical or surgical reasons.

Site(s) of bleeding	Number of patients	Median age in (years; min, max)	Surgical procedure (number of patients)*	Diagnosis/contributing conditions (including trauma) (number of patients)*
Surgical				
GI/abdominal	11	53 (<1, 84)	Hernia repair (1), repair duodenal ulcer (1), liver biopsy (1), repair of fistula (1), Whipple's procedure (1), colectomy (3), repair of liver laceration (1), laparotomy (1), splenectomy (1), internal fixation pelvis (1)	Sepsis (2), renal failure (1), liver failure (2), postpartum (1), acute myeloid leukaemia (1), blunt trauma (4), no underlying condition (2)
ICH	2	61 (50, 75)	Neurosurgery (2)	Thrombocytopenia (1), no underlying condition (1)
Cardiac	16	72 (41, 83)	CABG (6), AVR (10), MVR (2), repair aortic dissection (4)	No underlying condition (16)
Vascular	7	74 (69, 85)	AAA repair (6), amputation lower extremity (1)	Renal failure (1), no underlying condition (6)
GU/gynaecological	3	66 (36, 68)	TURP (1), biopsy of bladder mass (1), Caesarean section	Liver failure (1), renal failure (1), multiple myeloma (1), postpartum (1)
Prophylaxis [†]	3	69 (35, 72)	Neurosurgery (resection of neurofibroma) (1), liver resection (1), TURP (1)	No underlying condition (3) [‡]
Total	42	69 (<1, 85)		
Diagnosis/contributing conditions (including trauma) (number of patients)*				
Medical patients				
GI/abdominal	15	68 (31, 83)		Sepsis (1), renal failure (2), liver failure (4), pancreatitis (1), hepatic mass (1), acute myeloid leukaemia (1), myelofibrosis (1), non-Hodgkin's lymphoma (1), melanoma (1), no underlying condition (3) [†]
ICH	5	68 (20, 75)		Anticoagulant use (2), thrombocytopenia (1), blunt trauma (1), penetrating trauma (1), no underlying condition (1)
ENT	2	43.5 (15, 72)		Thrombocytopenia (2)
Multiple sites [§]	4	66 (<1, 72)		Thrombocytopenia (2), sepsis (1), renal failure (1), acute myeloid leukaemia (1)
Total	26	66 (<1, 83)		

Min, minimum value; Max, maximum value; GI, gastrointestinal; ICH, intracranial haemorrhage; GU, genitourinary; CABG, coronary artery bypass grafting; AVR, aortic valve replacement; MVR, mitral valve replacement; AAA, abdominal aortic aneurysm; TURP, trans-urethral resection of prostate; ENT, ear, nose or throat.

*Patients may have had more than one procedure or underlying condition.

[†]No bleeding.

[‡]Two patients with no underlying condition did not wish to receive blood for religious reasons.

[§]Multiple sites of bleeding including ENT (one patient), GI/abdominal (four patients), ICH (two patients) and diffuse bleeding (one patient).

[¶]One patient with no underlying condition did not wish to receive blood for religious reason.

patient did not wish to receive blood products for religious reasons. The most common site of bleeding was the gastrointestinal (GI) tract ($n = 19$). Five

patients had intracranial haemorrhage, three patients had epistaxis and one patient had diffuse bleeding. Four patients had bleeding from more than one site.

Forty-two patients received the rFVIIa for bleeding related to surgery. The sites of bleeding were GI/abdominal ($n = 11$), intracranial ($n = 2$), cardiac ($n = 16$), vascular ($n = 7$) and genitourinary/gynaecological ($n = 3$). Three patients were administered rFVIIa prophylactically. The conditions potentially contributing to surgical bleeding included sepsis ($n = 2$), renal failure ($n = 3$), liver failure ($n = 3$), postpartum ($n = 2$), acute myeloid leukaemia ($n = 1$), multiple myeloma ($n = 1$) and blunt trauma ($n = 4$). Three patients had more than one underlying medical condition and 28 patients had no underlying medical condition recorded.

