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Experience with Intravenous Biological Therapies among Iraqi Patients with Rheumatological Diseases

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Abstract: ***Background: Subcutaneous and intravenous administration of biologic agents differ not only in routes of administration but also in dosing schedules, costs, onset of efficacy, and immunogenicity, which are associated with patients' preferences and corresponding persistence in treatment utilization. Additionally, injection issues (depending on the route of administration and agent type) have been shown to influence patients' utilization of biological therapies. Objective: The main objective of this study was to describe patients' experiences with intravenous (IV) biologics for specific rheumatologic conditions, including rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis. Patients and Methods: A cross - sectional study was conducted through interviews with 196 patients with the above - mentioned autoimmune rheumatic diseases who were currently receiving IV biologics at Baghdad Teaching Hospital. Patients were asked to describe the advantages and disadvantages associated with their experience of IV infusion with biologic drugs. Results: On a 7 - point Likert scale (1 = not at all satisfied; 7 = very satisfied), 90.3% of patients rated their satisfaction as 5, 6, or 7. The most frequently perceived benefit of IV therapy was related to infusion center visits, which act as an additional assessment opportunity alongside regular doctor visits; this benefit was reported by 88.8% of patients. Fifty - one percent of patients reported experiencing "No disadvantage" in receiving IV biologic therapy, and 25% noted that the duration of infusion was too long as a perceived disadvantage. The two most common reasons for preferring IV therapy were the less frequent dosing regimen, reported by 81.6% of patients, and the belief held by 54.1% of patients that intravenous infusion was always effective; these patients had no experience with subcutaneous therapy. Conclusions: Patients using IV biologics are highly satisfied with their medications, with preferences driven by less frequent dosing, the perceived effectiveness of IV injections, and the ease of remembering dosing when an appointment is scheduled for them.***

Keywords: Rheumatological patients experience, Biologics, intravenous, subcutaneous, Anti - TNF, Preferences

1. Introduction

Inflammatory arthritis (IA) - including rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) - is characterized by severe pain, inflammation, progressive joint damage, and decline of physical function over time. [1, 2]

These autoimmune diseases can be caused, signified, or accompanied by systemic disruption that may result in acute or chronic inflammatory injury, sometimes severe, in any organ system.

Overview of treatment of inflammatory arthritis

More aggressive treatment approaches in the last two decades have led to improved patient outcomes and prevention of disability. The breakthrough in the treatment of IA happened with the introduction of biologics, specifically tumor necrosis factor alpha inhibitors in the late 1990s and early 2000s. More recently, biologics with other mechanisms of action were introduced and became available to rheumatologists. [1, 2]

A 2017 update of European League Against Rheumatism (EULAR) recommendations for RA reported that treatment with bDMARD plus csDMARD achieved better efficacy than treatment with csDMARD alone. Starting csDMARD therapy, escalating the dose, and adding a bDMARD in cases of nonresponse to therapy was considered an effective treat - to - target strategy. When a bDMARD fails, the European League Against Rheumatism (EULAR) guidelines suggest that switching to another bDMARD could produce a better response, although choosing an agent with a different mechanism of action showed no greater benefit with a similar agent. They further recommended continuation of therapy to maintain low disease activity, although bDMARD dose reduction, or extending the spacing of doses, did not appear to alter remission status. [3]

The following represents some of the most common intravenous and subcutaneous biologic therapies used in rheumatologic diseases:

Etanercept, Adalimumab, Infliximab & Rituximab.

Subcutaneous versus intravenous dosing

Subcutaneous and intravenous administration of biologic agents differs not only in routes of administration but also in dosing schedules, costs, onset of efficacy, and immunogenicity which are associated with patients'

preferences and corresponding persistence in treatment utilization. Additionally, injection issues (depending on the route of administration and agent type) have been shown to influence patients' utilization of biologic therapies. [4 - 6]

Prior research suggests variations in dosing frequency, delivery type, pH levels, and needle size may all influence whether patients discontinue using a particular biologic agent. [6]

Subcutaneous dosing

Because many SC injections are self - administered, an advantage of SC dosing is patient control over when and where the patient will receive his or her medication, and a lack of associated (namely office - related) costs. Physicians may prefer SC dosing for patients who would otherwise have to travel a long distance to receive an IV infusion.

