The Influence of HIV, HCV and Inhibitors on the Quality of Life and Behavior of the Disease in Patients with Haemophilia: An Observational Study

Ana Torres-Ortuño, Rubén Cuesta-Barriuso* and Joaquin Nieto-Munuera

1Departamento de Fisioterapia, Facultad de Ciencias de la Salud, Universidad Europea de Madrid, Madrid, España
2Departamento de Psiquiatría y Psicología Social, Facultad de Medicina. Universidad de Murcia, Murcia, España

Abstract

Background: Inhibitors are the main complication in the treatment of haemophilia. A high percentage of adult patients were infected in past decades by HIV and HCV through factor concentrates. This study compared the quality of life of patients with hemophilia (QoL) and illness behavior in adult patients with haemophilia according to the development of inhibitors and HIV or HCV co-infection.

Method: This is an observational clinical study. 69 adult patients with haemophilia participated. We used A36 Hemophilia-QoL and IBQ questionnaires to measure the QoL and illness behavior, respectively. The dependent variables were type and severity of hemophilia, type of treatment, development of inhibitors, HIV and HCV infection, or both.

Results: We observed significant differences in the perception of QoL and illness behavior in patients according to the development of inhibitor and coinfection with HIV-HCV. We obtained four groups: the first and second group, which comprise 67% of the sample, exhibit behavior patterns indicating good adaptation to the disease and good QoL. The other two groups, which comprise 33% of the sample show behavior that is not well adapted to the disease, and poor quality of life.

Conclusion: The development of inhibitors itself does not influence the quality of life and illness behavior in patients with haemophilia. Patients infected with HIV or HCV do not have a worse illness behavior compared to those uninfected. The development of inhibitors and HIV-HCV co-infection has a negative impact on quality of life and illness behavior in patients with haemophilia.

Keywords: Haemophilia; HIV; HVC; Inhibitors; Quality of life; Illness behavior

Introduction

Hemophilia is a congenital coagulopathy that occurs with a deficiency of factor VIII (hemophilia A) or factor IX (hemophilia B). Depending on the percentage of blood factor, there are three degrees of severity: severe (<1%), moderate (1-5%) and mild (5-20%). This rare disease, according to the World Federation of Hemophilia affects around 400,000 people around the world. In Spain, this disease affects 2,900 people, according to data from Spanish Federation of Hemophilia.

Clinical manifestations of hemophilia are the hemorrhages, which cause disabling physical effects (hemophilic arthropathy) that limit the quality of life of patients with hemophilia. Improvements in the treatment of hemophilia have resulted in better control of the disease, and with this, improved life expectancy [1-3]. The medical treatment currently recommended to prevent haemorrhages in patients with haemophilia is to give regular F VIII or FIX concentrate treatments, even when there have been no haemorrhages (prophylactic treatment) [4].

Chronic diseases affect patients’ well-being. Some studies [5,6] have described how haemorrhages and the physical sequelae of haemophilia not only affect physical functions but are also a threat to patients' psychological and social well-being, and may affect their quality of life.

Talaulikar et al. [7] observed that, for patients with haemophilia (PWH), the perceived quality of life is lower than that for healthy people; other studies [8], however, did not find such differences, except in certain domains (functioning and physical role, especially) and depending on the patients’ age range. One aspect that makes this perception worse is the appearance of antibodies to the FVIII/ FIX concentrates (inhibitors); these are currently the most serious complication in the treatment of haemophilia. Almost a third of patients with serious haemophilia A and 5% with severe haemophilia B develop inhibitors [9]. The development of inhibitors increases the prevalence of haemorrhages, and with them, the appearance of sequelae in the joints, from the first decades of a patient’s life [10,11].

During the 1970's and 1980's, many patients with haemophilia caught the human immunodeficiency virus (HIV) and/or hepatitis C virus (HCV) from the F VIII and FIX concentrates used in pharmacological treatment [12]. As a result, many patients contracted one or both of these infectious diseases, raising the percentage of comorbidity and mortality in adult PWH [13].

The physical limitations suffered by patients with haemophilia and inhibitor have been extensively evaluated in the bibliography, as has their influence on the perceived quality of life of such patients [9,14-21].