Concomitant therapies

In addition to receiving rFVIIa, 70 (82.4%) patients received additional haemostatic therapies including fresh-frozen plasma, cryoprecipitate, platelet transfusions, tranexamic acid, desmopressin acetate and vitamin K. If patients without a diagnosis of haemophilia, acquired haemophilia, FVII deficiency or other congenital bleeding disorders are considered ($n = 68$), 97% of these patients received some other haemostatic therapy before or at the time of the rFVIIa infusion. Overall, 67.1% of the rFVIIa was prescribed by a haematologist accounting for all of the on-label use and 64.1% of the off-label use.

Outcomes

Of the 85 patients treated with rFVIIa, 31 (36.5%) died. None of the patients receiving rFVIIa for on-label indications died compared with 39.7% ($n = 31$) of the patients receiving rFVIIa for off-label indications.

Trends in rFVIIa utilization

The total amount of rFVIIa infused increased each year from 2001 to 2004 then decreased in 2005 (Table 2 and Fig. 3). The total number of infusions of rFVIIa administered yearly has also increased from 100 in 2001 to 319 in 2005 (Fig. 3). On-label use of rFVIIa increased yearly from 650.4 mg (62.7% of the total yearly amount) in 2001 to a high of 2025.6 mg (86.3%) in 2004 and then decreased to 1266 mg (74.1%) in 2005. Off-label use has also increased over the 5 years but to a smaller degree: from 386.4 mg (37.3% of the yearly total) in 2001 to 441.6 mg (25.9%) in 2005 (Fig. 3).

The total number of patients who received rFVIIa has increased from six patients in 2001 up to 38 patients in 2005. The number of patients receiving

rFVIIa for on-label indications has remained low and relatively stable while the number of patients who received off-label rFVIIa has increased. The indications for rFVIIa administration are illustrated in Fig. 4. Because some patients received rFVIIa in more than 1 year, the number of individual patients receiving rFVIIa over the 5-year study period (85 patients) differs from the total of all years (100 patients). Many patients received multiple infusions of rFVIIa. In fact, one patient with haemophilia A and FVIII inhibitors accounted for 44.7% of all rFVIIa utilization in this region over the 5 years. In addition, the amount of rFVIIa infused per patient varied when one compared patients receiving rFVIIa for on-label or off-label indications (Table 3). Overall the median on-label use was 562.8 mg per patient (IQR: 273–1006.8 mg) compared with off-label use of 7.2 mg per patient (IQR: 4.89–14.4). Patients receiving rFVIIa for on-label indications received a greater number of infusions (median 63, IQR: 33–144) compared to those patients receiving rFVIIa for unlicensed indications (median 1, IQR: 1–2).

Discussion

This study presents the results of a retrospective cohort study analysing the use of rFVIIa in southern Ontario, Canada. The main strength of this study is the fact that use of the robust methodology of the tracking system enabled us to account for all of the use of rFVIIa in the area, regardless of whether the infusion occurred in the hospital, outpatient clinic or patient's home. Limitations of this study include the relatively small number of patients who received rFVIIa and the lack of outcome data.

Most of the rFVIIa used in this region from 2001 to 2005 was for the approved indication of the treatment or prevention of bleeding in patients with haemophilia and inhibitors (82.9% of all infusions). If one considers the licensed indications in the United States and Europe, such as congenital FVII deficiency, Glanzmann's thrombasthenia and acquired inhibitors to FVIII, the amount of rFVIIa for on-label indications increases to 90.5% of the total. During the first 4 years of the study period, there was a threefold increase in the utilization of rFVIIa for on-label indications. One possible reason for this is the increase in elective surgeries in these individuals, procedures which would have likely been previously deferred because of a high risk of bleeding complications. Individual patients with inhibitors often use large amounts of rFVIIa during surgery or trauma which explains why so patients ($n = 7$) were responsible for over 85% of the total rFVIIa administered

Table 2. Descriptions of infusions: 2001–05.

