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TREATING ANKYLOSING SPONDYLITIS OF PATIENTS IN ADJARA REGION: WHY BIOLOGICAL THERAPY?

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მაანკილოზებელი სპონდილიტის მკურნალობა აჭარის რეგიონში: რატომ ბიოლოგიური თერაპია?

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რეზიუმე

მაანკილოზებელი სპონდილიტი არის ქრონიკული აუტოიმუნური დაავადება, რომელიც გავლენას ახდენს ხერხემალზე, უკარგავს მას მოქნილობას და იწვევს მის დეფორმაციას - შერწყმას. დაავადება ჩვეულებრივ იწყება გვიან მოზარდებში ან საშუალო ასაკის ჯგუფში, რის გამოც მნიშვნელოვანია მისი დროული მკურნალობა. ბოლო წლებში განვითარებული ბიოლოგიური თერაპია, განსაკუთრებით TNF ინჰიბიტორები, როგორიცაა Simponi (გოლიმუმაბი), გვიჩვენებს ეფექტურ შედეგებს.

ჩვენს კვლევაში მონაწილეობდა 29 პაციენტი (22 მამაკაცი და 7 ქალი) ასაკი 24-65 წელი, რომლებსაც 12 თვის განმავლობაში უტარდებოდათ ბიოლოგიური თერაპიით მკურნალობა. შედეგები აჩვენებს, რომ მკურნალობის შემდეგ მნიშვნელოვნად შემცირდა ტკივილის ინტენსივობა, CRP და ESR დონეები. 12 თვის შემდეგ მამაკაცების 22%-ში და ქალების 0%-ში აღინიშნა მხოლოდ მსუბუქი ტკივილი. ასევე შემცირდა CRP და ESR დონეები, რაც მიუთითებს დაავადების პროგრესირების შემცირებაზე.

ბიოლოგიური თერაპია მნიშვნელოვნად აუმჯობესებს პაციენტების ცხოვრების ხარისხს, რაც განაპირობებს სხეულის მობილურობისა და მოქნილობის ზრდას. ასევე რეკომენდებულია ახალგაზრდებისათვის ბიოლოგიური მკურნალობის გამოყენება, რათა დაავადება არ განვითარდეს. ეს მეთოდი დღესდღეობით ერთ-ერთი ყველაზე ეფექტური საშუალებაა მაანკილოზებელი სპონდილიტის მართვისათვის.

BACKGROUND. Ankylosing Spondylitis is an autoimmune condition [1]. It is a chronic inflammatory disease of axial/central skeleton of human body that leads to partial or complete fusion and rigidity of spine [2,3]. Numerous factors involving both genetic as well as non-genetic which together lead to onset of Ankylosing Spondylitis [4], the exact mechanism and aetiology depends on many factors and is complex [5].

Usually, in 90% of cases, Ankylosing Spondylitis is related to HLA-B27 antigen [6], but other genes are also involved [7]. HLA-B27, the main contributing gene, is more prevalent in the Caucasian population, with up to 90% of patients being positive [8]. The risk of ankylosing spondylitis in 1st-degree relatives with the HLA-B27 allele is about 20%. Hence contributing to an increased prevalence of Ankylosing Spondylitis in Caucasians [9]. Incidence is much lower in the Asian and Black population. Ankylosing Spondylitis cases in Europe and Asia are estimated to be 1.30–1.56 million and 4.63–4.98 million, respectively. Ankylosing Spondylitis affects 0.1-1.4% of common population

worldwide [10]. HLA-B27's presence increases the manifestation of Ankylosing Spondylitis in the human body but even if it is positive, it does not confirm Ankylosing Spondylitis as diagnosis, because among patients with positive HLA-B27, only 1 to 2 % people may precipitate symptoms of Ankylosing Spondylitis.

Ankylosing Spondylitis usually start at an age of 20 to 30 years. Mostly seen in age-group <40 years, it is a chronic disease and progresses gradually. Earlier, it was thought that Ankylosing Spondylitis affects males mostly but nowadays even females are affected. In males with ankylosing spondylitis the possibility of joint stiffness is higher whereas in females with ankylosing spondylitis, in ammation is more common [11]. The Modified New York Criteria is used for Diagnosis and Classification of Ankylosing Spondylitis [12].