*Corresponding author: Rubén Cuesta-Barriuso, PhD. Departamento de Fisioterapia, Facultad de Ciencias de la Salud, Universidad Europea de Madrid, Madrid, España, Tel: +34 91 211 53 69; E-mail: ruben.cuestab@gmail.com

Received November 17, 2015; Accepted January 05, 2016; Published January 12, 2016

Citation: Torres-Ortuño A, Cuesta-Barriuso R, Nieto-Munuera J (2016) The Influence of HIV, HCV and Inhibitors on the Quality of Life and Behavior of the Disease in Patients with Haemophilia: An Observational Study. J AIDS Clin Res 7: 534. doi:10.4172/2155-6113.1000534

Copyright: © 2016 Torres-Ortuño A, et al. This is an open-access article distributed under the terms of the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.
The results are, however, very heterogeneous, depending on the size of the sample, the age of patients, the measuring instruments used and the patients’ musculoskeletal disorders [17,18]. The comorbidities associated with haemophilia, such as HIV and HCV, should also be taken into account [8,19].

Patients who develop a chronic disease in adult life have been described as tending to identify this as a biographical interruption in their life story [20]. Patients with a congenital disease, however perceive it differently, and are less likely to experience changes or feelings of loss as a result of developing the disease [21,22]. As a result, we need to know and understand the psychosocial reality of the disease, and know how PWH respond. We therefore use the concept of illness behaviour, which is a person’s disposition to respond to the disease in a given way, taking into account the way they perceive, feel, and give importance to, or not, the symptoms of the disease and their consequences [23]. This variable has already been studied in patients with different diseases by using cluster statistical analysis [24]. This variable has not, however, been evaluated for haemophilia in any study to date.

The objective of this study is to evaluate the perceived quality of life and illness behaviour in patients with haemophilia, as a function of the development of inhibitors and the presence of HIV, HCV or both.

Materials and Method

Study design

Cross-sectional and multi-center study, with adult patients with haemophilia.

Study cohort

The criteria for including the participants in the study were: I) patients diagnosed with haemophilia A or B; II) older than 18 years old; III) without cognitive disorders; and IV) work activity at the present (employment or academic).

Before their participation in the study, all the patients signed an informed consent document according to Helsinki standards (1975). This study was approved by the Ethics Committee of the Faculty of Medicine, University of Murcia.

Data collection

The patients with haemophilia included in the study were recruited in the Region of Murcia (Spain) between the months of September and October 2014, after the authors of the study contacted them by phone. Additionally, patients with inhibitor were recruited at the VIII Albergue (10th "Shelter" Summer School) for patients with haemophilia and inhibitor and their families, which was held at the Ongoing Haemophilia Training Centre “The Charca” (Murcia, Spain) in July, 2014.

Clinical and sociodemographical data was obtained from all the patients, including the age, the type and severity of haemophilia, type of treatment received at that time, presence of inhibitors, and infections caused by HIV and HCV.

Perception of quality of life

To evaluate perceived quality of life, we used a specific questionnaire, the A36 Hemophilia-Qol [25]. This scale consists of 36 items grouped into 9 dimensions (physical health, everyday activities, joint, pain, satisfaction and treatment difficulties, emotional functioning, mental health, social relationships and activities, and overall perception of quality of life). This questionnaire show good values in terms of reliability (internal consistency and test-retest reliability) and validity. This has good concurrent validity with the SF-36 multi-purpose scale and is sensitive to changes in a patient’s state of health [26].

Illness behavior

Illness behavior was evaluated with the Spanish version [27] of the Illness Behavior Questionnaire (IBQ) [28]. This scale comprises 62 items, to evaluate several domains: hypochondria, disease conviction, psychological and somatic perception, emotional inhibition and affective disruption, denial, irritability, emotional and somatic scale, and rate of hypochondriasis.

Statistical analysis

Statistical analysis was performed using SPSS 19.0 for Windows (IBM Corporation, Somers, NY, EE.UU.). A descriptive analysis was made of the clinical variables for the patients recruited for the study and the dependent variables evaluated in it.

The t-test for independent samples was used to observe the differences between the dependent variables as a function of the type of haemophilia, the pharmacological treatment, co-infections and inhibitors development. A cluster analysis was run in order to empirically obtain patterns of patients’ responses to the questionnaires. The level determined for the confidence interval estimate was 95% (CI).