Indication for infusion	2001	2002	2003	2004	2005	Total (2001–05)
Amount infused [mg (%)]						
On-label						
Haemophilia A or B with inhibitors	650.4 (62.7)	1047.6 (90.4)	1844.4 (92.4)	2025.6 (86.3)	1266 (74.1)	6834 (82.9)
Off-label						
Factor VII deficiency	204.0 (19.7)	37.2 (3.2)	12.0 (0.6)	0 (0)	24 (1.4)	277.2 (3.4)
Acquired inhibitor	182.4 (17.6)	0 (0)	38.4 (1.9)	79.2 (3.4)	52.8 (3.1)	352.8 (4.3)
Other congenital bleeding disorder	0 (0)	0 (0)	0 (0)	28.8 (1.2)	49.2 (2.9)	78.0 (0.9)
Other diagnosis or indication	0 (0)	74.4 (6.4)	100.8 (5.1)	213.6 (9.1)	315.6 (18.5)	704.4 (8.5)
All off-label	386.4 (37.3)	111.6 (9.6)	151.2 (7.6)	321.6 (13.7)	441.6 (25.9)	1412.4 (17.1)
Total	1036.8 (100)	1159.2 (100)	1995.6 (100)	2347.2 (100)	1707.6 (100)	8246.4 (100)
Number of patients [n (%)]						
On-label						
Haemophilia A or B with inhibitors	2 (33.3)	4 (33.3)	3 (20)	5 (17.2)	5 (13.2)	7 (8.2)
Off-label						
Factor VII deficiency	3 (50.0)	1 (8.3)	1 (6.7)	0 (0)	1 (2.6)	3 (3.5)
Acquired inhibitor	1 (16.7)	0 (0)	1 (6.7)	1 (3.4)	1 (2.6)	4 (4.7)
Other bleeding disorder	0 (0)	0 (0)	0 (0)	1 (3.4)	2 (5.3)	3 (3.5)
Other diagnosis/indication	0 (0)	7 (58.3)	10 (66.7)	22 (75.9)	29 (76.3)	68 (80.0)
All off-label	4 (66.7)	8 (66.7)	12 (80)	24 (82.8)	33 (86.8)	78 (91.8)
Total	6 (100)	12 (100)	15 (100)	29 (100)	38 (100)	85 (100)*
Number of infusions [n (%)]						
On-label						
Haemophilia A or B with inhibitors	56 (56)	71 (81.6)	300 (92.0)	280 (84.3)	247 (77.4)	954 (82.0)
Off-label						
Factor VII deficiency	34 (34)	7 (8.0)	2 (0.6)	0 (0)	10 (3.1)	53 (4.6)
Acquired inhibitor	10 (10)	0 (0)	7 (2.1)	14 (4.2)	11 (3.4)	42 (3.6)
Other bleeding disorder	0 (0)	0 (0)	0 (0)	3 (0.9)	13 (4.1)	16 (1.4)
Other diagnosis/indication	0 (0)	9 (10.3)	17 (5.2)	35 (10.5)	38 (11.9)	99 (8.5)
All off-label	44 (44)	16 (18.4)	26 (8.0)	52 (15.7)	72 (22.6)	210 (18.0)
Total	100 (100)	87 (100)	326 (100)	332 (100)	319 (100)	1164

*Because some patients received recombinant activated factor VIIa (rFVIIa) in more than 1 year, the number of individual patients receiving rFVIIa over 5 years differs from the total of the numbers for each year.

