

The Perspective of Patients with Hemophilia with Inhibitors and Their Care Givers: Preferences for Treatment Characteristics

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Background

- Clotting replacement therapy is a commonly-used effective treatment for hemophilia, however it is less effective among hemophilia patients with inhibitors.
- Inhibitors occur in 20-30% of patients with hemophilia A, and 2-5% of patients with hemophilia B.¹
- Common treatments for hemophilia with inhibitors include: porcine FVIII, immune tolerance therapy, activated prothrombin complex concentrate, and recombinant activated factor VII.²
- Lee et al (2005) identified attributes of treatment important to hematologists in making their decisions regarding optimal care for inhibitor patients in the United States.³

Objective

As a follow up to the study conducted on physician treatment preferences, this study sought to identify treatment attributes that hemophilia patients with inhibitors, or their caregivers, consider important. These results will be compared to a previous study conducted on the treatment preferences of hematologists [3], and will therefore yield conclusions that will be meaningful to the patients, caregivers, and hematologists.

Methods: Data Source and Approaches

- Hemophilia patients with inhibitors and their caregivers were identified at a series of conferences in 2006; 90 consented to participate in further research.
- 90 patients and caregivers were sent a survey requesting demographic and clinical information, as well as a conjoint analysis treatment preferences questionnaire. The questionnaire sent to the patients was the same as that sent to physicians in Lee et al 2005,³ in order to obtain easily comparable data.
- There were 12 relevant treatment attributes included in the questionnaire: risk of viral infections, possibility that the titer of the inhibitor may rise, number of infusions required to stop hemorrhaging, time required to stop bleeding, time required to alleviate pain, prophylaxis use and ability to undergo major surgery, cost of medication, likelihood of dose related thromboembolic events, infusion prep time, infusion time, and infusion volume.
- For each question there were two to four mutually exclusive levels, patients or their caregivers were asked to identify only the most appropriate level for each question. (Table 1 lists the twelve attributes and the applicable levels included in the questionnaire).

Statistical Analysis

- Data were analyzed using a discrete choice model with best worst scaling. Best worst scaling asks patients to identify the treatment scenario they are most and least likely to use, thereby increasing the amount of preference information collected.
- Treatment preferences were modeled using a standard utility function, and relative importance of preferences was obtained using a multinomial logit function.

Table 1. Questionnaire Attributes and Levels

Attributes	Levels
Risk of contracting a virus from the product	<input type="checkbox"/> A product derived from components of human blood <input type="checkbox"/> A product produced without blood-derived contents, using recombinant DNA technology
Possibility that the level of inhibitor may rise	<input type="checkbox"/> Yes <input type="checkbox"/> No
Reduces the likelihood that dangerous blood clots will occur with higher doses of the product	<input type="checkbox"/> Yes <input type="checkbox"/> No
Number of infusions required to stop a hemorrhage	<input type="checkbox"/> 1 infusion <input type="checkbox"/> 2 infusions <input type="checkbox"/> 3 infusions
Time required to prepare the infusion	<input type="checkbox"/> ≤ 5 minutes <input type="checkbox"/> > 10 to ≤ 30 minutes <input type="checkbox"/> > 5 to ≤ 10 minutes <input type="checkbox"/> > 30 minutes
The time required to inject the infusion (infusion time)	<input type="checkbox"/> ≤ 5 minutes <input type="checkbox"/> > 10 to ≤ 30 minutes <input type="checkbox"/> > 5 to ≤ 10 minutes <input type="checkbox"/> > 30 minutes
Infusion volume	<input type="checkbox"/> ≤ 15 mL <input type="checkbox"/> > 40 to ≤ 80 mL <input type="checkbox"/> > 15 to ≤ 40 mL <input type="checkbox"/> > 80 to 120 mL
Time required to stop bleeding	<input type="checkbox"/> ≤ 6 hours <input type="checkbox"/> > 12 to ≤ 24 hours <input type="checkbox"/> > 6 to ≤ 12 hours <input type="checkbox"/> > 24 hours
Time required to alleviate pain	<input type="checkbox"/> ≤ 2 hours <input type="checkbox"/> > 6 to ≤ 9 hours <input type="checkbox"/> > 2 to ≤ 6 hours <input type="checkbox"/> > 9 to 12 hours
Frequency of infusion needed on a regular basis for prevention of abnormal bleeding	<input type="checkbox"/> 1 infusion every 2 days <input type="checkbox"/> 1 infusion every day
Ability to undergo major surgery	<input type="checkbox"/> Yes <input type="checkbox"/> No
Out-of-pocket cost of medications	<input type="checkbox"/> Not really a consideration <input type="checkbox"/> Somewhat of a consideration <input type="checkbox"/> Very much a consideration