Results

Descriptive characteristics of all patients

69 patients with haemophilia took part. Their ages ranged between 19 and 61, with an average age of 38.17 (SD: 14.68). Most (88.4%) had haemophilia A, and a severe phenotype (68.1%). 18 of the patients had developed inhibitors. Of the patients in the study, 52.2% were receiving prophylactic treatment. In terms of co-infections, 38% had HIV, 68% had been infected with HCV and 32 of them had had both viral diseases. Only 4 patients with haemophilia had developed inhibitors and were also coinfected with both HIV and HCV. In Table 1 are shown descriptive characteristics of the studied sample.

| Variables                  | n   | %   |
|----------------------------|-----|-----|
| Type of hemophilia         |     |     |
| A                          | 61  | 88.4|
| B                          | 8   | 11.6|
| Severity of hemophilia     |     |     |
| Severe                     | 47  | 68.1|
| Moderate                   | 13  | 18.8|
| Mild                       | 9   | 13.0|
| Type of treatment          |     |     |
| Prophylactic               | 36  | 52.2|
| On demand                  | 33  | 47.8|
| Inhibitor                  |     |     |
| Yes                        | 18  | 26.1|
| No                         | 51  | 73.9|
| HIV                        |     |     |
| Yes                        | 26  | 37.7|
| No                         | 43  | 62.3|
| HCV                        |     |     |
| Yes                        | 47  | 68.1|
| No                         | 22  | 31.9|
| HIV and HCV                |     |     |
| Yes                        | 22  | 31.9|
| No                         | 47  | 68.1|
| Inhibitor, HIV and HCV     |     |     |
| Yes                        | 4   | 5.8 |
| No                         | 65  | 94.2|

HIV: Human Immunodeficiency Virus; HCV: Hepatitis C Virus; n: Number of Subjects; %: Percentage.

Table 1: Descriptive characteristic of the 69 patients with haemophilia who participated in this study.
The quality of life is worse for patients with inhibitor than for PWH without inhibitor, and this is especially significant in terms of social activities and relationships. Illness behaviour is also more affected in patients with inhibitor, but there are no significant differences in any dimension.

Taking into account the above-mentioned dependent variables, we can see that the type of haemophilia and the presence of HCV do not significantly affect quality of life or disease behaviour (Table 2). The type of treatment, and whether or not it is on demand, affects quality of life due to the difficulty of following the treatment. The presence of HIV affects disease behaviour, causing greater emotional disturbance. The presence of co-infection (HIV and HCV) does not, however, interfere with general quality of life, although it does affect illness behaviour (greater emotional disturbance and affective scale). Co-infection combined with inhibitor principally interferes with quality of life in general and, specifically, with everyday activities, pain, and relationships and social activities. The significant results of the statistical analysis using Student’s t-test are shown in the Table 3.

**Cluster analysis**

This type of analysis allows us to group the individuals in the sample on the basis of their degree of homogeneity and the variables used. In Table 4 are shown the results of this study based on the obtained groups.

On the basis of the questionnaires, we obtained four response patterns:

### Table 2: Descriptive analysis of the perception of quality of life and perception of illness (and their domains), measured in the study.

| Questionnaire | Variable | M     | SD    | Range |
|---------------|----------|-------|-------|-------|
| A36-Hemofilia QoL | Physical health | 23.17 | 6.11  | 7-32  |
|               | Everyday activities | 11.33 | 4.07  | 2-16  |
|               | Joints | 7.87  | 2.70  | 2-12  |
|               | Pain | 5.52  | 1.97  | 0-8   |
|               | Treatment satisfaction | 6.75  | 1.67  | 0-10  |
|               | Treatment difficulties | 12.03 | 3.04  | 1-16  |
|               | Emotional functioning | 15.41 | 3.33  | 5-20  |
|               | Mental health | 9.23  | 2.49  | 2-12  |
|               | Social relationships and activities | 16.71 | 3.78  | 6-20  |
|               | Overall perception of quality of life | 108.03 | 22.11 | 38-142 |
| Illness behaviour | Hypochondria | 1.94  | 2.12  | 0-8   |
|               | Disease conviction | 1.9   | 1.43  | 0-5   |
|               | Psychological and somatic perception | 2.48  | 1.25  | 0-5   |
|               | Emotional inhibition | 2.01  | 1.14  | 0-5   |
|               | Affective disruption | 1.61  | 1.46  | 0-5   |
|               | Denial | 3.25  | 1.02  | 1-5   |
|               | Irritability | 1.35  | 1.28  | 0-5   |
|               | Emotional scale | 4.88  | 4.08  | 0-17  |
|               | Somatic scale | 4.42  | 2.14  | 1-10  |
|               | Discriminant function | 45.94 | 17.31 | 15-84 |
|               | Rate of hypochondriasis | 4.75  | 2.75  | 1-12  |

