Research article

Adalimumab effect in a cohort of Libyan patients with rheumatic diseases

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Abstract

Background: Adalimumab is a recombinant human IgG1 monoclonal antibody. It is a tumour necrosis factor-inhibiting, anti-inflammatory, biologic medication. It binds to tumour necrosis factor alpha (TNF), which normally binds to TNF receptor, leading to the inflammatory response of autoimmune disease. By binding to TNF, adalimumab reduces this inflammatory response.

Objective: The study was done to monitor the effects and side effects of adalimumab in our Libyan patients with rheumatic diseases.

Methods: The inclusion criteria for the study were all patients with rheumatic diseases who were treated with adalimumab in the period from April 2013 to April 2016 in the Rheumatology Department, Tripoli Medical Center, Tripoli, Libya. There were 31 patients, 10 of them had RA, 16 patients had Ankylosing Spondylitis (AS), 4 patients had Psoriatic Arthropathy (PsA) and 1 patient had Adult Onset Still's Disease (AOSD). Adalimumab 40mg subcutaneous was given every 2 weeks. Demographic details such as age and sex were recorded. Clinical characteristics as rheumatoid factor in RA patients, disease duration, duration of taking adalimumab and drugs used before starting adalimumab were noted. Assessment of disease activity was measured by DAS28 for RA patients, by BASDAI for AS patients and by DAPsA for PsA patients. For all patients, complete blood count, erythrocyte sedimentation rate, liver function test, hepatitis screen, urine routine examination and tuberculin test before adalimumab were requested to monitor its side effects during follow up.

Results: All patients with rheumatic diseases who took adalimumab in the period between April 2013 and April 2016 were included in the study. Ten patients had rheumatoid arthritis, their mean age was 39.1 years, 10% were male and 90% were female. Rheumatoid factor was positive in 60%, negative in 30% and unknown in 10%. Sixteen patients were ankylosing spondylitis; their mean age was 39 years, 81.25% were male and 18.75% were female. Four patients had psoriatic arthritis, mean age was 40 years, two were females and two were males. One patient had AOSD; she was a female aged 58 years. All RA patients were on prednisolone and/or one or two DMARD before starting adalimumab and failed to show a response. Fourteen AS patients were on one or two NSAIDs and/or salazopyrine and failed to show a response before starting adalimumab and two patients were on infliximab which was not responding to it. Two psoriatic arthritis patients were on methotrexate (MTX) alone, two patients were on leflunomide alone. The AOSD patient was on MTX and prednisolone. The mean of DAS28 before starting adalimumab for RA patients was 4.06 and the mean of DAS28 at the last dose was 2.7 (P-value =0.0135). The mean of BASDAI before using adalimumab was 5.13 and the mean of BASDAI at the last dose was 1.656 (P-value <0.0001). PsA patients had moderate disease activity (mean of DAPsA=20$\pm$SD1.6) and became (mean of DAPsA=6$\pm$SD1.2) which means low disease activity (P-value <0.02). The AOSD patient showed significant improvement clinically and ESR dropped from 53 at the start to 12 at the last dose.

Conclusion: During three years of follow up of our rheumatic diseased patients on adalimumab, we noticed a significant improvement in disease activity scores with minimal side effects.

Introduction

Adalimumab is a recombinant human IgG1 monoclonal antibody. It is a tumour necrosis factor- inhibiting, anti-inflammatory, biologic medication. It binds to tumour necrosis factor alpha (TNF), which normally binds to TNF receptor, leading to the inflammatory response of autoimmune disease. By binding to TNF, adalimumab reduces this

inflammatory response. Adalimumab is administered by subcutaneous injection. For most indications, the maintenance treatment is an injection every other week.

In Rheumatoid Arthritis (RA), it has been approved for use alone or with methotrexate or similar medicines, in the U.S since 2002[1,2]. Adalimumab in RA has a response rate similar to methotrexate, and in combination, it nearly doubles the response rate of methotrexate alone[3].

