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RESEARCH ARTICLE

Medicolegal Aspects of Disclosure of Side Effects of Biologic Drugs in Rheumatology: A Pilot Study

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Abstract:

Background:

Management of rheumatoid arthritis is complicated due to different disease presentations and the multiplicity of drugs. Although most patients are informed about the risks of treatment, there remain possible side-effects, which patients are not informed about to avoid the 'information dump.' Rheumatologists have to balance what they believe is essential to tell patients *versus* what reasonable patients believe they need to know to make an informed consent.

Objective:

To determine differences in information that the physicians give, regarding the possible side effects of treatment options for rheumatoid arthritis, and what the patients actually want to know.

Methods:

To conduct this pilot study, a questionnaire was devised to assess what patients and prescribing rheumatologists, from the Gulf Cooperative Council, consider important for being informed about, including the possible adverse events with biologic drugs in rheumatoid arthritis.

Results:

A total of 20 patients and 13 physicians completed the questionnaire. Physicians routinely discussed the increased risk of infections (100%), skin rashes at injection sites (92%),falling white blood cell counts, and alterations in liver enzymes (84%). Patients were less interested in learning about infections (72%) and more interested in learning about rare complications, such as an increased risk of heart failure and cancer (81%), which doctors were less likely to discuss.

Conclusion:

There is a discordance between what doctors inform patients about and what patients want to know regarding the risks of biologic therapy in rheumatoid arthritis. This information gap can have a significant legal implications in routine practice if a patient develops a rare side effect of which they have not been informed. We propose a solution of both verbal and signed informed consent to bridge the gap.

Keywords: Side effects, Biologics, Rheumatoid arthritis, Disclosure, Informed consent, Medicolegal.

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1. INTRODUCTION

Informing patients about possible risks associated with treatment options for rheumatological conditions is a complex process. Patient autonomy applies to treatment in rheumatology, where patients are an integral part of decision-making for choosing optimal therapy. Patients should have the right and timely information to enable them to make decisions for the best approach to the management of their condition [1, 2]. Physicians should make all efforts to educate patients about the disease, available treatment options, and support groups, and respect the patients' decisions for their health. These efforts may require repeated and elaborate discussions after patients have been allowed time to understand, explore, and make

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decisions regarding a particular therapy [1].

Informed consent is an integral part of patient engagement in rheumatology [3]. The patient should be provided with adequate and relevant information about any treatment and the possible associated risks. Patients should be able to make a voluntary and individual decision to consent for the treatment after understanding the benefits and risks of the same. The components of disclosure, understanding, voluntariness, and authorization in the informed consent process apply to the safety of all therapies, including biologics in rheumatology [4]. Also, patients should be aware of their rights to discontinue the therapy at any stage during treatment.

Rheumatologists are known to be at risk for litigation due to the complex, lengthy, and uncertain course of the disease, varying outcomes in patients with different therapies, and the possibilities of adverse events [5]. With increasingly available pharmacological therapies in rheumatology, both physicians and patients need to stay informed about the right and safe use of these agents. The initiation, continuation, and switch of therapy should involve active decision making with the patient and informed consent for the same. Any potential risks associated with therapy should be explained to patients, and they should be able to seek additional information and understand the nature and extent of risks before they can consent to adopt any therapy [6]. Efforts have been made to assess the understanding and desire of trial participants for various components of sought consent. The participants' understanding of side effects and risks of treatment is reported to be inadequate despite this being an essential element of informed consent [7].

The physician-patient relationship in rheumatology is asymmetric and disproportional, resulting in paternalism. When compared to what the patient knows, physicians have a stronger and more in-depth understanding of the disease and the available options for management. This higher level of technical knowledge may lead to physician decisions imposed on the patient [3]. Physicians should make sustained efforts to eliminate paternalism and allow patients to make self-decisions with integrity and individuality.

Patients should be encouraged to adopt any therapy with full willingness after all their concerns have been answered. Patients should not be victimized to any therapeutic misconceptions as newer therapeutic targets emerge in rheumatology [8, 9]. This approach not only requires the physicians to share information with the patients, but also allows them time and opportunity to fully understand the recommended therapy, more specifically, when there are newer and advanced therapeutic options. Physicians should adopt an ethical approach in routine clinical practice by offering the right therapeutic options to patients and disclosing any conflicts of interest [10]. Effective and timely communication of possible side effects of therapy can lead to a sustained professional relationship between the physician and the patient and build trust in the patient. Physicians should make every attempt to provide a complete and honest picture of the safety of any treatment [11].

