



## EDITORIAL

Bilingual edition English/Spanish

## Adherence to biologic treatments: a balance between need and concern

### Adherencia a los tratamientos biológicos: un equilibrio entre necesidad y preocupación

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Received 3 June 2019;  
Accepted 10 June 2019.

DOI: 10.7399/fh.11289

#### How to cite this paper

Vázquez-Díaz M, Bachiller-Corral J. Adherence to biologic treatments: a balance between need and concern. Farm Hosp. 2019;43(4):119-20

*"It is beneath human dignity to lose one's individuality and become a mere cog in the machine".  
Gandhi*

Adherence to treatment is a complex process involving more than 250 factors related to the patient, disease and health system. WHO considers that "multiple comorbidities and complex medical regimens further compromise adherence". According to a report by the same organization, it is estimated that, in developed countries, adherence among patients suffering chronic diseases averages only 50%, a percentage that has remained unchanged over the last 30 years<sup>1</sup>.

In a practical way, non-adherence is usually classified into two overlapping categories: unintentional (forgetting medication, not understanding the instructions, lack of financial resources, etc.) and intentional, which is what the patient decides based on the balance between beliefs in the medical necessity and concern for adverse effects (Horne and Weinman's necessity-concerns framework)<sup>2</sup>.

Numerous studies show that stronger beliefs of necessity measured with the Beliefs about Medicines Questionnaire (BMQ), are associated with better adherence, while the beliefs of concern relate to a reduction in adhesion. With every increase of one standard deviation in the beliefs of necessity, the chances of adherence are multiplied by 1.7, while the same increase in concerns multiplies by 2 the decreased likelihood of adherence<sup>3</sup>.

The National Institute for Health and Care Excellence developed in 2009 a clinical adherence to medicines guideline<sup>4</sup>, whose basic rule is a patient-centered health care. Based on this guideline, the medical consultation is adapted to the needs of patients with recommendations for individualized interventions, and periodic monitoring of medication concerns, as well as necessity perceptions are set in its fundamental principles.

Over the last 40 years, many effectiveness studies of different strategies aimed at increasing treatment adherence in several chronic diseases have been published with conflicting results. However, a recent 711 meta-analysis of these studies shows that only those approaches based on patient habit and behavior, the on-site dispensation by the pharmacist and the compliance with visits to the patient's doctor, were associated with better adherence<sup>5</sup>.

Biologic therapies have offered an effective therapeutic alternative for chronic inflammatory arthropathies (rheumatoid arthritis, psoriatic arthritis

and ankylosing spondylitis) for those patients whose remission has not been achieved through chemical disease modifying drugs. Those are hospital dispensing, either subcutaneous or intravenously administered and high cost drugs.

There is no consensus on the definition of adherence to specific biologic therapies in different chronic inflammatory arthropathies, nor a standard reference measurement. There are multiple measurement methods (self-referred questionnaires, dispensing records or electronic devices), but none has good sensitivity in isolation. Thus, a combination of several methods is recommended. In this regard, the most commonly used measurements are the average medication possession ratio with a greater than 80% or 90% adherence threshold, according to the authors, along with the Morisky-Green test, which is based on a questionnaire of four questions<sup>6</sup>. In rheumatoid arthritis, an adherence to these therapies ranging between 11% and 88% has been described, according to the studies and methods of measurement used<sup>7</sup>.

Additionally, a recent study in Canada<sup>8</sup> shows a 78% adherence for anti-tumor necrosis factor subcutaneous biological drugs in all chronic inflammatory arthritides. Out of these, golimumab (monthly administered) was the one who scored significantly higher rates of adherence. However, it should be noted that, although the highest rate of adherence loss takes place during the first six months of treatment, patients in this study had to take two years of therapy in order to be included.



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In the current issue of this journal, a retrospective observational study by N. Martínez *et al.* is published, where adherence to biologic therapies (intravenous and subcutaneous) in 362 patients with chronic inflammatory arthropathies is analyzed by evaluating medication possession ratio<sup>9</sup>. Results show an 89% overall adherence with no significant differences between the three diseases. In accordance with the conclusions of the aforementioned Conn VS' meta-analysis, adherence also appears to be significantly related to visits to the pharmacy service, and inversely related to absences in rheumatology consultations. In addition, it should also be noted that, with an 80% adherence threshold, a greater use of resources was not evidenced by the non-adherent (hospitalizations, emergency room visits and/or more consultations), although activity data in different diseases were not collected. Papers published in rheumatoid arthritis with non-biological disease modifying drugs show that patients in remission or with a reduced disease activity have weaker beliefs about the medical necessity, which is associated with a lower adherence<sup>10</sup>.

Generally, there are few published studies on the effectiveness of different interventions to improve adherence in rheumatoid diseases. Results show an inconsistent non-adherence effect on the outcome of the disease. Experience in other chronic diseases with the use of electronic devices (Apps, SMS reminders, etc.) to improve unintentional non-adherence, seems promising. However, avoiding unintentional adherence entails greater complexity, as it requires a deeper change in the doctor-patient relationship, in which patients educated and trained could work together with professionals in a less rigid health system.

Therefore, strategies to improve adherence in these diseases should probably be focused on education, shared decision-making and patients' self-management, along with a continued motivation by professionals based on the knowledge of the individual circumstances of each patient (their environment, their beliefs on the disease, their fears, their time availability, employment status, etc.).

Trends in health policy in recent years emphasize the need to empower the patient, which is associated with better health outcomes and better use of resources. However, this model requires a real change in health systems, as they remain focused on a biomedical care concept. Currently, an empowered patient who would consider to have their disease controlled based on their personal scheme and expectations (one who can do their personal, social and occupational activities normally) could try to reduce or suspend the biologic therapy for fear of side effects, as they are aware that rheumatologists use the strategy of spacing out doses in cases of low activity or remission. The doctor would assume this to be a case of non-adherence, but what if the doctor had explored all his patient's circumstances, had the time and willingness to be aware of them and therefore both had agreed a therapeutic change?

A recent study in psoriatic arthritis<sup>11</sup> shows a significant discrepancy on the rheumatologist's concept of remission, based on multidimensional levels of activity concerning the patient. It would be reasonable to assume that the medical necessity perception would have shown a disagreement as well if it had been analyzed in this study.

Better strategies have been introduced in hospitals to improve adherence to hospital-distributed, among others, biologic-therapies, both in Pharmacy Services by monographic dispensing consultations<sup>12</sup>, and in Rheumatology by introducing nursing consultations and monographic day hospitals. Even so, these initiatives tend to have a paternalistic approach, as it is aimed essentially at adapting patients to a rigid healthcare system.

Decision making in Medicine is based on probabilistic schemes through protocols and/or clinical guidelines that do not take into account the individuality<sup>13</sup>, or, as Ortega y Gasset said, the 'individual and their circumstances'. Consequently, effective models are being sought in target patient groups models to universally implement them, ignoring the fact that society is increasingly evolving towards increasingly taking individualism and freedom of decision into account.

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