Ankylosing Spondylitis is a disease with multiple diverse manifestations which can be potentially severe, if left untreated or under-treated. Ankylosing Spondylitis not only involves the central skeleton or joints, gradually it can affect the other body systems too [13]. As many parts of the body are getting affected due to Ankylosing Spondylitis, hence it should be managed correctly [14]. If the treatment lacks anywhere other problems may be manifested in such patients as the disease progresses like, risk of thrombotic/cerebrovascular stroke increases by 50 to 60 % and it also increases the risk of heart attack [15].

Management can be followed according to the treatment guidelines and criteria given in the ACR/SAA/SPARTAN and the ASAS/EULAR [16,17]. Therefore, a multidisciplinary management is followed for providing the best possible care [18].

- A first inseparable mode of management is to do any form of physical exercises, as it helps in subsiding the ankylosing spondylitis symptoms by reducing in ammation.
- Then comes the NSAIDs (first line drugs) but is only for symptomatic relief and management, also it is always to be taken with doctor's advise as it is contraindicated in few situations along with this it has various side-effects.
- Now comes the Steroid medications, which again have contraindications and numerous side effects. Steroids reduce the inflammation and pain but routine use of steroid medication is non-advisable. Local injections of corticosteroids are given for peripheral arthritis. Using systemic glucocorticoids is not recommended in long term.
- Methotrexate has a very restricted role in Ankylosing Spondylitis management and is prescribed in a very few cases only. Sulfasalazine is recommended only for persistent peripheral arthritis when TNF-α inhibitors are contraindicated.
- Biological Therapy (These biologic therapies cannot reverse any damage or fusion of the spine and sacroiliac joints that has already occurred, but research has shown than many people with long-standing disease can still have significant improvement with them. People who do not respond sufficiently (it may take 3-6 months to be certain), or who get serious side effects, will usually be recommended to stop their biologic therapy).
- TNF-α inhibitors (second line drugs) are the first line of treatment in those who cannot take NSAIDs. It includes a few biologic preparations such as Infliximab (5 mg/kg intravenous over at least 2 hours at 0,2,6 weeks than every 6 week), Adalimumab (40 mg subcutaneous every 2 weeks), Etanercept (50 mg subcutaneous once weekly), Golimumab (50 mg subcutaneously once a month), Certolizumab Pegol.

They help to reduce the inflammation by inhibiting TNF-α[19]. Side-effects of TNF-α inhibitors are that, it increases risk for infections as it causes immunosuppression and it may cause reactivation of hepatitis B or latent tuberculosis infection.

- On Failure of second line drugs or any contraindications to TNF-α, Anti IL-17 antibodies as third line of treatment which include Secukinumab (starts with 5 weekly doses and then moves to once monthly) and Ixekizumab (monthly dosing).

Patients with AS have very high levels of IL-17A in their body and that it plays a very important role in causing the inflammation associated with AS. By decreasing the IL-17A, this biologic reduces inflammation in your body and joints.

ACR/SAA/SPARTAN do not mention use of IL-17i because the literature review in 2015 preceded the approval of IL-17i (secukinumab) in February 2016, while the 2016 ASAS-EULAR included IL-17i in the step-up approach to be used as an alternative to switching to another TNFi, when the initial TNFi fails [20].

A recent review of ACR 2019 guidelines mentions that TNF-α inhibitors held a reasonable prospect of benefit and should be used in most patients, rather than immediately switching to a different class of biologics [21].

ACR 2019 guidelines also states that [21]:

- Adding methotrexate or sulfasalazine to biologics is not recommended.
- Switching to other biologics is not good approach.
- Switching from a biologic to biosimilars is also not appreciated.
- in any co-existent condition with ankylosing spondylitis such as recurrent uveitis, IBD treatment with TNF-α inhibitor monoclonal antibodies is advised over treatment with other biologics.
- In adults with active AS despite treatment with NSAIDs, treatment with TNF-α inhibitor over treatment with secukinumab or ixekizumab is conditionally recommended.
- Surgery - Some patients may be diagnosed in late stages they can manifest ankylosed hip joint which is a very problematic situation as they are not able to sit, stand or walk so in such patients Hip replacement surgery is recommended, we face a problem of intubation in them because of AS which can be easily managed by a good anaesthesiologist.