Patients often express dissatisfaction regarding their communication with physicians. Patients and their families have often reported the inability or unwillingness of physicians to listen and warn them of the possible challenges with therapy [12]. In such situations, gaps in communication can result in litigation when adverse events occur. The objectives of our study are to determine differences in what physicians inform patients about and what patients want to know regarding the possible side effects of treatment options for Rheumatoid Arthritis (RA). The objective was to raise awareness about side effects, which occur due to the lack in communication between doctors and patients.

Based on the gained insights, we also describe an effective informed consent process that practicing rheumatologists can deploy for RA patients in the Middle East.

2. METHODOLOGY

For the purpose of this pilot study, practicing rheumatologists and patients from 3 health care centers in the gulf region were selected. All the participants were informed about the purpose of the study and those expressing interest in the study were chosen. The participation was based on the informed consent of both practitioners and patients, which comprised the inclusion criteria of the research. Following this, exclusion criteria were applied and those without a confirmed diagnosis of RA were excluded from the study. All selected patients had a confirmed diagnosis of RA, according to the ACR criteria [13].

A total of 20 patients with RA and 13 practicing rheumatologists from the Gulf Co-operative Council (GCC) were finally selected. These patients were receiving DMARDs for the management of RA and belonged to a multi-ethnic population. All the participants, including patients and practitioners, were provided with questionnaires that were intended to explore the gap in the process of disclosure provided to the patients. For this purpose, close-ended questions were devised to assess the understanding of patients and prescribing physicians about the possible adverse events associated with biologic disease-modifying antirheumatic drugs (bDMARDs) for the management of RA. Two different sets of questionnaires were designed for rheumatologists and patients. The questionnaires comprised common questions, which included the 12 possible side effects listed in the American College of Rheumatology (ACR) information leaflet on anti-TNF drugs, and other conventional biological DMARDs (Table **1**). Patients and physicians were asked to attempt the written format of the questionnaires.

Patients were asked to identify the side effects, which they would want to be informed about. Rheumatologists listed the possible side effects that they routinely listed for patients.

2.1. Practice Standards

The concepts of Medical Practice Standards (MPS) and Reasonable Person Standards (RPS) were applied to the responses gathered from the participants [14]. According to MPS, physicians can use their discretion to share information with the patients. On the other hand, RPS binds, upon the physicians, as a duty to give their patients all the information they might want. Those items that were selected by at least

50% of the doctors were classified as MPS, and those selected by at least 50% of the patients were classified as RPS.

Table 1. Possible side effects with biologic pharmacological options used in the management of rheumatoid arthritis.

Increased Risk of Infections	Can Worsen Heart Failure
Increased risk of tuberculosis	Neurological disease, such as MS, are very rare
Very slight increased risk of cancer	Raised cholesterol very slight risk
Very slight increased risk of skin cancer	Risk of intestinal perforation very slight risk
Very slight increased risk of lymphoma (blood cancer)	Reactions during intravenous infusions
Skin rashes at the area of injection	Low white cell count and increased liver function test (very slight risk)

The second step consisted of open-ended informal interviews of patients by the Patient Liaison Officer of the Middle East Arthritis Foundation. The interviews focused on asking patients how they would like to be informed of the drugs they were prescribed. There was no specific format to these interviews and patients responded to an open-ended question as to how they would prefer to be informed of the side effects of medications. All the feedback was compiled and analyzed.

The proportions of patients and physicians who responded to each of the component side effects in the questionnaires were determined. Each of the listed side effect was classified as MPS or RPS. Since the study population was very small, no statistical tests were applied.

An informed consent format was developed with information specific to the use of treatment options in RA.

3. RESULTS

All physicians routinely discussed the increased risk of infections, including tuberculosis, and the possibility of reactions during intravenous infusions with the patients. The following common possible side effects which most physicians discussed with patients included skin rashes at injection sites (92%), falling white blood cell counts and alterations in liver enzymes (84%). Less than half of the physicians were interested in discussing the possibilities of skin cancer, heart failure, and intestinal perforation (Fig. **1**).

Most patients (81%) expressed interest in being informed about the possible reactions during intravenous injections, rashes at injection sites, and the increased risk of blood cancer. The other common interests reported by 72% of the patients included the increased risk of infections, including tuberculosis, the possibility of worsening of heart failure, changes in blood cell counts, and alterations in liver function tests. Less than half of the patients were keen to know about the possibility of neurological diseases and an increase in cholesterol (Fig. **1**).

