THE STUDY ON THE MEDICAL ADHERENCE OF PATIENTS TO RHEUMATOID ARTHRITIS TREATMENT

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Abstract:
Patients adherence to treatment in rheumatoid arthritis case is less than optimal (patients do not take their medications half of the time) and the economic costs are emphasizing this problem. A non-adherent patient is costly and time-consuming. It was demonstrated that every dollar spent improving adherence saves seven dollars in total healthcare costs. The level of adherence can be improved if we can understand the correlation between patients behavior in taking their medication and the advices from doctors providing medical services. In order to assess the correct adherence, it is necessary to start using pharmacoeconomic instruments such as CQR-19, DAS, Morisky scale etc. These tools will guide the conversation and alert the physician or the pharmacist to discuss any potential issues during the patient's meeting. Patients who are involved in decisions about the medications they are prescribed are more likely to adhere their rheumatoid arthritis treatment plan. If medication costs are a barrier to adherence for the patients, they should use generic medicines. Other research wrote about the health impact of non-adherence and this analysis will emphasize the health-economics consequences of low adherence to medication-taking in rheumatoid arthritis.

Keywords: adherence, rheumatoid arthritis, cost-effectiveness, economics consequences

1. Introduction

Rheumatoid arthritis is a chronic autoimmune disease of the congenital tissue of unknown etiology, characterized by symmetric erosive synovitis (generating severe joint lesions). Most patients present a fluctuating course of the disease, leaved untreated lead to progressive joint destruction, permanent joint deformities, accompanied by motor deficiencies. The socio-economic costs that this disease generates are impressive, but economic studies have shown that the size of the

expenses generated by complications, hospitalization, surgical interventions exceeds the costs caused by medical consultations and intensive treatment of the more early cases; this underlines the importance of prophylaxis and early treatment. That is why we aim to look at this affection, from the pharmacoeconomic perspective, but also in terms of the patient's quality of life.

Even if no treatment for rheumatoid arthritis has been found, doctors change patients' administration methods at least once during their lifetime. The treatment begins with disease-modifying anti-rheumatic drugs – referred to as DMARDs (hydroxychloroquine, cyclophoshamide, gold injections, methotrexate, leflunomide, cyclosporine, mycophenolate, sulfasalazine), that relieve symptoms and slow progression of the disease. Along with DMARDs, doctors often prescribe drugs that are non-steroidal anti-inflammatory – NSAIDs and low-dose corticosteroids.

The pharmacoeconomic instruments (PRO's) are perceived as standardized measures, directly taken from patients. These characterize the subjective perception of patients on the disease, but also on prescribed treatment. Direct measurements, from the patients' perspective are increasingly used methods in clinical trials. Measuring patients' experiences, extrapolating how they can carry out their daily activities, demonstrates the patient's key role in the disease management. Experts in quality of life of patients have suggested that researchers should develop tools whose main characteristic is to identify the changes of the organism after the administration of various treatments. The pharmacoeconomic instruments are most useful when measuring concepts that are appropriate in patients' perspective. In terms of rheumatic affections, these questionnaires are important just because the socio-economic costs that they generate.

Improving treatment adherence is critical for better health outcomes and for decreasing healthcare costs. Many factors have been analyzed for predictability of medication non-adherence. In particular, we can say that inflammatory musculoskeletal; disease are complex and often have negative impact on the patient from a social, physical and physiological point of view. The patients' education with rheumatoid disease is regarded as an indispensable part of the general treatment (Ware et al., 1983).

The management and prognosis rely mostly on standardized physician and patient-reported outcomes measures (PROMS). With the recognition of patients' perspectives as key outcomes measure for improving the quality of care, the inclusion of PROMS in the process of healthcare was a good choice.

2. Research objectives

Our main objectives are to demonstrate the connection between correct adherence to treatment for rheumatoid arthritis and several socio-economic factors. This will be verified through pharmacoeconomic instruments used by specialists such as doctors or pharmacists. If a patient is adherent to the treatment the doctor prescribed him, the evolution of the disease will be favorable and the condition of the patient will improve. The final goal in treatment the rheumatoid arthritis is for the patient to adhere correctly to the medication and to relief the pain, swelling, also to prevent other bone erosions to happen.

