Abstract

Objective: To check the occurrence of viral infections resulting from treatment with blood products and their impact on quality of life in the health of adult patients with hemophilia.

Method: This is a cross-sectional study with a convenience sample conducted with an association of patients. Data collection took place in November and December 2015. The evaluation protocol used the application of the SF-36 questionnaire and a form to collect demographic and clinical data.

Results: The participants were 49 adult patients with hemophilia, male, with an average age of 32±8.5 years old. They had a higher prevalence of hemophilia A in its severe form. Viral infections were more prevalent in those who had hemophilia when hepatitis C was the most frequent infection. Viral infections had a negative impact on quality of life in the “physical capacity,” “pain,” “general health” and “mental health.” The age of the participants who experienced viral infections resulting from treatment with blood transfusions were significantly higher than the uninfected participants.

Conclusion: Viral infections resulting from treatment with blood products in hemophiliac patients have repercussions in a lower quality of life of patients with hemophilia. The infections were more frequent with increasing age, suggesting special attention to older patients.

Introduction

Hemophilia A and B are hereditary hemorrhagic coagulopathies linked to the chromosome X, characterized by a quantitative deficiency of clotting factors VIII and IX. Data from the “Profile of inherited coagulopathies in Brazil: 2014” show that the country has 21,066 patients with inherited coagulopathies, and 9,616 (45.65%) of them

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Keywords

Hemophilia A; Hemophilia B; Adult; Comorbidity; Hepatitis; HIV infections.
are hemophilia A, 1,881 (8.93%) are hemophilia B and 9569 (45.42%) are other coagulopathies and bleeding disorders [1, 2].

Treatment for hemophilia until the 40s consisted of rest, use of compression bandages, immobilization, and ice as palliative care in the hemarthroses [3]. From the 50s, the use of fresh or frozen plasma infusion has started as a source of factor VIII, with difficulty to obtain adequate plasma levels without risk of circulatory overload in hospitals [4].

In 1964, Judith Pool created the cryoprecipitate from a fraction of the plasma removed containing large amounts of factor VIII. The product could be administered to the patient and reduce mortality rates as well as school and work absenteeism at the time [5].

The introduction to prophylactic treatment during the 70s proved its effectiveness as a treatment on demand. However, patients who were frequent using plasma transfusions or their derivatives were infected by viruses such as HIV and hepatitis C during the 80s and 90s [6, 7]. However, from 1993 the donor would undergo a screening when identifying items such as infectious diseases to be a donor [8].

In the early 90s, the scientific community started researching on DNA technologies to provide treatment with recombinant factor VIII and IX and the development of viral inactivation methods in blood products [6].

The replacement of factors VIII and IX of coagulation synthesized by recombinant technology do not give the risk of infection by the hepatitis B and C or HIV viruses [1]. With this technology, there was a safer therapy, and the possibilities for prevention and treatment of the consequences of hemophilia were increased.

Hemophilia can interfere with the individual’s life due to its complexity, effects and associated comorbidities. Due to the chronic nature of the disease, it can lead to physical and/or psychological changes of the patients. When considering the aspects mentioned, the investigation of the quality of life (QOL) in the perception of the individual with hemophilia is necessary. The quality of life is understood as the patients’ perception of their well-being in several areas, including the physical, emotional, mental, social and behavioral [10].

In this context, this study aimed to check the occurrence of viral infections resulting from treatment with blood products and their impact on quality of life related to the health of adult patients with hemophilia.

Method
This is a cross-sectional study with a quantitative approach, conducted with patients with a hemophilia diagnosis, linked to the Association of volunteers, researchers, and patients with coagulopathy (AJU-DE-C) located in Brasília/DF, the capital of Brazil.

The sampling was by convenience for the eligibility criteria and methods of selection of participants. The population consisted of all members of the studied patients association. The final sample included 49 hemophilia patients, male, 18 years old who agreed to participate voluntarily and signed the Informed Consent Form (TCLE). Those with cognitive impairment and those not present in the Association during data collection were not included.

Data collection took place between November and December 2015, with meetings and events on dates previously reported by the Association. An individual invitation was made to patients with the approach of the research objectives and after the volunteers accepted to participate the TCLE was presented for its consideration and signature. After including the subjects, the instruments adopted to collect data of the study were administered in an individual and reserved way.