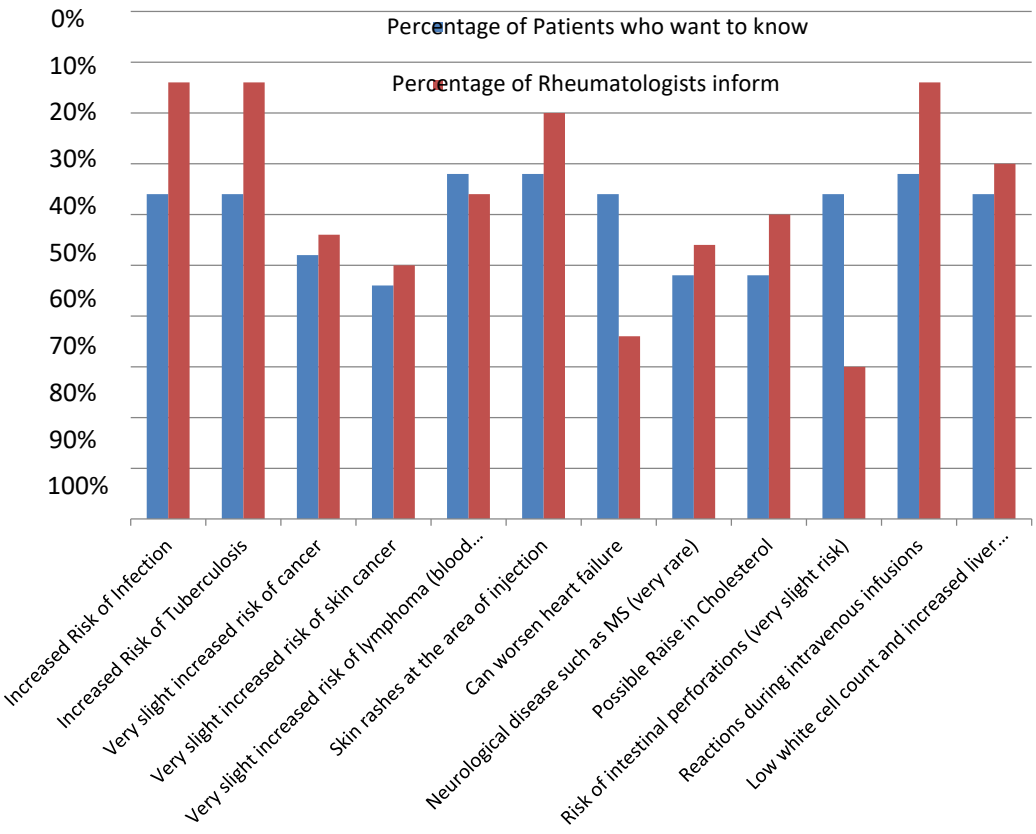

Fig. (1). Physician and patient willingness to share or know possible side effects with pharmacotherapy in rheumatoid arthritis.

All listed side effects qualified for MPS except the increased risk of cancer and intestinal perforation and the possibility of worsening heart failure. Most doctors were not informing patients about all possible adverse events, as these were considered to be rare. Patients wanted to know about most side effects except increased risk for high cholesterol and neurological diseases, and these did not meet the criteria for RPS.

Patients were given a copy of their medical report with the plan for their treatment. Below the plan was included that the patient was informed of the risks and benefits of the medication X and they were given a pamphlet on this from the American College of Rheumatology. By signing they acknowledge that they have received this information and they agree to come for blood tests and monitoring, as recommended.

4. DISCUSSION

Understanding of possible adverse events is equally important for physicians and patients. Patients need to understand the risks of treatment without being overburdened with information or fearing treatment to the point that they do not take the proposed medication course [11]. Patients often want to know information, which may pertain to rare but severe side effects, such as cancer and heart failure. Rheumatologists, however, do not inform patients about adverse effects that are considered to be rare as they do not want to alarm patients or lead to a nocebo effect [15]. However, if the majority of patients want to know of a particular side effect, it can be considered as RPS. If the RPS is not followed, there can be grounds for litigation against the rheumatologist [14].