A disadvantage of SC dosing is limited flexibility; patients must adhere to specific incremental dosage increases. In addition, there can be functional limitations to SC dosing, because not all patients are physically able to inject themselves, possibly as a result of progressive disease.

Compared with IV infusions in hospital, patients tend to prefer, be more satisfied with, and report better health - related quality of life with SC administration of the same drug at home, primarily due to greater convenience Bril V et al 2024 [7]

The likelihood of an immune response to a biological agent is greater after SC administration than after an IV infusion. However, the rate of anti - product antibody formation, allergic reactions, efficacy, and the incidence of autoimmune syndromes (for example, systemic lupus erythematosus) after SC administration remains to be determined. [8]

Intravenous dosing

Intravenous dosing allows continuous dosage adjustments to be made, affording flexibility in matching patient needs at any given time during the infusion and helping to optimize overall treatment outcomes. Healthcare workers who administer IV medications should be familiar with the toxicities that can occur after infusing any IV agent and should be able to manage these reactions. Other methods of ensuring safety include the adherence to standardized protocols for the infusion procedure; patient assessments before, during, and after the procedure; and careful follow - up. Ancillary benefits of IV therapy include continuity of care, better patient education, peer support, and access to other medical specialists and support staff (such as social workers, nutritionists, and occupational/physical therapists). [8]

Patient adherence, satisfaction, and preference for biological therapies

Since it has been recognized that patient preferences play an important role in adherence to prescribed medication, the patient's perspective is increasingly important in assessing the therapy's value. Treatment regimens in line with patient preferences will be more likely associated with higher drug satisfaction and willingness to adhere to one's prescription, which will ultimately lead to higher real - life efficacy. [9, 10]

In line with this reasoning, EULAR and ACR recommendations suggest a process of shared decision - making between rheumatologists and patients, taking into account patient preferences when choosing a suitable medication. ([11.12])

Objectives

The main objective of this study was to describe patient experience with intravenous (IV) biologics for specific rheumatologic conditions including ankylosing spondylitis, psoriatic arthritis, and rheumatoid arthritis.

Specific objectives include the evaluation of perceived advantages and disadvantages of IV biologic therapy and the patient's experience at the site of care.

2. Patients and Methods

Study design

This was a cross - sectional study conducted through interviews performed with 196 patients from July 2017 to May 2018 at the Rheumatology Unit – Baghdad Teaching Hospital. The sample included patients with certain Rheumatic diseases who were currently being treated with IV biologic therapy. Patients were asked to describe the advantages and disadvantages associated with their IV infusion experience. Ethical approval was obtained from the Ethics Committee in the Medical Department - College of Medicine - University of Baghdad. All 196 patients from July 2017 to May 2018 were informed about the details of the study and verbal consent was obtained from each one of them according to the declaration of Helsinki for enrolment in the study.

Patient selection

Patients were selected from the Biologic Infusion Unit and Rheumatology unit. Structured brief individual interviews with the selected patients were conducted in the mentioned location and inquiry data were collected.

Inclusion criteria

1) The patient's age was 16 years or older.
2) Patients were already diagnosed with specific rheumatologic conditions including ankylosing spondylitis, psoriatic arthritis, and rheumatoid arthritis according to Modified New York classification criteria [13], CASPAR criteria [14], and the 2010 American College of Rheumatology/European League Against Rheumatism Classification Criteria for RA, ([15]) respectively.
3) Each patient was currently being treated with IV biologic therapy who received more than 3 doses.