Table 2. Demographics and Clinical Characteristics of Hemophilia Patients with Inhibitors

Demographics			Clinical Characteristics		
Variable	Value	n	Variable	Value	n
Age (years)		51	Type of Hemophilia		52
Mean (SD)	20.7 (18.8)		A	88.5%	
Median (min-max)	15.0 (2-84)		B	11.5%	
Current Student and Employment Status		53	Seriousness of Hemophilia		52
No work, school, or daycare	32.1%		Serious	88.5%	
Work	5.7%		Moderate	11.5%	
School or daycare	49.1%		Current Level of Factor		37
Both work and school	13.2%		Mean (SD)	3.3 (8.6)	
Gender		51	Median (min-max)	1.0 (0.0-40.0)	
Male	96.1%		Highest Titer		31
Female	3.9%		Mean (SD)	3230 (14,277)	
Family Annual Income (\$US)		53	Median (min-max)	192 (9.2-80,000)	
<\$20,000	19.0%		Hemorrhages (last 12 mo.)		50
\$20,000 - \$49,000	21.0%		Mean (SD)	11.6 (12.2)	
\$50,000 - \$74,000	28.0%		Median (min-max)	8.0 (0.0-50.0)	
\$75,000 - \$100,000	6.0%		Patient Surgery (last 12 mo.)		52
>\$100,000	17.0%		Yes	32.7%	
Would rather not respond	9.0%		No	67.3%	
Health Insurance Status		53			
Medicaid	37.7%				
Medicare	17.0%				
Through employer	58.5%				
Self-pay/private	5.7%				
None	3.8%				

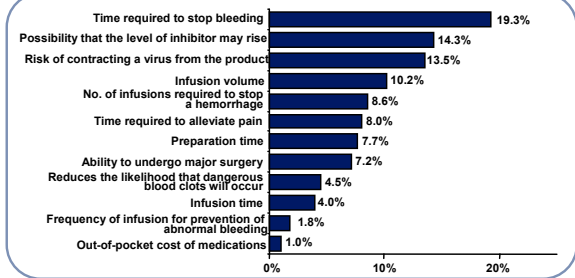
Results

- The sample of hemophilia patients with inhibitors (n=53) was predominantly male (96.1%) and mean age was 20.7 years (SD=18.8), with 58.8% of the sample representing children under the age of 18. (Further demographic and clinical characteristics and results are included in Table 2).
- Caregivers (70% mothers of patients, 16.7% fathers of patients, and 13.3% other) completed 64.7% of the survey packets on behalf of patients, including all children patients (100%) and three adult patients (14.3%).
- The majority of patients had hemophilia type A (88.5%), while the remaining had type B (11.5%).
- The data showed the three most important treatment attributes to be time required to stop bleeding (19.3% relative importance), possibility that the level of inhibitor may rise (14.3% relative importance), and risk of contracting a virus (13.5% relative importance). (Complete relative importance and part worth utilities results can be found in Table 3 and Figure 1).
- Preferences between different levels were pronounced in the three most important treatment attributes. The following levels were significantly preferred: time required to stop bleeding – ≤ 6 hours (p<.05), possibility that inhibitor level may rise – “no” (p<.01), and risk for contracting a virus – the lowest risk option, (product produced without blood-derived contents using recombinant DNA technology) (p<.01).