M: Mean; SD: Standard Deviation

### Table 3: Results of t-test for independent samples to analyze the quality of life and perception of disease with clinical characteristics of patients.

| Independent variables | Dependent variables | Subtypes | Mean (SD) | Sig. |
|-----------------------|---------------------|----------|-----------|------|
| Inhibitor | Social relationships and activities | Patients who develop inhibitors | 14.67 (3.86) | 0.013 |
| | | Patients who do not develop inhibitors | 17.43 (3.51) |  |
| Treatment | Treatment difficulties | Patients in prophylaxis treatment | 12.75 (2.64) | 0.041 |
| | | Patients on demand treatment | 11.24 (3.27) |  |
| HIV-HCV | Affective disruption | Patients with HIV and HCV | 2.27 (1.66) | 0.021 |
| | | Patients without HIV and HCV | 1.30 (1.26) |  |
| | Emotional scale | Patients with HIV and HCV | 6.55 (4.62) | 0.036 |
| | | Patients without HIV and HCV | 4.11 (3.60) |  |
| HIV-HCV-Inhibitor | Everyday activities | Patients with HIV, HCV and inhibitors | 6.00 (2.70) | 0.019 |
| | | Patients without HIV, HCV and inhibitors | 11.66 (3.93) |  |
| | Pain | Patients with HIV, HCV and inhibitors | 4.50 (0.57) | 0.019 |
| | | Patients without HIV, HCV and inhibitors | 5.58 (2.01) |  |
| | Social relationships and activities | Patients with HIV, HCV and inhibitors | 10.75 (2.98) | 0.020 |
| | | Patients without HIV, HCV and inhibitors | 17.08 (3.52) |  |
| | Overall perception of quality of life | Patients with HIV, HCV and inhibitors | 80.25 (15.15) | 0.024 |
| | | Patients without HIV, HCV and inhibitors | 109.74 (21.39) |  |

HIV: Human Immunodeficiency Virus; HCV: Hepatitis C Virus; SD: Standard Deviation; Sig.: Signification
Table 4: Descriptive characteristics of the 4 groups of patients resulting from cluster analysis.

| Variables                        | Good adaptation group | Regular adaptation group | Poor adaptation group | Bad adaptation group | F     | Sig.  |
|----------------------------------|-----------------------|--------------------------|-----------------------|---------------------|-------|-------|
| Physical health                  | 28.03                 | 23.37                    | 13.14                 | 19.33               | 38.798| 0.000 |
| Everyday activities              | 14.03                 | 12.43                    | 4.14                  | 8.94                | 33.703| 0.000 |
| Joints                           | 9.32                  | 8.93                     | 4.14                  | 6.11                | 18.769| 0.000 |
| Pain                             | 6.67                  | 6.06                     | 3.42                  | 4.05                | 15.719| 0.000 |
| Treatment satisfaction           | 6.96                  | 6.43                     | 6.85                  | 6.66                | 0.352 | 0.780 |
| Treatment difficulties           | 13.32                 | 11.87                    | 9.57                  | 11.11               | 3.430 | 0.008 |
| Emotional functioning            | 17.57                 | 16.12                    | 9.42                  | 13.72               | 30.611| 0.000 |
| Mental health                    | 10.92                 | 9.25                     | 5.00                  | 8.22                | 24.305| 0.000 |
| Social relationships and activities| 19.03                | 18.57                    | 9.85                  | 14.27               | 40.073| 0.000 |
| Overall perception of quality of life | 125.89              | 112.87                   | 65.57                 | 92.44               | 82.035| 0.000 |
| Hypochondria                     | 1.00                  | 1.27                     | 3.00                  | 3.87                | 10.491| 0.000 |
| Disease conviction               | 0.60                  | 2.44                     | 3.42                  | 2.87                | 32.049| 0.000 |
| Psychological and somatic perception | 2.85              | 3.50                     | 0.85                  | 1.37                | 28.253| 0.000 |
| Emotional inhibition             | 1.92                  | 1.50                     | 2.71                  | 2.43                | 3.140 | 0.031 |
| Affective disruption             | 1.00                  | 1.27                     | 2.28                  | 2.75                | 7.186 | 0.000 |
| Denial                           | 3.14                  | 2.83                     | 3.71                  | 3.68                | 2.766 | 0.049 |
| Irritability                     | 0.92                  | 1.33                     | 2.00                  | 1.81                | 2.454 | 0.071 |
| Emotional scale                  | 2.92                  | 3.68                     | 7.28                  | 8.37                | 10.048| 0.000 |
| Somatic scale                    | 2.75                  | 3.94                     | 7.57                  | 6.50                | 52.076| 0.000 |
| Discriminant function            | 34.46                 | 38.11                    | 71.85                 | 63.50               | 52.536| 0.000 |
| Rate of hypochondriasis          | 2.89                  | 4.11                     | 8.57                  | 7.06                | 28.328| 0.000 |