Initial assessment

We applied demographical inquiries about patient age, sex, and current residency to our selected sample. The educational level of the patients was recorded and categorized into either educated (primary school, secondary school, college, and postgraduate) or illiterate. The inquiry also included information about the patients' diagnosed condition, duration, current disease activity (CDAI for RA [16], BASDAI for As [17], DAPSA for PsA [18]), smoking status reported, height in centimeters and weight in kilograms were

measured for all patients, body mass index (BMI) was calculated according to the equation BMI=weight (kg) /height (m^2). According to WHO classification, ([19]) BMI of adults >20 years old has been classified into the following categories:

<18.5 Underweight, 18.4 - 24.9 Normal weight, 25.0 - 29.9 Overweight, 30.0 - 34.9 Obese, and >35.0 Severe obesity. The patient's residency was reported. Other non - autoimmune comorbid conditions were also assessed if they existed including hypertension, gastrointestinal problems, fibromyalgia, osteoarthritis, and others. Uses and types of current IV biological agents were recorded for each patient in addition to the duration of IV biological treatment. The patients were divided into 4 groups for the duration of IV biologic treatment as follows: less than 1 year, 1 - 2 years, 3 - 5 years, and more than 5 years of treatment duration. The patient's prior experience with subcutaneous therapy was also recorded in addition to reasons why patients might receive their biological treatment as an IV infusion rather than as a subcutaneous injection; what patients might like/dislike about receiving their medication as an infusion and why patients might switch from a subcutaneous to an IV biologic therapy. Uses of methotrexate, prednisolone, or other synthetic DMARDs were reported.

The patients were asked to tell us their satisfaction with IV biologic therapy and this was measured by a 7 - point Likert scale (where 1 indicates that the patient is not satisfied at all and 7 indicates that the patient is fully satisfied). Likert scale explanation was conducted to the patients so that they could choose their satisfaction score by themselves.

We used an inquiry guide composed of 29 questions that focused on specific issues surrounding the IV therapy experience to demonstrate the perceived advantages and disadvantages of IV biologic therapy, and reasons for preferring IV biologics, Which were chosen from a topic guide comprised of 45 questions that focused on specific issues surrounding the IV therapy experience which was structured by Bolge SC et al 2017. ([20])

Statistical analysis

In this study, Descriptive statistics for means and standard deviation of age, height, weight, and BMI of the studied patients were included. Frequency tables show age, sex, educational level, residency, smoking, BMI, diagnosed conditions, disease activity, DMARDS, prednisolone intake, non - autoimmune comorbid conditions, type of biologic therapy, duration of IV biologic treatment, prior experience with a subcutaneous therapy (etanercept/ adalimumab), satisfaction with IV biologic, perceived advantage, perceived disadvantages and the reasons for preferring IV biologic treatment.

In logistic regression model analysis was made to determine which of the independent variables had a statistically significant effect on the satisfaction of the patients who used IV biological treatment. The independent t - test and Kruskal - Wallis H test show if there are statistically significant differences between the categories of patients' characteristics on satisfaction with IV biologic treatment.

All the data collected was analyzed by using Microsoft Excel 2013 for Windows, and statistical package for the social sciences (SPSS version 24) Program. P value < 0.05 was considered to be statistically significant with a confidence interval of 95%.

3. Results

General descriptive statistics

This study included 196 patients distributed as 80 (40.8%) males and 116 (59.2%) females. The patients' age range was distributed between 16 and 70 years with a mean of 43.13 years and a standard deviation of ±11.178 years. The descriptive statistics also showed that patients' BMI was distributed between 16, and 48 kg /m2 with a mean equal to 28.81 kg /m2, and a standard deviation equal to ± 5.500 kg /m2. A new variable has been used to classify the BMI into five groups according to WHO classification. ([19]) Three patients were underweight, 32 were normal weight 82 were overweight, 76 were obese and none were of severe obesity. The educational level of patients was 45 graduates of primary school, 81 from secondary school, 60 from college, and 10 were illiterate. There were 37 smokers.

Descriptive statistics in relation to rheumatologic diseases

The patients that were included in this study were diagnosed as rheumatoid arthritis, ankylosing spondylitis, or psoriatic arthritis with a percentage equal to 55.6%, 35.2%, and 9.2% respectively with disease duration of 1 to 27 years (their mean was 7.62 years and standard deviation _+ 5.871 years). Each diagnosed condition was classified according to disease activity.47.7% of patients were treated with methotrexate and 17.9% of patients were on prednisolone medication.