2.1 Data collection

Data collection was carried out in Craiova, Romania, at a large public teaching hospital. The local institution approved the study. All the patients (n=75)) were

splintered into 2 groups: one with cheaper treatment (n=64) and one with more expensive one (n=11).

The criteria to include the study participants were: 1) age, 2) diagnosis of RA, 3) treatment by a rheumatologist in an ambulatory setting, 4) taking at least a disease-modifying anti-rheumatic drug or anti-inflammatory drug for RA.

Patients who met the inclusion criteria, gave their consent for using their medical record, and were interviewed by a rheumatologist to collect the data related to RA diagnosis and treatment. After completing the consent, patients answered the CQR -19 (compliance questionnaire for rheumatology) in Romanian, with help from a specialist in the field.

2.2 Survey instruments

We used the Compliance Questionnaire for rheumatology (CQR-19) translated in Romanian (Subtirelu et al., 2017) to assess the adherence of patients with rheumatoid arthritis. The list of RA treatment attributes was defined after reviewing published literature in Pub Med database by using as search terms: "adherence", "rheumatoid arthritis", "cost-effectiveness" and "economics consequences". However, as early arthritis and disease remission became the targets of management, the interest has shifted towards specific patient-reported symptoms such as pain, fatigue, duration of morning stiffness, quality of life as well as function ability. Patient reported tender joints were also introduced into standard clinical practice, and found comparable to the physician reported joint tenderness. Some other predictor factors could be introduced in the clinical practice (Firulescu et al., 2017). For validation of the questionnaire in Romanian, we used two native specialists in English and rheumatic disease to translate from English to Romanian, and backwards in English to verify if the patients will understand the correct meaning of the questions.

Table 1

Compliance Questionnaire for rheumatology (CQR-19) (translated from English to Romanian, and backwards in English)

Questions	1. Definitely do not agree	2. Do not agree	3. Agree	4. Definitely agree
1. If the doctor tells me to take my medicine, I do so.				
2. I surely take my anti-rheumatic medicines, because I have less pain this way.				
3. I surely do not forget to take my anti-rheumatic medication.				
4. If alternative medicine can help me, I prefer those in favor to what my doctor prescribes.				
5. My medicine is always in the same place, that's why I do not forget to take them.				

6. I take always my medicine, because I trust my rheumatologist.				
7. I always take my medicine, because this way I can still do what I like.				
8. I do not like to take my medication. If I can live without them, I surely will.				
9. When I go someplace in vacation, it happens to not take my medication.				
10. I definitely take my prescription, otherwise why I am consulting a rheumatologist?				
11. I do not expect something amazing after taking my anti-rheumatic medication.				
12. If you do not like the medicine, do not take them at all.				
13. If I do not take regularly my medication, the pain and inflammation returns.				
14. If I do not take my medication, my body feels the change.				
15. My personal health is the most important thing, and if I have to take my medication in order to feel well, I will.				
16. I use an organizer for my medication.				
17. I follow strictly what my doctor tells me.				
18. If I do not take regularly my medication, I have more pain.				
19. It is common that I forget to take my medication, when I go out for the weekend.				

Each question has 4 answers (four point Likert answering scale): "Definitely don't agree" (scored with 1), "Don't agree" (scored with 2), "Agree" (scored with 3) and "Definitely agree" (scored with 4) (Costa et al., 2017). Lower scores indicate lower levels of adherence. The Adherence score is calculated with the formula:

$$\textbf{Adherence score}=(\sum_{i=1}^{19} Qi\text{-}19)/0,57 \quad (1)$$

where Qi is the answer for the question Qi from the CQR19.

If the **Adherence score** is higher than 80, the patient is adherent to treatment.