F=Function; Sig.: Signification

- Good adaptation (group 1), comprising 41% of the total sample (28 cases). The average age of this group is 30, severe haemophilia A, 25% with inhibitor, 54% in prophylaxis, 43% with HCV, 22% HIV and 14% co-infected (HIV and HCV). Their quality of life rating is high, both in general and on all the sub-scales. They have low scores on all the sub-scales of disease behaviour. This is a behaviour pattern that is well adapted to the disease.

- Regular adaptation (group 2), comprising 26% of the total sample (18 cases). The average age of this group is 37, severe haemophilia A, 28% with inhibitor, 56% in prophylaxis, 61% with HCV, 39% HIV, 33% co-infected y 11 with inhibitor and co-infection (HCV-VIH). With respect to illness behaviour, they have high marks on the P/S sub-scale (Somatic Vs psychological perception) and low marks on the N sub-scale (Denial), as well as low marks for hypochondria (GH), Witteley index (WI), Somatic scale and Discriminant function (DF). This is a behaviour pattern of relatively good adaptation to the disease.

- Poor adaptation (group 3), comprising 10% of the total sample (7 cases). The average age of this group is 34, severe haemophilia A, 38% with inhibitor, 29% in prophylaxis, 61% with HCV, 39% HIV, 57% HCV, 43% co-infected and 29% with co-infection and inhibitor. They have low marks for quality of life and high marks on disease perception, high marks on the somatic scale, Discriminant function, Denial and Somatic Perception disease. These patients therefore have a pattern of “conversion” behaviour in the face of the disease.

- Bad adaptation (group 4), comprising 23% of the total sample (16 cases). The average age of this group is 51, severe haemophilia A, 13% with inhibitor, 50% in prophylaxis, 50% HIV, 81% HCV and 50% co-infected. They have low marks for quality of life and very high marks in Illness behaviour, especially for emotional disturbance, Affective Scale, Irritability and Hypochondria. Subjects in this group therefore show a pattern of “dysthymic” (depressed) behaviour in the face of the disease.

The first two groups, which comprise 67% of the sample, exhibit behaviour patterns indicating good adaptation to the disease and good quality of life. The other two groups, which comprise 33% of the sample show behaviour that is not well adapted to the disease, and poor quality of life.

Discussion

Psychosocial variables are clearly of great importance in chronic physical disease, and it is also evident that illness behaviour plays a decisive role in the patient’s progress.

Illness behaviour

Each patient’s illness behaviour contributes to his or her symptoms and the clinical course of this disease, and decisively conditions the way they relate to their doctor and social group of reference and how they respond to the prescribed treatment and therapeutic instructions [23]. Not all patients respond to their situation in the same way. In some cases, they follow the recommendations for treatment and have a good relationship with the doctors. Other patients, however, do not follow instructions and have difficult relationships with doctors.

The progress of the disease varies considerably, as does the number of hospital admissions and adverse events. Patients with haemophilia and inhibitor suffer more bleeds and greater degenerative arthropathy, and consequently more psychosocial difficulties.

We found no significant differences in disease behaviour related to the presence or absence of inhibitors. Patients suffering from HIV and HCV co-infections were affected differently in terms of emotional disturbance. That is to say, these patients have difficulty expressing their emotions, feel anxiety, and easily become sad.

Patients who had only been infected with either HIV or HCV did not show significant differences in illness behaviour.
In a longitudinal study of patients with haemophilia and HIV, Theorell et al. [29] found that limited emotional support has a negative effect on these patients' immune status. That is to say, patients' illness behaviour and emotional awareness may be of great use for developing programmes that increase their well-being and quality of life, and thus improve their strategies for facing up to, and adhering to, medical treatments.