Patients in this study were either treated with infliximab (82.1%) or rituximab (17.9%) for durations that were subdivided into less than one year, 1 - 2 years, 3 - 5 years, and more than 5 years of treatment. Patients were also asked if they had prior experience with subcutaneous biologic treatment and the result showed that 36.2% were treated with Etanercept (Enbrel) and 8.2% were treated with adalimumab. Patients were shifted to biologic treatment because of either primary failure (14.8%), secondary failure (25%), or drug unavailability (2%). Further details are available in table (1).

Table 1: Descriptive statistics in relation to rheumatologic diseases

Patients' characteristic	Parameter	N	(%)
Diagnosed condition	RA	109	(55.6)
	AS	69	(35.2)
	PsA	18	(9.2)
Disease Activity of RA	Low	33	(16.8)
	Moderate	63	(32.1)
	High	18	(9.2)
Disease Activity of PsA	Mild	11	(5.6)
	Moderate	6	(3.1)
	High	1	(0.5)
Disease Activity of AS	Inactive	42	(21.4)
	Active	27	(13.8)
Methotrexate	No	103	(52.6)

	Yes	93	(47.4)
Prednisolone	No	159	(81.1)
	Yes	35	(17.9)
Type of biologic	Infliximab	161	(82.1)
	Rituximab	35	(17.9)
Duration of IV biologic treatment	<1 year	74	(37.9)
	1 - 2 years	76	(39.0)
	3 - 5 years	41	(21.0)
	>5 years	4	(2.1)
Prior experience with a SC therapy etanercept (Enbrel)	No	124	(63.3)
	Yes	71	(36.2)
Prior experience with a SC therapy adalimumab (Humera)	No	180	(91.8)
	Yes	16	(8.2)
Causes of shifting to IV treatment	Primary failure	29	(14.8)
	Secondary failure	49	(25.0)
	Unavailable	4	(2.0)
Non - autoimmune comorbid conditions	No	108	(55.1)
	Yes	88	(44.9)

N: number; (%): Percent

Descriptive statistics in relation to non - autoimmune comorbid conditions

The results showed the frequencies of non - autoimmune comorbid conditions (Hypertension was reported among 53, GI problems among 44, Fibromyalgia among 41, and Osteoarthritis among 21 patients). A total of 88 patients 45% of studied patients were presented with the above - mentioned comorbidities. The studied patients may have more than one non - autoimmune comorbid condition.

Descriptive statistics in relation to satisfaction with IV biologic based on the Likert scale.

In this study, our patients showed a high satisfaction score with IV biologic treatment based on the Likert scale. Nine point seven percent showed 7/7 satisfaction score, 42.3% showed 6/7 score, 38.3% showed 5/7 score, 8.7% showed 4/7 score and 1% showed 3/7 score

Intravenous biologic treatment perceived advantages and disadvantages

The results also showed the causes of the perceived advantages, the perceived disadvantages, and the reasons for preferring IV biologic treatment. There were 174 patients considered "Infusion center visits act as an additional assessment to a regular doctor visit" as perceived advantages which represents 88.8% while 100 patients (51%) expressed that there was "No disadvantage" in receiving IV biologic therapy and 49 patients (25%) considered that "The infusion takes too long" as perceived disadvantages. One hundred sixty patients (81.6%) considered "Less frequent dosing" as the reason for preferring IV biologic treatment, other frequencies and percentages are demonstrated in Tables (2 and 3)

Table 2: Perceived advantages and disadvantages of intravenous biological therapy

Perceived advantages	number	(%)
Staff at the infusion center can monitor for side effects	161	(82.1)
The medication is administered by a professional	152	(77.6)
Infusion center visits act as an additional assessment to a regular doctor visit	174	(88.8)
Infusion center staff keep track of the patient's dosing regimen	116	(59.2)
Emotional support is provided by infusion center staff	43	(21.9)
Center staff can check medical issues beyond the autoimmune disease for which the biologic is being received	57	(29.1)
Learning from the experiences of other patients attending the infusion center	15	(7.7)
Social interaction with other patients at the infusion center	46	(23.5)
Infusion center visits can complement activities such as shopping or dining out	1	(0.5)
Perceived of disadvantages		
The infusion takes too long	49	(25)
Scheduling appointments is inconvenient	4	(2)
Travel to the infusion center is inconvenient	31	(15.8)
Infusion side effects/reactions	35	(17.9)
Multiple attempts may be required to start infusion; veins may be difficult to find	16	(8.2)
Cost of infusion	1	(0.5)
No disadvantage	100	(51)