Informed consent in rheumatology is an elaborate process that includes confirmation for the patients' understanding of the underlying condition and any risks associated with a chosen therapy. Based on insights from the conducted survey, we have devised a simple format for informed consent, which can be applied to rheumatology practices in the Middle East. We add an addendum to the medical report stating that the patient has been informed of the risks and benefits of the treatment proposed and that they have also been given a pamphlet on the medication from an official organization, such as the ACR. The addendum further goes on to state that the patient understands the information and agrees to come for follow up tests and visits as recommended. The patient signs this report, a copy of which is maintained in the file. A translation can further refine this addendum into the spoken language of the patient. Adoption of explicit informed consent in rheumatology can lead to enhanced patient satisfaction and reduced risks of litigation for the treating physicians.

4.1. Physician Perspective

Rheumatologists need to understand the importance of educating patients about risks associated with therapy and should make intensive efforts to enable them to make an informed choice. Increased communication is reported to reduce the risk of malpractice claims. Differences in physician-patient communications were compared for physicians with (≥2-lifetime claims) and without malpractice claims. In this study, the no-claims physicians were reported to spend more time educating patients when compared to physicians with claims. Additionally, the no-claims physicians spent a long time on routine visits, encouraged patients to talk and express opinions, and made attempts to check the understanding of the patients [16].

Irrespective of the frequency and significance of adverse effects, the failure on the part of the physicians to effectively communicate the possible risks associated with a medication, can account for medical negligence [17]. Though physicians seek professional satisfaction in sharing the required and relevant information with patients, they also report a professional dissatisfaction due to the constant threat of potential litigation [18].

It is prudent to determine the frequency and clinical presentations of various features that can occur during a disease [19]. This applies explicitly to rheumatological conditions that have a chronic and variable course and different clinical presentations. Some of these features may have an overlap with the possible side effects with a chosen therapy.

Treating physicians should be trained for patient experiences with therapy and how patients select one therapy over another [11]. Physicians need to consider patient preferences, affordability, and other factors that can influence the choice of therapy. Physicians should make all efforts to make the treatment safe, effective, and convenient for the patients.

4.2. Patient Perspective

Patients have opinions and perceptions about the timeliness and quality of information they receive from the treating physicians. When in collaboration, both physicians and patients meet more success in handling adverse events with therapy. The negative emotions of helplessness, anger, and frustrations are lesser when patients and physicians are better prepared to manage these events with therapies [11]. Patients need to understand the benefit-risk profiles of therapies and participate in decisions for selecting a treatment.

Patients should be made aware of their rights to know the available treatment options and how these can potentially impact their health. Legal reforms are needed to limit errors in medical care and also allow compensation to victims when errors occur [20]. Patients should be able to trust the physicians for safe and effective treatment. Patients often delegate the task of decision-making to the treating physicians for identifying the best treatment for their condition [21]. Physicians should further safeguard this trust by encouraging more active participation of patients in the management of their condition.

Fear of adverse effects is a conventional deterrent to adherence to therapy in patients with rheumatological conditions [22]. Informed patients are more likely to complete treatment and have better outcomes.

5. LIMITATIONS OF THE STUDY

Small samples of patients and physicians limit our study. Another limitation is that we did not evaluate what factors may influence the willingness of patients to know the side effects of

the therapy they were receiving. In an informed consent survey, factors like age and education influenced the willingness of trial participants to know about the possible risks associated with an intervention [7]. Studies with adequate samples may be conducted in the future to explore the knowledge and attitudes of patients and physicians for the disease and treatment options in rheumatology. Besides these, our study has the inherent limitations of the design and development of questionnaires, including interviewer bias, inaccurate respondent recall, and nonblinding [23].

CONCLUSION

There is a significant discordance between what patients with RA want to know and what their doctors inform them about regarding side effects of bDMARDs. The physician-patient discussions about treatment should include any possible associated risks. Effective and timely communication can help both physicians and patients to improve outcomes and enhance satisfaction with available treatment options. We suggest the adoption of the proposed format of informed consent in rheumatology practices. The impact of the use of this new format should be evaluated in future studies in more comprehensive patient and physician groups. However, a larger sample size study should be carried out to further understand the physician and patient relationship.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Ethical approval was waived off due to nature of the study.

HUMAN AND ANIMAL RIGHTS

Not applicable.

CONSENT FOR PUBLICATION

Written informed consent was obtained from all the participants.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

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None.

CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

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All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authorship for this manuscript, take responsibility for the integrity of the work, and have given final approval for the version to be published.

Key Messages:

1. Physicians should inform patients about possible side effects with therapy.

2. Patients should understand safety concerns before choosing a therapy.

3. Effective communication can mitigate the fear of side effects in patients.

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