This study had two instruments for data collection; the first instrument was the “Medical Outcomes Study 36 - Item Short-Form Health Survey” (SF - 36) and the second instrument was an Evaluation Form.
The instrument “Medical Outcomes Study 36-Item Short-Form Health Survey” (SF-36) is a generic questionnaire to assess the quality of life. It was translated into Portuguese (Brazilian version) and validated to use it in Brazilian Portuguese. [11]

The Evaluation Form was developed specifically for this study, and it has items to design the socio-demographic characteristics such as age, race/skin color, educational level and marital status, as well as items for the clinical characterization with topics on the type of hemophilia, its clinical severity and viral infections resulting from the treatment.

The descriptive results statistically analyzed were presented as average and standard deviations, categorical results for absolute frequency and/or relative measurements. The comparison between the types of hemophilia and the variables “clinical severity,” “viral infection by the use of blood products” and “type of viral infection” was performed by the chi-square test.

The comparison between hemophiliacs who had viral infections from treatment with blood products and those that did not about the scores in each domain of the SF-36 and relation to age of the patients was performed using the Mann-Whitney test. Statistical analysis was performed using SPSS, version 22.0. The study adopted 5% significance level.

The research study protocol was previously approved in its ethical, and methodological aspects by the Ethics Committee in Research with Human Beings of the Federal University of Mato Grosso do Sul (UFMS), in the opinion N° 1,300,316 and CAAE N° 46914215.6.0000.0021.

Table 1. Socio-demographic characteristics of the sample of patients with hemophilia. Brasília/DF, 2016 (n=49).

<table>
<thead>
<tr>
<th>Variable</th>
<th>n</th>
<th>%</th>
<th>Average±SD*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years old)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20-29</td>
<td>23</td>
<td>46.9</td>
<td></td>
</tr>
<tr>
<td>30-39</td>
<td>17</td>
<td>34.7</td>
<td>32.3±8.61</td>
</tr>
<tr>
<td>40-49</td>
<td>06</td>
<td>12.2</td>
<td></td>
</tr>
<tr>
<td>50-59</td>
<td>03</td>
<td>6.1</td>
<td></td>
</tr>
<tr>
<td>Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brown</td>
<td>24</td>
<td>49.0</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>19</td>
<td>38.8</td>
<td></td>
</tr>
<tr>
<td>Black</td>
<td>06</td>
<td>12.2</td>
<td></td>
</tr>
<tr>
<td>Marital Status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Single</td>
<td>30</td>
<td>61.2</td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>19</td>
<td>38.8</td>
<td></td>
</tr>
</tbody>
</table>

*: Standard deviation

Table 2 shows the results for the association between the type of hemophilia and the variables “clinical severity,” “presence of viral infections by blood transfusion” and “type of viral infection.” There was

Table 2. Clinical severity and viral infection by the use of blood products of hemophilia patients. Brasilia/DF, 2016 (n=49).

<table>
<thead>
<tr>
<th>Variable</th>
<th>Hemophilia A</th>
<th>Hemophilia B</th>
<th>p1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical severity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>01 (2.6)</td>
<td>01 (9.1)</td>
<td>0.286</td>
</tr>
<tr>
<td>Moderate</td>
<td>06 (15.4)</td>
<td>03 (36.4)</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>32 (82.1)</td>
<td>06 (54.5)</td>
<td></td>
</tr>
<tr>
<td>Viral infection by the use of blood products</td>
<td></td>
<td></td>
<td>0.282</td>
</tr>
<tr>
<td>Yes</td>
<td>23 (59.0)</td>
<td>04 (40.0)</td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>16 (41.0)</td>
<td>06 (60.0)</td>
<td></td>
</tr>
<tr>
<td>Type of viral infection</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV2</td>
<td>01 (4.3)</td>
<td>00 (0.0)</td>
<td>0.738</td>
</tr>
<tr>
<td>VHC3</td>
<td>18 (78.3)</td>
<td>04 (100.0)</td>
<td></td>
</tr>
<tr>
<td>VHC e HIV</td>
<td>02 (8.7)</td>
<td>00 (0.0)</td>
<td></td>
</tr>
<tr>
<td>VHC e VHB4</td>
<td>02 (8.7)</td>
<td>00 (0.0)</td>
<td></td>
</tr>
</tbody>
</table>

1: Chi-square test, 2: Human immunodeficiency virus, 3: Hepatitis C Virus, 4: Hepatitis B Virus.