Table 3: Reasons for preferring IV biologic treatment

Reason	N	(%)
Dislike of self - injection/needles; lack of comfort with self - injection	22	(11.2)
Less frequent dosing	160	(81.6)
Administered by a professional; self - injection may not be carried out safely	11	(5.6)
Staff interaction at the infusion center	28	(14.2)
Easier to remember doses when an appointment is scheduled	71	(36.2)
IV infusion is perceived to be more effective than SC injection	83	(42.3)
IV has always been effective/no experience with SC administration	106	(54.1)
Infusion is easier/everything is taken care for you	57	(29.1)
IV infusion is less painful	1	(0.5)

Patients' characteristics affect satisfaction

A logistic regression model was used to determine which of the patients' characteristics have a statistically significant effect on the Satisfaction of the patients who used IV biologic treatment. The analysis in this model showed that gender, disease activity of rheumatoid arthritis, disease activity of psoriatic arthritis, comorbid diseases, hypertension, osteoarthritis, type of biologic treatment, and the duration of IV treatment have a significant predicted effect on patient's satisfaction with IV biologic treatment. The test values, p - values, and confidence intervals are demonstrated in Table (4).

Table 4: Logistic regression model for the predicted patients' characteristics in relation to the satisfaction with IV biologic treatment

Factors	Test value	P - value	Cl.
Age	0.003	0.813	- 0.023 - 0.030
Gender	0.847	0.040*	0.038 - 1.656
Educational level	0.158	0.668	- 0.564 - 0.880
Disease duration	0.034	0.177	- 0.015 - 0.083
Smoking	0.211	0.592	- 0.981 - 0.559
Weight	0.047	0.626	- 0.145 - 0.233
Height	0.018	0.851	- 0.205 - 0.170
BMI	0.106	0.689	- 0.613 - 0.419
Disease activity of RA	0.796	0.003*	- 1.344 - 0.847
Disease activity of AS	0.468	0.314	- 0.442 - 1.378
Disease activity of PsA	18.839	0.000*	16.960 - 20.719
Diagnosed condition	0.853	0.077	- 1.798 - 0.893
MTX	0.424	0.136	- 0.133 - 0.980
Prednisolone	0.367	0.292	- 0.315 - 1.049
Comorbid diseases	0.050	0.001*	- 0.574 - 0.474
Hypertension	0.059	0.039*	- 0.646 - 0.528
GI problems	0.229	0.058	- 0.967 - 0.310
Fibromyalgia	0.298	0.082	- 0.355 - 0.951
Osteoarthritis	5.818	0.001*	- 0.141 - 6.559
Type of IV biologics used	0.189	0.012*	- 1.074 - 0.296
Duration of IV treatment	0.788	0.000*	0.442 - 1.133
SC therapy etanercept	0.150	0.589	- 0.693 - 0.394
SC therapy adalimumab	0.243	0.740	- 1.226 - 0.740
"Satisfaction with IV biologic" as a dependent Variable *Statistically significant.			

Further analysis was carried out in this study to demonstrate which category within the patients' characteristics showed a significant effect on patient's satisfaction with IV biologic treatment are shown in Table (5).

Table 5: Detailed patients' characteristics in relation to satisfaction with IV biologic treatment

Factors	Test value	P - value
Sex	Male Female	0.026* NS
Disease activity of RA	Low Moderate High	0.002* 0.005* NS
Disease activity of PsA	Mild Moderate High	0.000* NS NS
Comorbid diseases	Yes No	0.001* NS
Hypertension	Yes No	0.039* NS
Osteoarthritis	Yes No	0.001* NS
Type of IV biologics used	infliximab Rituximab	0.005* NS
Duration of IV	<1 year 1 - 2 Years 3 - 5 Years >5 Years	0.014* 0.012* NS NS
"Satisfaction with IV biologic" as a dependent Variable *Statistically significant. NS: not significant.		