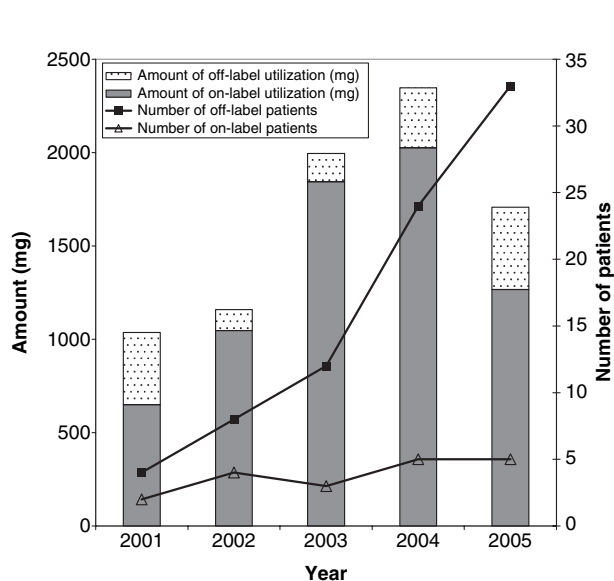


Fig. 3. Trends in recombinant activated factor VIIa utilization (amount and number of patients) by indication for the years 2001–05.

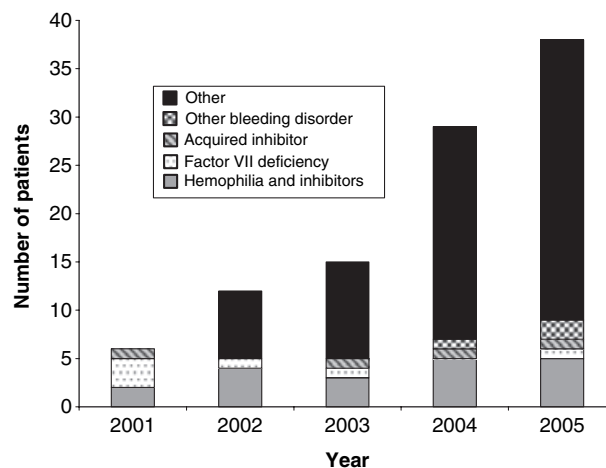


Fig. 4. Classification of patients receiving recombinant activated factor VIIa for the years 2001–05. Patients were classified as having: haemophilia and inhibitors to factor VIII; factor VII deficiency; an acquired inhibitor to factor VIII; other bleeding disorder (which included α_2 -antiplasmin deficiency, factor X deficiency and von Willebrand's disease) or other. The 'other' category includes patients with medical or surgical indications.

Table 3. Descriptions of infusions (number and dose) for on-label and off-label indications.

Infusion characteristic	Indication	Year					Overall (2001–05)
		2001	2001	2003	2004	2005	
Median amount infused per patient (mg) (IQR: Q1, Q3)	On-label	325.2 (178.2, 472.2)	124.8 (22.5, 364.2)	562.8 (343.8, 859.8)	142.8 (117.6, 420.0)	93.6 (26.4, 123.6)	562.8 (273, 1006.8)
	Off-label	80.4 (61.2, 115.8)	7.2 (4.8, 22.2)	9.6 (4.8, 16.2)	7.2 (4.8, 15.6)	7.2 (4.8, 14.4)	7.2 (4.8, 14.4)
Median number of infusions per patient (IQR: Q1, Q3)	On-label	28 (16, 41)	10 (4, 24)	84 (49, 144)	21 (9, 59)	19 (6, 20)	63 (33, 144)
	Off-label	11 (9, 14)	1 (1, 2)	2 (1, 2)	1 (1, 2)	1 (1, 2)	1 (1, 2)

IQR, interquartile range.

during the study period. The amount of rFVIIa used annually for on-label indications is subject to wide yearly fluctuations because of few patients using large amounts of factor. The amount of rFVIIa decreased in 2005 and, although the reasons for this are unclear, fewer surgeries or cases of trauma occurred in patients with haemophilia and acquired inhibitors during that year.

A small proportion of the rFVIIa infused was for 'off-label' indications. Off-label use was lower both in terms of number of infusions and total use per patient. The smaller amount used per patient was because of fewer infusions (usually only one or two per patient) rather than a difference in dose per infusion. Of concern, despite the relatively modest use for off-label indications, is the fact that the number of patients in this group far exceeds the number of patients with haemophilia and has increased steadily over the 5 years studied. Furthermore, the potential for growth in this group is also much greater. Given the high cost of rFVIIa, concern has been raised about the need to monitor its utilization, especially for off-label indications. Our study suggests that, currently, off-label use is not contributing greatly to the increased utilization of rFVIIa, but may in the future if the number of such patients continues to increase. While the number of patients in Canada with the potential for on-label use is small (i.e. there are <100 patients with haemophilia A or B and inhibitors currently in Canada and this number is relatively stable), the potential for increased off-label use of rFVIIa is great.