Quality of life

During the course of the disease, the quality of life of PWH is compromised and worsens as a result of joint bleeds, chronic pain and other clinical complications. Despite recent progress in the treatment of haemophilia for patients with inhibitor, their QoL is worse than that for patients with haemophilia who have not developed an inhibitor [9,30]. Several studies have stated [9,11] that the QoL of patients with haemophilia and inhibitor is strongly determined by the state of their joints, which especially affects their physical functions and physical health. In our study, however, we observed that, for patients with inhibitor, it was their social activities and relationships that were most seriously impacted in perceived QoL. Similarly, in those patients who had treatment on demand, we observed differences in terms of difficulties with the treatment.

Progress in pharmacological treatments has improved life expectancy for patients with haemophilia and inhibitor. Although joint deterioration continues to exist, it is not such a clearly determining factor in their perceived quality of life as it is in other aspects [6,11,15]. In these patients, the development of inhibitors leads to greater difficulties in managing in their surroundings and integrating into society [31,32]. A factor to be taken into account is that, in patients with haemophilia, whether or not they have developed inhibitors, exercise not only protects their joints but also improves their physical, emotional and social [33].

In those patients in our study who had only been infected with either HIV or HCV this variable did not significantly influence their quality of life or illness behaviour.

Development of inhibitor antibodies continues to be the most serious complication in the treatment of patients with haemophilia [9,11,34]. It also has a major impact on their quality of life [16,18,35]. Morfini et al. [36] observed that patients with inhibitor reported more joint pain together with more restricted movement, and required technical aids. However, as in our study, they did not find significant differences between different age groups.

We also found that patients who had developed inhibitor and were suffering from a co-infection (HIV-HCV) had worse overall quality of life. Specifically, their everyday activities, perceived pain and relationships and social activities were affected. On the basis of these studies, the presence of inhibitor alone is not a factor that worsens the quality of life of patients with haemophilia. Although some studies [37,38] have highlighted the number of bleeds and consequent joint deterioration - which makes activities and social relationships difficult - as the most relevant factor in perceived quality of life, in our study the development of an inhibitor alone only has an influence in that it makes activities and social relationships difficult.

Cluster analysis

Of the subjects in the sample (46 cases), 67% were in groups 1 (28 cases), and 2 (18 cases). They display well-adapted behaviour patterns with respect to the disease and enjoy a good quality of life.

Good adaptation group is made up of younger subjects, of whom a lower proportion has been infected with HIV, HCV and co-infection (HIV-HCV). This group is the best adapted to their disease and enjoys the best quality of life.

Regular adaptation group has the highest proportion of patients infected with HCV. This group contains subjects who have a high awareness of disease, are aware of the stress resulting from the everyday problems of life and who realise that these problems can have psychological repercussions on the progress of their disease. The behaviour of patients in this group is also well adapted to their disease, and they enjoy an acceptable quality of life.

The remaining 33% (23 cases) fall into groups 3 (7 cases) and 4 (16 cases). These groups show behaviour that is not well adapted to the disease and poor quality of life.

Poor adaptation group has the highest number of patients with treatment on demand and inhibitor and co-infection (HIV-HCV) and inhibitor. This group is made up of patients who have a tendency to see the disease from a somatic point of view, denying the influence of everyday stress and attributing their problems to the direct effects of the disease. This translates into a high probability of expressing pain and symptoms, which can be considered to be "conversion disorder", i.e. showing psychological stress in physical ways and consequently adhering too closely to the role of a sick person. All this leads to considerable difficulty in expressing their feelings, especially negative ones.

Bad adaptation group includes the older patients and has the highest percentage of patients with HIV, HCV and co-infection (HIV-HCV). It also has the lowest percentage of patients with inhibitor. This response pattern corresponds to a profile of chronic patients predominantly with dysthymic disorder (depressive illness) and a process of secondary hypochondrias, with attitudes of being biographically "installed" in the disease situation.

On the basis of these results, we can state that adaptation to disease and quality of life are influenced more by the patient's personal and psychosocial characteristics than by HIV or HCV infection or the presence of inhibitors. However, in cases of comorbidity (the presence of inhibitor with HIV and/or HVC), those conditions do indeed have an influence and result in poorer adaptation to the disease and a poor quality of life.