Patients' characteristics categories affect satisfaction

The results showed that there were statistically significant differences between the categories of patients' characteristics on the satisfaction with IV biologic treatment of the patients. Within the parametric tests, gender, hypertension, and osteoarthritis categories' differences showed a significant effect on patient satisfaction with IV biologic treatment. Within the non - parametric tests, the disease activity of rheumatoid arthritis, disease activity of psoriatic arthritis, and duration of IV biologic categories' differences showed a significant effect on patients' satisfaction with IV biologic treatment. More details and p - values are demonstrated in Table (6).

Table 6: P - values of significant differences between the categories of patients' characteristics in relation to Satisfaction with IV biologic treatment

Parametric tests		Non - Parametric tests	
Factors	p - value	Factors	p - value
Sex	0.049*	Age	0.401
Smoking	0.659	Disease Duration	0.244
Prednisolone	0.386	Weight	0.671
MTX	0.144	Height	0.080
Hypertension	0.003*	BMI	0.246
GI problems	0.598	Dose of prednisolone	0.414
Fibromyalgia	0.536	Disease activity of RA	0.040*
Osteoarthritis	0.044*	Disease activity of AS	0.060
SC therapy etanercept	0.596	Disease activity of PsA	0.014*
SC therapy adalimumab	0.563	Duration of IV biologic	0.000*
"Satisfaction with IV biologic" as a dependent Variable *Statistically significant.			

4. Discussion

Among the available choices are biologic drugs administered either as SC injection or IV infusion. It is increasingly evident that the physician should discuss the advantages and disadvantages of each treatment option with the patient. [21 - 23]

This study enrolled 196 patients with a mean age of 43 years. The results showed that patients with RA, AS, and PsA who were treated with IV biologics were satisfied with their medications. The overall treatment experience showed that 38.3% expressed 5/7 and 42.3% expressed 6/7 satisfaction scores, whilst 9.7% were fully satisfied 7/7. These results align with another study by Susan Bolge et al, 2017 which involved studying patient experience with intravenous biologic therapies for some autoimmune diseases. Four hundred patients were enrolled in the study with a mean age of 50 years, their results showed a high satisfaction score (77% equals to or more than 6/7), ([20]) however, their Patients gave top - two ratings satisfaction scores (equal to or more than 6/7) percentage was higher than our findings. We think this is due to their larger sample size and to the multicenter study which provided a uniform better patient care. In another study done by Norman B. Gaylis involving 100 patients, there was a high level of satisfaction among all patients with regard to their experience with IV - administered biological therapy with a total of 90% of patients ranked their satisfaction with IV therapy as 4 or 5, with 77% ranking satisfaction as 5 (very satisfied). ([24]) Another prospective study in Spain, in 2008 was conducted on 198 patients initiating therapy with infliximab to assess patient expectations in relation to

treatment efficacy. This was carried out through a series of questions at multiple time points, including at baseline, 2, 6, and 14 weeks. After 2 weeks, 90% of patients reported that their expectations for treatment had been met, and for 50% expectations were surpassed. Patients satisfied with treatment were 19.4%, 76.9%, and 85.5% at baseline, 2 weeks and 14 weeks respectively. [25]

This study, showed patients' characteristics that affect satisfaction rate with IV biologic treatment were analyzed in two ways (logistic regression model and categorical effect of the patients' characteristics). According to logistic regression; it was found that patient sex, disease activity of rheumatoid arthritis, disease activity of psoriatic arthritis, comorbid diseases, hypertension, osteoarthritis, type of biologic treatment, and the duration of IV treatment have a significant predicted effect on patients' satisfaction with IV biologic treatment. According to the difference in the patients' characteristics categories on the satisfaction with IV biologic treatment of the patients; it was found that sex, hypertension, osteoarthritis, disease activity of rheumatoid arthritis, disease activity of psoriatic arthritis, and duration of IV biologic had a significant effect. Although the study which was done by Susan Bolge et al involved almost the same inquiry variables, their analysis was not done by the same methods. [20]