Results

The study participants were 49 adult hemophilia patients and male. The average age and the standard deviation was 32±8.61 years old, respectively. The most prevalent age group was between 20 to 29 years old (46.9%). There was a higher prevalence of brown ethnicity hemophiliacs (49%) and single marital status (61.2%) (Table 1).
no statistically significant association between the type of hemophilia and other variables. Hemophilia A was classified as severe, and it was the most prevalent in this study (82.1%). Regarding the viral infections by blood transfusion, 23 cases (58.97%) occurred in patients with hemophilia A and four cases (40%) in patients with hemophilia B.

Table 3 shows the analysis of the variables related to the quality of life of affected patients with hemophilia by viral infections related to the use of blood products contaminated according to each SF-36 domain. There were statistically significant differences in the domains of “physical capacity,” “pain,” “general health” and “mental health,” since in these areas the scores in patients with viral infections by blood products was lower than in those without this type of infection.

A relevant fact was the age of the participants with viral infection by blood products (37.55±8.10 years old), significantly higher than the participants who did not have it (p <0.001), as shown in Figure 1.

Table 3. Analysis of the quality of life according to the scores of the SF-36 among patients with hemophilia who had viral infections by blood transfusion and those without infection Brasília/DF, 2016 (n=49).

<table>
<thead>
<tr>
<th>Domains of SF-36</th>
<th>Viral infection by the use of blood transfusion</th>
<th>p²</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Average±SD¹</td>
<td>Average±SD¹</td>
<td></td>
</tr>
<tr>
<td>Physical capacity</td>
<td>52.78±24.54</td>
<td>72.72±23.18</td>
</tr>
<tr>
<td>Physical aspects</td>
<td>57.40±44.29</td>
<td>75.00±37.79</td>
</tr>
<tr>
<td>Pain</td>
<td>52.93±21.20</td>
<td>67.50±19.77</td>
</tr>
<tr>
<td>General health</td>
<td>54.30±23.13</td>
<td>71.45±17.20</td>
</tr>
<tr>
<td>Vitality</td>
<td>60.74±26.15</td>
<td>72.72±13.42</td>
</tr>
<tr>
<td>Social aspects</td>
<td>73.61±29.28</td>
<td>87.50±14.94</td>
</tr>
<tr>
<td>Emotional aspects</td>
<td>60.48±44.37</td>
<td>83.33±35.26</td>
</tr>
<tr>
<td>Mental health</td>
<td>68.44±22.08</td>
<td>79.09±11.10</td>
</tr>
</tbody>
</table>

¹: Standard deviation, ²: Mann-Whitney test.

Discussion

The age of the participants in this study ranged from 21-54 years old, average of 32 years old, so there was no presence of elderly in the sample. Garbin and colleagues [12] conducted research with hemophilic adults and they found an average age of 34.36±11.9 years old (between 18 and 66 years old) and prevalence of individuals aged 21-29 years old. The lower portion of hemophilic elderly of that study was probably due to the high mortality, especially due to HIV infection when using contaminated blood transfusions occurred in the 80s.

In this work, most subjects were reported as brown (49%), followed by whites (38.8%) and blacks (12.2%). Zago, Hawk, and Pasquini reported that the prevalence of hemophilia A and B show no racial differences. However, rare cases are present in Chinese and African [13].

In the center-west region of Brazil, there is a predominance of brown subjects (50.6%) [14]. However, research conducted by Almeida and colleagues [15] with 34 hemophilic participants from a public
reference center of Brasília/DF found a predominance of Caucasians (63.7%), followed by brown (33.3%) and black (3%).

Regarding marital status, the research showed a predominance of hemophiliac singles (61%). These findings corroborate those found by Garbin et al. [12], where 60% of hemophiliac adults lived alone (single or divorced), as well as research of Nunes et al. [16] with 78.3% of the sample and of the study Almeida et al. [15], with 69.7% of participants.

These results can be explained by the difficulty of coping with the disease and its social repercussions, the presence of concomitant viral infections due to the use of contaminated blood products, physical limitations and therefore difficult to work [12]. Caio et al. [17] mentioned that the establishment of a family is an important point of support for hemophiliac adults. However, the lack of access to a satisfactory regular employment is a major factor of social inadequacy. Also, 65% of hemophiliacs prefer not to have children if the hypothetical risk of generating a hemophiliac child increases.

The results of this study demonstrate a higher prevalence of hemophilia in the participants (82.5%) compared with hemophilia B (17.5%). Thus, a Brazilian study by Ferreira et al. [18] included 39 hemophilia participants, of which 33 were hemophiliacs A (84.6%). Other research conducted by Adams and colleagues [15] found a prevalence of hemophilia A in 91% of the sample. Hemophilia A is considered to be more prevalent than B with a prevalence of 1/20,000 and 1/10,000 individuals, while for hemophilia B is 1/30,000 to 1/50,000 individuals [13].