Limits of the study

According to the Spanish Haemophilia Federation census, 33% (18/54) of patients with haemophilia have also developed inhibitor antibodies. Although our study does include representatives of this group, the small size of the sample is one of the principal limitations of this study.

This work has not taken into account the pharmacological treatment for HIV and HCV that the patients were receiving at the time of the evaluation. These treatments, which are very aggressive due to their secondary effects, can significantly influence disease behaviour and quality of life.

Future lines of research

Multi-centre studies, which recruit a larger sample of patients, are required to confirm the results of this study.

Other clinical variables that may also influence patients' perceptions should be taken into account. Examples are the pharmacological
treatment they are undergoing for co-infections and the severity of their haemophilic arthropathy.

**Conclusion**

The development of inhibitors does not, on its own, have a negative influence on the perceived quality of life or the disease behaviour of patients with haemophilia.

Patients who had only been infected with HIV or HCV did not exhibit behaviour that was poorly adapted to the disease.

The patients with haemophilia who were co-infected (HIV-HCV) and had inhibitors, did exhibit poorer adaptation to the disease and a poor quality of life.

A multidisciplinary approach to patients with haemophilia is required, which emphasizes their personal and psychosocial characteristics independently of the infectious diseases they may suffer from or whether they have developed inhibitors.

**References**

1. Franchini M, Tagliaferri A, Mannucci PM (2007) The management of haemophilia in elderly patients. Clin InterV Anging 2: 361-368.
2. Sournic JM, Nuss R, Eavatt B, Abdelhak A, Cowan L, et al. (2000) Mortality among males with haemophilia: relations with source of medical care. The Hemophilia Surveillance System Project Investigators. Blood 96: 437-442.
3. von Mackensen S, Gringeri A, Siboni SM, Mannucci PM; Italian Association Of Haemophilia Centres (AICE) (2012) Health-related quality of life and psychological well-being in elderly patients with haemophilia. Haemophilia 18: 345-352.
4. Nilsson IM, Berntorp E, Löfqvist T, Petersson H (1992) Twenty-five years' experience of prophylactic treatment in severe haemophila A and B. J Intern Med 232: 25-32.
5. Groves M, Muskin PR (2011) Psychological responses to illness. Textbook of Psychosomatic Medicine, Arlington (2nd edn), American Psychiatric Publishing.
6. Poon JL, Zhou ZY, Doctor NJ, Wu J, Ullman MM, et al. (2012) Quality of life in haemophilia A: Hemophilia Utilization Group Study Va (HUGS-Va). Haemophilia 18: 699-707.
7. Talaulikar D, Shadbolt B, McDonald A, Piccock M (2006) Health-related quality of life in chronic coagulation disorders. Haemophilia 12: 633-642.
8. Lindvall K, Von Mackensen S, Berntorp E (2012) Quality of life in adult patients with haemophilia--a single centre experience from Sweden. Haemophilia 18: 527-531.
9. Gringeri A, Mantovani LG, Scalone L, Mannucci PM; COCIS Study Group (2003) Cost of care and quality of life for patients with hemophilia complicated by inhibitors: the COCIS Study Group. Blood 102: 2358-2363.
10. Dimichele D (2002) Inhibitors: resolving diagnostic and therapeutic dilemmas. Haemophilia 8: 280-287.
11. Scalone L, Mantovani LG, Mannucci PM, Gringeri A, Investigators CS (2006) Quality of life is associated to the orthopaedic status in haemophilic patients with inhibitors. Haemophilia 12: 154-162.
12. Aznar JA1, Lucía F, Abad-Franch L, Jiménez-Yuste V, Pérez R, et al. (2009) Haemophilia in Spain. Haemophilia 15: 665-675.
13. Katsarou O, Touloumi G, Antoniou A, Kouramba A, Hatzakis A, et al. (2005) Progression of HIV infection in the post-HAART era among a cohort of HIV+ Greek haemophilia patients. Haemophilia 11: 360-365.
14. Gringeri A1, von Mackensen S, Auerwald G, Bullinger M, Perez Garrido R, et al. (2004) Health status and health-related quality of life of children with haemophilia from six West European countries. Haemophilia 10 Suppl 1: 26-33.
15. Remor E, Arranz P, Miller R (2002) Psychosocial impact of inhibitors on haemophilia patients' quality of life: Rodriguez-Merchan EC, Lee C eds., Blackwell Science, Inhibitors in Patients with Haemophilia, Oxford, UK.