The most prominent perceived advantages of IV infusion, in this study, were related to Infusion center visits which act as an additional assessment to a regular doctor visit which was equal to 88.8% of patients. Patients were able to receive counseling about their IV infusion therapy before initiating treatment and were able to seek further evaluation of other concurrent medical and health issues, also the staff on site of care could monitor the patient for side effects which were reported by 82.1% of patients. Fifty - one percent of patients expressed that there was "No disadvantage" in receiving IV biologic therapy and 25% of patients reported that the duration of infusion takes too long as perceived disadvantages. While in Susan Bolge et al [20] study, the most frequently cited advantage of infusion therapy (mentioned by 98% of the sample) was that it was administered by a professional, and the staff on - site could monitor the patient for side effects. The most commonly reported disadvantages of IV infusion were related to inconvenience. A total of 41%, 23%, and 19% of patients reported that duration of infusion, appointment scheduling, and travel to their SOC, respectively, could be problematic; 13% mentioned the fear of side effects or infusion reactions which correspond to 14.8% in this study. In Norman B. Gaylis's study, the highest - ranking potential advantages of IV treatment suggest that constant professional reinforcement of disease management, readily available health - care resources to assist with any problem, and relationships developed with the staff are meaningful to patients receiving IV biologic treatment, and no outstanding disadvantage to using IV biologics was identified by their patients. [24]

The most frequently cited reason for preferring IV infusion to SC injection was a less frequent dosing regimen reported by 81.6% of our patients. Another reason to prefer IV therapy reported by 54.1% of patients where they believe that the intravenous infusion has always been effective they had no experience with subcutaneous therapy. In Susan Bolge et al, 82% of the patients in the sample preferred IV to SC therapy. The most common reason for preferring IV therapy to SC was a dislike of self - injection (mentioned by 43%). In addition, 34% of patients preferred the less frequent dosing regimen associated with IV infusion. [20] In two other studies from the United Kingdom and one from Denmark, RA patients preferred subcutaneous (SC) agents over intravenous (IV) agents. [4.26.27] However, Scarpato et al, who have done the largest study of 802 anti - TNF - naïve RA patients from 50 Italian rheumatology centers (the RIVIERA study) revealed similar preferences between SC and IV routes (49.8% and 50.2%, respectively). [28] Notably, Scarpato et al evaluated only RA patients. By contrast, the present study examined patients with RA, AS, and PsA. In addition, the patients sampled by Scarpato et al had never received an anti - TNF biologic and could only describe their expectations. [28] In the present study, patients were included only if they were currently receiving an IV biologic and could therefore describe their experience. Indeed, most patients (62.1%) in the present study had maintained their IV biologics for more than 1 year. The varied preferences of study subjects cannot be directly compared between studies because different questionnaires were used. However, the reasons for the patient's preferences for routes of drug administration could help to identify the contributing factors to their preferences and thereby further guide the decision - making process.

In the present study, 87 patients had previous experience with SC biologics for their inflammatory arthritis, and they have reported reasons for their switching from SC to IV biologics. Twenty - nine patients (33.3%) reported primary failure 49 patients (56.3%) reported secondary failure and only 4 patients (2%) switched off due to drug unavailability. Among patients who switched from SC therapy to IV therapy in Norman B Gaylis et al, [24] the primary reason for switching pertained to efficacy. A total of 67.8% of patients reported that the switch to IV infusion was related to the SC medication "not working". Another reason for switching was that patients did not like giving themselves SC injections (38.7%). Overall, patients who had previously received SC therapy and later switched to IV therapy identified multiple benefits of infusion therapy that were not available to them while they were injecting themself SC, although the differences were insignificant. [24]

In a survey done by Christos Ermeidis et al.2[9], Sample consisted of 244 patients (65.2% women), with a mean age of 50.4 years. The most common diagnosis was rheumatoid arthritis (37.3%), followed by Ankylosing spondylitis (18.9%). Almost two - thirds of the patients (60.7%) were on intravenous biologic drugs, half of which (48.8%) received their treatment in a public hospital. Overall, 80.5% of the patients stated that biologic treatment had a positive/very positive effect on their lives, with>80% admitting being satisfied or very satisfied regardless of the route of administration. Traveling to the hospital was difficult for 28.6% of the patients, in comparison with the current study traveling represented 15.8% of perceived disadvantages; the waiting period for administration was characterized as an unimportant issue by the majority of the participants while it

was considered as the most perceived disadvantage for 25%of the patients in current study [29].