2.3 Treatment (pharmacological strategies)

Rheumatoid arthritis has no cure, but specialists recommend using early treatments to decrease the severity of symptoms. The treatment of rheumatoid arthritis is composed of three classes of drugs. One of those is non-steroidal anti-inflammatory drugs, named as well NSAIDs, which are commonly used in relieving the pain from the patients. The last two are corticosteroids and also disease modifying anti-rheumatic drugs, known as DMARDs, the last one are very effective in the treatment of this affection but the clinical effect is seen only after weeks. The most frequent situation in the case of rheumatoid arthritis is when the cartilage starts to break and the bone fractures are common, that is the point when physicians move towards a more aggressive treatment (American College of Rheumatology Subcommittee, 2002).

Other drugs used in rheumatoid arthritis are anti-inflammatory drugs; they have moderate action on rheumatic pain, but also action on inflammation. Recently, anti-inflammatory drugs have been found to produce increases in blood pressure and blood flow effects. Lately, important findings have been made regarding the treatment of rheumatologic arthritis, especially for patients who are not responding to treatment with specific anti-rheumatic drugs. The problem of financial issues has started to be solved with the appearance of biosimilars that are reimbursed (Kawalec et al., 2017).

Monitoring the evolution of rheumatoid arthritis and the response to treatment depends on the severity of the disease and the therapeutic regimen used, all patients having to be followed virtually for an indefinite period of time. Those during the remission period will be examined every 6 months; patients in the initial period of the disease, or in persistent active forms, require more frequent controls (every 4-8 weeks) until the disease can be tempered. At every consultation, the essential question that must be answered is whether the disease is still active or not. The persistence of the signs of articular inflammation, active synovitis, prolonged morning pain, asthenia, all these signs indicating an active form of disease (American College of Rheumatology Subcommittee, 2002).

3. Results

3.1. Response rate

All of the patients were diagnosed with rheumatoid arthritis and are under treatment. Positive changes in patient activation were reported as able to lead to positive self-management behavior changes in patients with chronic conditions such as rheumatoid arthritis (Hibard et al., 2007).

3.2. Influence of demographic factors

Gender, living place and level of education did not influence the level of adherence.

3.3 Adherence factors

Factors influencing the adherence:

- Socioeconomic factors: income, education, employment, race/ethnicity, neighborhood conditions;
- Patient factors:
  - gender,
  - age,
  - race/ethnicity,

- co morbidities,
- coping mechanism/social support;

- Rheumatoid arthritis disease factors: inflammation, disease activity, pain, functional status/disability, clinical remission.

Table 2

Methods to evaluate the adherence

Method
Self-report from discussions
• Advantages: sensitive for non-adherence, cheap, noninvasive, easy to use; • Disadvantages: not accurate, no clear evidence;
Questionnaires
• Advantages: easy to use, noninvasive; • Disadvantages: no clear evidence, patients is aware of the adherence’s measurement;
Drug concentration/metabolites
• Advantages: accurate, clear evidence; • Disadvantages: invasive, expensive, unavaible non-adherence factors;
Prescription refill from pharmacies
• Advantages: easy to use, noninvasive, patient is aware of the adherence’s measurement; • Disadvantages: no clear evidence, difficulties in electronic monitoring, unavailable non-adherence factors;

The easiest way to find non-adherence factors is the direct contact with patients. They will immediately respond if they take their prescriptions as the specialist told them to. The difficult task for the doctors is to evaluate if the patient is adherent because he is afraid of the doctor disapproval, or he understands the responsibility that he has to be actively involved in the management of his/her disease.

The patient may fail to improve, worsen or (especially in long-term therapy) relapse, so the doctors need to make them understand the importance of the relationship between noncompliance with medications and relapse especially in patients with arthritis. The adherence in our group was middle to high (Fig.1), with no adherence patients. There was no statistical significant difference between the two financial groups ($p>0.05$).