Most of the patients included in our study received additional haemostatic therapies. In fact, if one excludes patients with haemophilia, acquired haemophilia, FVII deficiency and other congenital bleeding disorders, 97% of patients received concomitant haemostatic therapy before or at the time of the rFVIIa infusion. This proportion may have been high because, in many cases, the rFVIIa was

prescribed by a haematologist. Others have suggested that the requirement of a haematology consult has possible benefits which include: the provision of assistance in managing appropriate supportive care and other haemostatic therapies; the evaluation of the appropriateness of dose and the evaluation of the effect of rFVIIa on clinical outcome [21].

An increasing amount of haemophilia care, particularly the infusion of coagulation FVIII and FIX, is now administered in the patients' home. However, the majority of the rFVIIa infusions were given in the clinic or hospital. This is likely a reflection of the increased use of rFVIIa in patients other than those patients with haemophilia and the increased use of rFVIIa for prevention and treatment of bleeding at the time of surgery or traumatic bleeding in patients with haemophilia.

The approved indications for rFVIIa (NovoSeven®) in Europe and in the USA also include the treatment and prevention of bleeding episodes in patients with congenital FVII deficiency, patients with acquired haemophilia and patients with Glanzmann's thrombasthenia refractory to platelet transfusions. Furthermore, several clinical trials exploring the use of rFVIIa in currently off-label indications have been performed or are in process which may result in expansion of approved indications [8,14,16,23,24]. Alternately, as many of the trials have failed to demonstrate a beneficial effect of rFVII administration, it is possible that the utilization of rFVIIa may decrease for some indications. For example, in patients with acute intracerebral haemorrhage, a phase 2 trial looking at treatment of rFVIIa within 4 h of the onset of the bleed was found to limit the growth of the haematoma, decrease mortality and improve functional outcomes at 90 days [16]. However, according to a preliminary report of a subsequent phase 3 trial the more important end points of mortality and severe disability at 90 days were not improved [25]. Furthermore, in a randomized-clinical

trial including severely injured trauma patients, rFVIIa administration was suggested to result in a significant reduction in RBC transfusion in blunt trauma but not in penetrating trauma [8]. However, there was no difference in the primary outcome of RBC transfusion when the entire trauma cohort was included [8,26]. In two randomized-controlled trials studying patients with cirrhosis undergoing partial hepatectomy and non-cirrhotic patients undergoing partial hepatectomy, the administration of rFVIIa did not change the requirement for RBC transfusion [23,24]. Finally, in a randomized-controlled trial studying the administration of rFVIIa to a small number of patients undergoing retroperitoneal prostatectomy, perioperative blood loss and need for RBC transfusion was significantly reduced [14]. However, the clinical utility of this intervention requires further investigation [27,28].

Therefore, one can expect the pattern of utilization of rFVIIa to evolve as further evidence accumulates, and the need to monitor the use of rFVIIa to become increasingly important. Effective utilization management and demand forecasting of blood products are dependent on the availability of accurate and timely data, both on trends in utilization and indications for use. In Canada, distribution data, describing issuing information from CBS to hospitals, is not accompanied by utilization data describing the actual use of the product. The tracking system used in this study, with CHARMS software and the haemophilia clinic as the coordinating data centre, allowed investigators to coordinate information gathering between CBS and hospitals and to provide utilization data within hospitals and homes.

Conclusions

The utilization of rFVIIa in southern Ontario is increasing. The majority of this increase is due to approved indications; however, the number of patients being prescribed rFVIIa for off-label indications is high. The tracking system used in this study could be a valuable tool to describe ongoing utilization patterns of rFVIIa.

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