In a multi - center study in Korea [30] of 307 patients (162 males, 145 females); had median age: 48 years, 139 had RA, and 168 had AS. A total of 80.1% of the patients indicated being satisfied or very satisfied with the therapeutic effect of the current bDMARD. Most patients were open to intravenous or subcutaneous injection, with the most preferred route of administration being subcutaneous (41.3%), followed by intravenous (32.0%), and oral (26.7%). Unlike this study, we did not include the oral route as most biological therapies are injectable. Most AS patients preferred subcutaneous administration (50.0%), while RA patients mostly preferred intravenous administration (39.3%). Most current users of intravenous administration methods preferred intravenous infusion (68.9%), and the majority of current users of subcutaneous methods preferred subcutaneous injection (58.4%). The patients considered therapeutic effect to be more important than cost or convenience while choosing a bDMARD (69.3%), and 86.6% consider their physicians to be the primary information source about biological therapy [30], in the current study the cost of infusion reported by 0.5% and the infusion center visits act as an additional assessment to a regular doctor visit in 88.8% of patients.

In a web - based survey in Japan [31] of the 400 RA patients 69.5% were female, the mean age was 55.7 years surveyed for preferred treatment mode, 15.3% preferred infusion, 18.0% preferred in - hospital injection, and 66.8% preferred self - injection. A preference for infusion and in - hospital injection versus self - injection was significantly associated with a higher current frequency of hospital visits and anxiety or other hurdles related to self - injection. A flexible administration setting was significantly associated with a preference for self - injection versus infusion and in - hospital injection. Many patients reported no discrepancy between their current and preferred treatment mode (patients receiving infusion 68.0%; in - hospital injection 71.2%; and self - injection 94.0%). However, > 90% of patients responded that they would change their current mode in the future following a recommendation by a medical professional, aging, or a change in RA symptoms. The most common reasons for preferring but not receiving in - hospital IV infusion were “healthcare cost may increase upon switching. In other words, patients receiving in - hospital IV infusion of a bDMARD tended to focus on the effectiveness of the medication, whereas those receiving self - administered SC injection were influenced by the relationship between their treatment mode and lifesty[31]. This survey was carried out between October and November of 2020, The spread of COVID - 19 infection during that period may have affected the selection of and preference for treatment mode among patients with RA. They suggest that this survey was hardly affected by COVID - 19, Unlike the current study this survey was Web - based so it is limited to respondents who had Internet access also they were unable to assess disease activity by physical examination or laboratory investigation and therefore did not assess the Disease Activity Score 28 (DAS28). Rituximab was not included as a bDMARD in the study because it is not indicated for the treatment of RA in Japan, bDenosumab, an antiresorptive drug, is approved in Japan for the treatment of RA, and was therefore included in the study 31. In the current study, the disease activity of RA and the type of IV biological treatment have a significant predicted effect on patient satisfaction.

5. Limitations

- The current study is limited by its sample size of 196 patients, which means that some subgroups were small for reliable statistical comparisons. Moreover, the quality of the data presented is reliant upon the accuracy of patients’ anonymous self - reporting of their condition. Nevertheless, it is important to stress that the self - reported nature of this study is also a strength with respect to the evaluation of patient perception.
- The current study was carried out in a single infusion unit and only included patients currently using IV biologics. Although some patients had previous experience with SC biologics, most did not. Preferences may differ among patients based on actual experience. Those currently using IV biologics may simply be satisfied with their current experience. It would be difficult for patients to provide their opinion on treatment modes that they had not experienced.

6. Conclusions

Most patients receiving IV biologics are satisfied with their medications and their preferences are due to less frequent dosing, the perceived IV injection effectiveness, and the easier - to - remember dosing when an appointment is scheduled for them.

Conflict of interest: the authors declare no conflict of interest

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