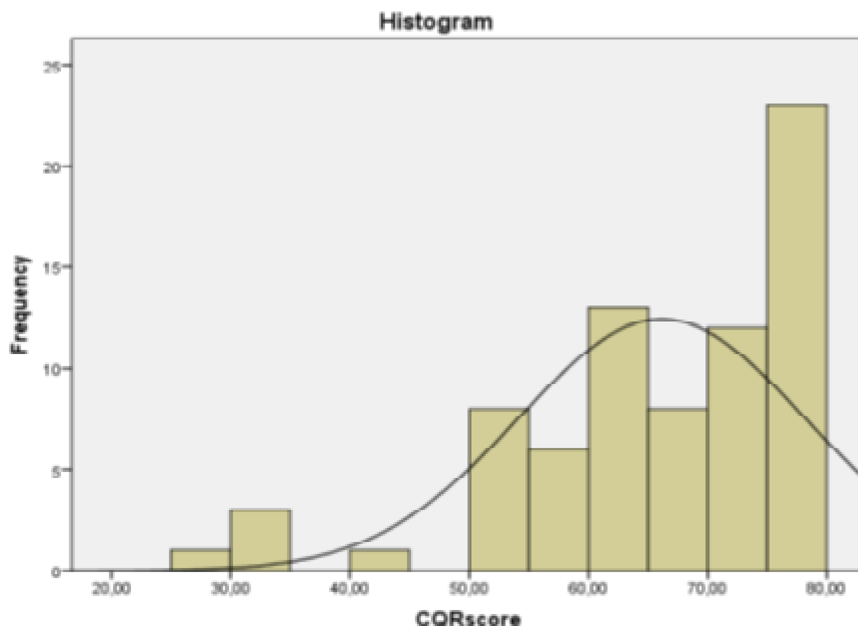

Fig. 1. The distribution of CQR-19

4. Discussion

From our study, we can say that inflammatory musculoskeletal diseases are particularly complex and often have a negative impact on the patient from a social, physical and physiological point of view. Even if in specialized clinics, patients with rheumatoid arthritis receive quality medical care, their daily life is hampered by the disabilities that the disease creates. While it is very important to minimize the negative musculoskeletal aspects of arthritis, attention has begun to move towards other complications of the disease. For each case of rheumatoid arthritis it is necessary to establish an individual treatment plan, which will be discussed in detail with the patient. It is necessary to specify the disease stage, in order to evaluate the therapeutic options: in the choice of background therapy, the time required to install the therapeutic effect, the cost of the therapy and the patients' preferences.

Moreover not taking the required medication prescribed can have both personal health impact and health economics consequences. Some studies found direct impact on patient health that could increase the overall costs of treatment, like, for example, the post-traumatic stress disorder. Recently patients have shown increased interest in their own health care possibilities, raising the overall rate of adherence to treatment. However, the cost-effectiveness is still a parameter that is often ignored when a medical expert chooses to treat different kinds of conditions. This study didn't prove that costs are a factor of low adherence because the expensive treatment is reimbursed almost 100% and the patients don't pay a very large amount of money.

5. Conclusions

The domains of PRO's in rheumatoid arthritis is clearly more relevant in these days, and have received recognition as being very important in both clinical and standard rheumatologic care. The economic perspective will always be a fundamental point of view; many patients will think about the necessity of their medication and also they concern about the potential adverse effects of taking it, all of these are related to the medication adherence.

The effectiveness and efficiency of treatments used in rheumatoid arthritis can improve patient's quality of life, but only when the therapy is continuous and correct. The rather slow reaction of the disease to treatment, along with new side effects, when patients decide to discontinue the treatment, leads to an erroneous approach to this disease.

When intentional non-adherence of a patient to treatment occurs after analyzing the cost vs. benefit ratio, it means that the patient has reached a significant degree of discomfort and the medication they take does not reach the expected benefits, so it does not justify the discomfort experienced. In this case, the best alternative is to use PRO's instruments in order to check on the patient's condition, but not only that, to ensure a high quality of life through the treatment. A good approach for any medical specialist is to check the quality of the treatment chosen in close connection with the patient's quality of life, even after the end of the medication period.

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