OREGON HEALTH AND SCIENCES UNIVERSITY

Improved Utilization of rFVIIa with Usage Policy and Periodic Review

Dawn Nye DO*, Per Thorborg MD, PhD, FCCM*, Thomas DeLoughery MD, FACP**
Departments of Anesthesiology and Perioperative Medicine* and Hematology**, Oregon Health and Sciences University Portland, OR

INTRODUCTION

With the rise of off-label use of recombinant factor VIIa (rFVIIa), there is concern about the impact of over utilization of this drug on patient outcomes and hospital budgets. The best way to control use of this expensive drug is uncertain.

At OHSU, preauthorization by the Chief Medical Officer was initially used for approval of rFVIIa. In 2005, a new drug usage policy was instituted outlining approved indications based on current randomized controlled trials (RCTs).

POLICY
Statement:
Three indications for rVIIa do not require approval by Roy Magnusson, his designee, or the pharmacist carrying the non-formulary pager.
1.Use of rVIIa in bleeding hemophilia patients with inhibitors to factor VIII or IX (up to 3 doses).
2.Patients with known or suspected intracranial bleeding who are on warfarin therapy (40 mcg/kg x 1 dose).
3.Trauma patients not responding to the massive transfusion protocol (90 mcg/kg x 1 dose).

Any subsequent doses for the above indications, or indications other than those listed above, require approval from Roy Magnusson, Associate Hospital Director (pager 12282).

PROCEDURE
The Trauma service will screen patients against the following inclusion criteria before calling Pharmacy or writing an order for rVIIa.
1.Trauma patient (blunt or penetrating injury)
2.Minimum of 4 units of red cells transfused
3.Refractory coagulopathy with microvascular bleeding identified by trauma surgeon or transfusion/coagulation staff
4.Massive transfusion protocol initiated and patient not responding to initial therapy
5.Injuries thought to be survivable
6.pH > 7.1

Hypothesis: The combination of usage policy and review will have a positive impact on the off-label use of rVIIa.

METHODS

- Quarterly chart review using pharmacy generated lists of patients at OHSU who had rFVIIa ordered between 1/2002 and 6/2009
- Of the 413 patients who had physician orders for rFVIIa, 307 patients received this medication for off-label indications (74%)
- Data collected included: age, sex, date received, number and type of blood products received, dose (mcg/kg), indication, INR, outcome, date and cause of death (if applicable) and occurrence of thromboembolic events
- Uses were categorized into 5 major indications: perioperative bleed, body trauma, brain injury, end stage liver disease (ESLD) and last ditch
- Calculations to determine mean age, percent male, in-hospital mortality (%) and percentage of patients who had an improvement in their INR were performed

RESULTS

Figure 1: Annual Off-Label Use of rFVIIa at OHSU

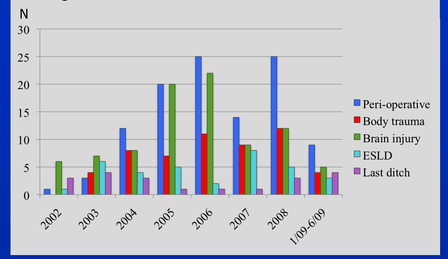


Figure 2: In-Hospital Survival Rates for Off-Label Indications of rFVIIa at OHSU

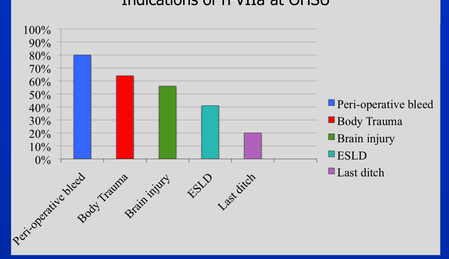
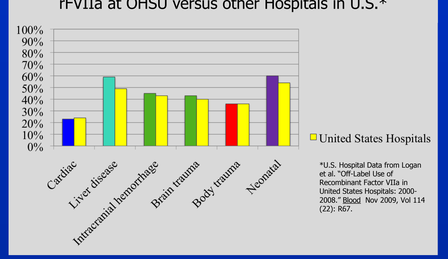


Figure 3: In-Hospital Mortality Rates for Off-Label Uses of rFVIIa at OHSU versus other Hospitals in U.S.*

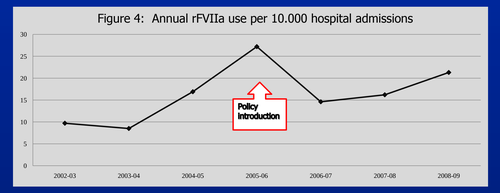


*U.S. Hospital Data from Logan et al. "Off-Label Use of Recombinant Factor VIIa in United States Hospitals: 2000-2008." Blood Nov 2009, Vol 114 (22): R67.

Table 1: Annual Use, Patient Characteristics, and Outcomes for Off-Label Use of rFVIIa at OHSU

Indication	2002	2003	2004	2005	2006	2007	2008	1/09 -6/09	Total	Age	Male %	Survival %	INR improved %
Periop	1	3	12	20	25	14	25	9	109	39	61.5	79.8	88.6
Body Trauma	0	4	8	7	11	9	12	4	55	41	76.4	63.6	88.9
Brain Injury	6	7	8	20	22	9	12	5	89	61	57.3	56.2	91.7
ESLD	1	6	4	5	2	8	5	3	34	43	58.8	41.2	83.9
Last Ditch	3	4	3	1	1	1	3	4	20	22	45	20	72.2

Figure 4: Annual rFVIIa use per 10.000 hospital admissions



- Since implementing the policy there has been no further escalation of total drug use (Fig 4)
- While perioperative use has increased, use in last ditch and ESLD categories have leveled off (Fig 1)
- Perioperative use (79.8%) and body trauma (63.6%) have the highest rates of in-hospital survival (Fig 2)
- ESLD (41.2%) and last ditch (20%) categories have the lowest rates of in-hospital survival (Fig 2)
- OHSU in-hospital mortality rates are comparable to other U.S. hospital rates using data reported by Logan et al "Off-Label use of Recombinant Factor VIIa in United States Hospitals: 2000-2008." Blood Nov 2009, Vol 114 (22): R67 (Fig 3)

CONCLUSION & DISCUSSION

rFVIIa is FDA approved for bleeding and surgery in patients with the following: hemophilia A, B with inhibitors, congenital FVII deficiency or acquired hemophilia. However, 74% of our use at OHSU from 1/02-6/09 was for off-label indications. For FDA indications, there is a large database showing good efficacy and extremely few thromboembolic events.

While there is no shortage of case reports; to date no RCTs have been performed or show benefit for use in our off-label indications. There is a potential for increased incidence of thromboembolic events, however, they have not materialized at our institution.

In addition, cost is a factor. At OHSU, the average dose is $5607. Yet, in situations where rFVIIa is used off-label, there are often few therapeutic alternatives.

An explicit usage policy with subsequent quarterly utilization review has been instrumental in controlling rFVIIa usage at OHSU to indications with higher likelihood of patient survival. Generally, physician compliance has been good

There appears to be a recent trend for increased utilization. Possible explanations include an increased percentage of surgical or trauma patients as the total number of hospital admissions. This is an area for review in the near future.