METHODS AND MATERIALS. Our latest investigation includes 29 patients of Ankylosing Spondylitis from Adjara region. Their Management Strategy with biologic medication TNF inhibitor Simponi from Golimumab group monotherapy was closely recorded and followed since the first day for every 3 months upto totally 12 months.

22 patients were males (age group 27 yrs to 65 yrs) and 7 patients were females (age group 24 yrs to 65 yrs). None of these female patients were pregnant. 25 patients were HLA positive and 4 patients were HLA negative. These patients had Ankylosing Spondylitis for a wide range of duration from 1 year to 40 years. This long suffering came to an end as Golimumab was recently approved for treatment of this disease by EMA (European Medicines Agency) recently.

Before giving Golimumab all contraindications and side effects were kept in mind. Also, none of these patients had a prior HBV infection and they all were tested for Tuberculosis before starting Golimumab monotherapy. 50 mg of Golimumab was injected once a month subcutaneously in the beginning of therapy. We documented the disease progression in these patients on biological therapy by recording their pain intensity, levels of CRP and ESR from the first day of using golimumab over a time duration of every 3 months till 12 months. The study was conducted at the clinic “Solo-med” during the period of 2022 October to 2023 December.

RESULTS. Biological therapy/biological mono treatment Golimumab showed a reasonable improvement in the progression of Ankylosing Spondylitis, by consequential reduction in the pain intensity along with a fall in increased levels of CRP and ESR over the course of therapy. The pain intensity

in both male and female patients shifted from severe to moderate and moderate to light gradually (Table 1). At the beginning of biological therapy, 83% of patients (82% males, 86% females) had severe pain intensity, 17% of patients (18% males, 14% females) had moderate pain intensity and none of them had light pain intensity. After 3 months, 21% of patients (18% males, 28% females) had severe pain intensity, 65% of patients (64% males, 71% females) had moderate pain intensity and 14% of patients (18% males, 0% females) had light pain intensity. After 6 months, none of the patients had severe pain intensity, 69% of patients (69% males, 72% females) had moderate pain intensity and 31% of patients (31% males, 28% females) had light pain intensity. After 12 months, none of the patients had severe pain intensity, only 17% patients (22% males, 0% females) had moderate intensity and 83% patients (78% males, 100% females) had light pain intensity.

Table 1. Percentage (%) of patients with variable pain intensity

Course of Therapy	Light pain			Moderate pain			Severe pain		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
At the Beginning	0	0	0	18	14	17	82	86	83
After 3 months	18	0	14	64	71	65	18	28	21
After 6 months	31	28	31	69	72	69	0	0	0
After 12 months	78	100	83	22	0	17	0	0	0

The increased levels of CRP (>6mg/L) also exhibited a gradual fall over the course of therapy (Table 2). At the beginning 100% of patients (100% males, 100% females) had an increased CRP. After 3 months, 96% of patients (95% males, 100% females) had high CRP. After 6 months, 55% of patients (54% males, 57% females) had high CRP. After 12 months, only 10% of patients (9% males, 8% females) had an increased CRP.

Table 2. Increased levels of CRP (>6 mg/L)

Course of therapy	Male		Female		Total	
	n	%	n	%	n	%
At the Beginning	22	100	7	100	29	100
After 3 months	21	95	7	100	28	96
After 6 months	12	54	4	57	16	55
After 12 months	2	9	1	8	3	10
n = number of patients; % = percentage of patients						

The elevated ESR declined quickly over the course of therapy (Table 3). At the beginning 93% of patients (95% males, 85% females) had high ESR. After 3 months, only 34% of patients (36% males, 28% females) had high ESR. After 6 months, just 4% of patients (4% males, 0% females) had high ESR.

Table 3. Increased levels of ESR (>22mm/hr)

Course of therapy	Male		Female		Total	
	n	%	n	%	n	%
At the Beginning	21	95	6	85	27	93
After 3 months	8	36	2	28	10	34
After 6 months	1	4	0	0	1	4
After 12 months	0	0	0	0	0	0
n = number of patients; % = percentage of patients						

After receiving Simponi 3 patients had episodes of acute rhinitis within 2 months, 2 patients had minor sneezing for 3 months as side effects, 5 patients had general weakness just after getting the injection. 3 patients had urinary tract infection (UTI) for 1 month as complication. And, none of them had any serious complications. This UTI can be easily managed first and then Golimumab therapy can be continued after it, if required.