The results of this study in the clinical severity of hemophilia classification pointed to the prevalence of a severe disease (77.6%), followed by moderate (18.4%) and light (4.1%). Almeida et al. (2011) corroborated these findings and reported that the clinical classification of the participants was severe in 60.6%, moderate in 33.4% and mild in 6%. Severe hemophilia is present in approximately 50% of patients, 10% are classified as moderate, and 40% with mild categorization [13].

There were 27 participants of the 49 subjects in this study having viral infections, when there was a predominance of Hepatitis C. Similar results were presented by Garbin et al. [12], where 20 (66.6%) participants reported infectious comorbidities, with a prevalence of hepatitis C infection (40%). Carmo et al. [19] reported that hemophiliacs were at high risk of hepatitis C infection before to the viral inactivation treatments. They showed that hepatitis C infection is a major problem in the Brazilian hemophiliacs, associated with age, co-infection with hepatitis B and inhibitor development of coagulation factor.

When comparing hemophiliacs who had a viral infection due to the use of blood products and those who showed no differences the quality of life (QOL) statistics in the domain scores “physical capacity”, “pain”, “general health” and “mental health”. Ferreira et al. [18] found statistically significant differences when comparing hemophiliacs with HCV infection (p=0.017) and HIV (p=0.025) compared to those not infected and reported that QOL in hemophiliac adult patients, measured by the use of HAEM-A-QoL instrument was diminished by the presence of hemophilic arthropathy and infectious diseases transmitted by blood products.

Mauser-Bunschoten, Fransen van de Putte and Schutgens [20] agree and indicate that the hemophiliac adults and the elderly have different problems compared to the new generation. They show premature hemophilic arthropathy due to lack of treatment as well as viral infections with HCV and/or HIV, which can lead to physical and psychological implications. The psychological aspects can be triggered mainly by job loss, early retirement, health decline and change in family dynamics, with decreasing autonomy.

Similar results of this study were presented by Posthouwer and colleagues [21], where hemophili-
acs infected with HCV had low QOL compared to uninfected hemophiliacs, with lower scores for “general health” and “vitality.”

HIV infection in hemophiliac adults has been shown to cause significant deterioration in QOL observed by the decrease in scores on “mental health” in the SF-36 [22] instrument. However, different results were found for Miners and colleagues [23] when there was no evidence that HIV infection has affected the QOL of the evaluated hemophiliacs.

A study [15] found decreased in all scores of the SF-36 questionnaire and HAEM-A-QOL compared hemophiliacs with infections with hepatitis B and C with those without infection. The largest differences were observed in the functional capacity, general health, vitality, functional capacity, bleeding and emotional impact (p <0.05). Barr et al. [24] reported that hepatitis and HIV confer additional morbidity, especially on items such as “mobility” and “pain,” generating statistical differences.

In this study, the age of the hemophiliac participants infected with virus resulting from blood transfusions treatment was significantly higher than those who did not show this type of infection, when all individuals born from 1994 were free of viral infection.

Only from November 1993 through the Decree 1376 of the Ministry of Health of Brazil criteria for selection and screening of blood donors were established, as well as laboratory and virus techniques in blood products [8]. Viral infections have declined due to the careful screening blood donors as well as individual testing for antiviral antibodies, antigens, and nucleic acids. These techniques were further supplemented by non-specific viral reduction by physical inactivation of pathogens (heat) and chemical inactivation (solvent-detergent) [25].

In the 70s and 80s, transfusions with plasma pool led to the contamination of many individuals with HIV and hepatitis C, triggering the development of free blood products for viral contamination, and they combined improvement in the screening and selection of blood donors with effective virus techniques and the use of recombinant technology for genetic engineering [26].

**Conclusion**

The age of the participants who experienced viral infections resulting from treatment with contaminated blood products is significantly higher than the uninfected participants. This may be associated with the chronological period without selection criteria for blood donors and viral inactivation techniques.

It was found that viral infections, particularly hepatitis C, are factors that diminish the quality of life of hemophiliac adults, especially in the items “physical capacity,” “pain,” “general health” and “mental health.”

Such infections arose from the treatment with blood products contaminated before the implementation of stringent selection criteria and screening for donors associated with the use of virus techniques. The use of recombinant technology, not derived from human or animal plasma, brought safely to patients in need of treatment for replacement of the deficient coagulation factor on a regular basis.

**References**