Table 3. Relative Importance and Part-worth Utility of Attributes

Attribute and Levels	Attribute Relative Importance	Levels		
		Part-Worth Utility	T-test	Sig. (p-value)
Time Required to Stop the Bleeding	19.33			
≤ 6 hours		0.28	2.38	0.02
> 6 to ≤ 12 hours		0.07	0.53	0.60
> 12 to ≤ 24 hours		-0.10	-0.83	0.41
> 24 hours		-0.25		
Possibility That The Titer Of The Inhibitor May Rise	14.25			
Yes		-0.20	-3.22	0.00
No		0.20		
Risk Of Human Viral Infections	13.48			
Very pure concentrate extracted from human blood		-0.19	-3.05	0.00
Recombinant concentrate		0.19		
Infusion Volume	10.17			
≤ 15 mL		0.18	1.41	0.16
> 15 to ≤ 40 mL		-0.05	-0.42	0.67
> 40 to ≤ 80 mL		-0.03	-0.23	0.82
> 80 to 120 mL		-0.10		
Number Of Infusions Required to Stop a Hemorrhage	8.62			
Only 1 infusion		0.07	0.75	0.45
2 infusions		0.08	0.91	0.37
3 infusions		-0.16		
Time Required to Alleviate Pain	8.03			
≤ 2 hours		0.12	1.05	0.29
> 2 to ≤ 6 hours		-0.03	-0.28	0.78
> 6 to ≤ 9 hours		0.01	0.1	0.92
> 9 to 12 hours		-0.10		
Time Required to Prepare the Infusion	7.69			
≤ 5 minutes		-0.03	-0.3	0.77
> 5 to ≤ 10 minutes		0.13	1.26	0.21
> 10 to ≤ 30 minutes		-0.01	-0.13	0.89
> 30 minutes		-0.08		
Ability to Undergo Major Surgery	7.18			
Yes		0.10	1.59	0.11
No		-0.10		
Reduces The Likelihood Of Dose-Related Thromboembolic Events	4.48			
Yes		0.06	0.85	0.40
No		-0.06		
Time Required to Inject the Infusion (Infusion Time)	3.95			
≤ 5 minutes		-0.05	-0.4	0.69
> 5 to ≤ 10 minutes		0.06	0.52	0.60
> 10 to ≤ 30 minutes		0.04	0.43	0.67
> 30 minutes		-0.05		
If it is Used in Prophylaxis	1.78			
1 infusion every 2 days		0.02	0.36	0.72
1 infusion every day		-0.02		
Cost of Medications	1.04			
Not really a consideration		0.01	0.11	0.92
Somewhat of a consideration		0.01	0.11	0.91
Very much a consideration		-0.02		

Figure 1. Relative Importance of Attributes



Discussion

- A treatment that is painful and time consuming is more acceptable than a treatment that risks extensive bleeding, infection, and increased levels of inhibitors, as evidenced by the finding that infusion volume, number of infusions needed, preparation time, and time required to alleviate the pain were ranked comparatively low.
- Cost of treatment had extremely low relative importance among patients and physicians.
- Although physicians placed more on the time to alleviate pain, patients placed more importance on the risk of viral transmission. In contrast, other research (Mantovani, et al., 2005) suggests greater importance of perceived viral safety among both physicians and pharmacists relative to patients.
- Perceptions of inflated risk of viral infection is perhaps expected among patients; however, consistent findings among physicians, placing more relative importance on this attribute above other treatment procedural and outcome attributes is noteworthy.
- Overall, patient preferences were similar to physicians (Lee, 2005).

References

- Aademak, J. Why do inhibitors develop? Principles of and factors influencing the risk for inhibitor development in haemophilia. Haemophilia 2005; 11:589-597.
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