DISCUSSION. The results of our study showed that the pain intensity was reduced with using Golimumab from severe to moderate and moderate to light in both males and females in every 3 months over the course of therapy. The increased CRP levels also declined simultaneously which is a marker of reduction in the in ammation inside body. An increased CRP was noted in 100% of patients at the very start, and by the end of 12 months only 10% of patients had an increased CRP. ESR reflects the several acute phase reactants, which was elevated initially also dropped quickly from 93% patients to 0% in 12 months. Hence, it suggests that now we are having a control over body's autoimmunity.

CONCLUSION. Our data analysis clearly depicts, that the use of Golimumab is an effective option after the failure of first line TNF-α inhibitors [22], Ankylosing Spondylitis can be easily managed by Golimumab monotherapy on doctor's recommendation with approximately no side effects contracted in Adjara region. The results are tremendously good over a span of 12 months use exhibiting a significant reduction in the remission period of Ankylosing Spondylitis. Therefore, Golimumab is an effective strategy for treating ankylosing spondylitis.

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TREATING ANKYLOSING SPONDYLITIS OF PATIENTS IN ADJARA REGION: WHY BIOLOGICAL THERAPY?

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SUMMARY

BACKGROUND. Ankylosing Spondylitis is an autoimmune chronic inflammatory disease of the axial/central skeleton of human body that leads to partial or complete fusion and rigidity of spine. As Ankylosing Spondylitis have its onset typically in late adolescents or middle age group, it is quite necessary to have a hold on it. Ankylosing Spondylitis was thought of having a bad prognosis earlier but in recent few years, with help of research advancement techniques a totally new and highly effective treatment known as biological therapy is used.

OBJECTIVE. Our aim was to identify the outcome with biological treatment of 29 patients which got biological medication TNF (tumor necrosis factor) inhibitor Simponi (Golimumab). We evaluated the effectiveness of managing Ankylosing Spondylitis with biological therapy in Adjara region. As this is an

autoimmunity disorder and it may affect any person especially the young and middle age people, everyone must be educated about getting biologic treatment as soon as possible so that they immediately get control over the disease progression.

MATERIALS AND METHODS. We investigated 29 patients of Ankylosing Spondylitis (22 males and 7 females) from 24 yrs. old to 65 yrs. old age-group. We used the biological therapy with TNF-α inhibitor named Simponi (Golimumab). 50 mg of Golimumab was injected once a month subcutaneously in the beginning of therapy. We identified pain intensity, levels of CRP and ESR in all recruited patients since the first day over a period of 3 months, 6 months, and 12 months. Accordingly, doses were decreased from once a month to once in three months. The study was conducted at the clinic "Solo-med" during the period of 2022 October to 2023 December.

RESULTS. The effectiveness of biological treatment with Simponi (Golimumab) is appreciated as it has shown a significant reduction in symptoms of Ankylosing Spondylitis such as the pain intensity, levels of CRP and ESR. About Pain intensity – After 3 months, light pain intensity was in about 18% of males with 14% of females and moderate pain intensity was in about 64% of males with 71% of females. It decreased and after 12 months, now moderate pain intensity was in about 22% of males and severe pain intensity was in none of the males. But in contrast, the female patients had neither severe nor moderate pain intensity rather they all had light pain intensity. About CRP – In the beginning all patients including both males and females had an increased level of CRP. It decreased and after 12 months only 9% of males and 8% of females had an increased CRP. About ESR – In the beginning 95% of males and 85% of females had an increased ESR. It decreased quickly with biological therapy and consequently after 12 months of treatment only 1 patient had increased ESR. After receiving Golimumab, 3 patients had episodes of acute rhinitis within 2 months, 2 patients had minor sneezing for 3 months as side effects, 5 patients had general weakness just after getting injection. 3 patients had urinary tract infection for 1 month as complication. And, no one had any serious complications.

CONCLUSION. According to these studies, it can be said that biologics have improved the quality of life of these patients by improving body mobility, flexibility and preventing complications from internal organs. To take care of the youth, use of biological therapy is advised so that the disease do not progress any further. Biological therapy is a present-day superlative method to manage Ankylosing Spondylitis as it reaches a stable remission period and alleviates the symptoms of Ankylosing Spondylitis.

Keywords: Ankylosing Spondylitis, Biological therapy, Simponi (Golimumab), Autoimmune disease, Treatment effectiveness.