In ankylosing spondylitis, adalimumab is indicated for reducing signs and symptoms in adult patients with active disease. Adalimumab is also indicated for reducing signs and symptoms, inhibiting the progression of structural damage and improving physical function in adult patients with psoriatic arthritis. Other indications of adalimumab are juvenile idiopathic arthritis, adult Crohn's disease, paediatric Crohn's disease, ulcerative colitis, plaque psoriasis, hidradenitis suppurativa and uveitis.

Materials and Methods

The inclusion criteria for the study were all patients with rheumatic diseases who were treated with adalimumab in the period from April 2013 to April 2016 in Rheumatology department, Tripoli Medical Center, Tripoli, Libya. There were 31 patients, 10 of them had RA, 16 patients had AS, 4 patients had PsA and 1 patient had Adult Onset Still's Disease (AOSD). All patients consented to participate in the study. The study was done after receiving consent from the Tripoli Medical Center ethical and research committee. Adalimumab 40mg subcutaneous was given every 2 weeks.

Demographic details such as age and sex were recorded. Clinical characteristics such as rheumatoid factor in RA patients, disease duration, duration of taking adalimumab and drugs used before starting adalimumab were noted. Assessment of disease activity was measured by DAS28 for RA patients, by BASDAI for AS patients and by DAPSA for PsA patients.

Disease activity scores were measured at the start of adalimumab and every month thereafter. For all patients, complete blood count, erythrocyte sedimentation rate, liver function test, hepatitis screen, urine routine examination and tuberculin test before starting adalimumab were requested to monitor its side effects during follow up. Data was analysed using SPSS computer software package. The mean and standard deviations of the age, disease duration and duration of taking adalimumab were calculated. P-value to measure if there was significant difference between the means of DAS28, BASDAI or DAPSA (according to the patient either RA, AS or PsA) at the start of adalimumab and at the last follow up were calculated using t-test.

Results

All patients with rheumatic diseases who took adalimumab in the period between April 2013 and April 2016 were included in the study. Ten patients had rheumatoid arthritis, their mean age was 39.1±SD8.6 years, 10% were male and 90% were female. Rheumatoid factor was positive in 60%, negative in 30% and unknown in 10%. Sixteen patients were ankylosing spondylitis; their mean age was 39±SD9.95 years, 81.25% were male and 18.75% were female. Four patients had psoriatic arthritis, mean age was 40±SD4.3 years, two were females and two were males. One patient had AOSD; she was a female aged 58 years. The mean duration of rheumatic diseases and the mean duration of taking adalimumab are shown in Table 1. All RA patients were on prednisolone and/or one or two DMARD before starting adalimumab and failed to show a response.

Table 1: The mean duration of rheumatic diseases and the mean duration of taking adalimumab

No. of patients (n=31)	Mean of disease duration (years)	Mean duration of taking adalimumab (months)
RA (10)	6+SD3.0	9.77+SD5.3
AS (16)	6.13+SD7.08	17.5+SD14.8
PsA (4)	11.5+SD9.8	10.5+SD6.4
AOSD (1)	Duration = 4 years	Duration = 3 months

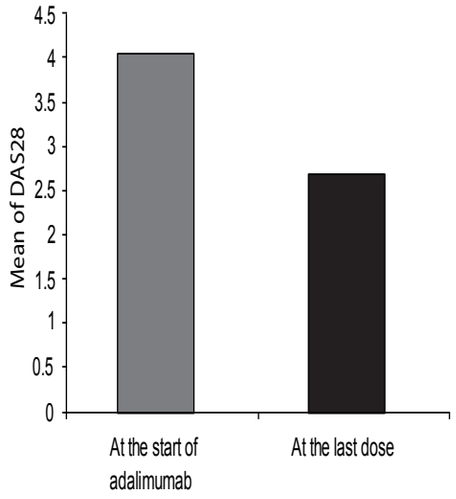
Fourteen AS patients were on one or two NSAIDs and/or salazopyrine and failed to show a response before starting adalimumab and two patients were on infliximab which was not responding to it. Two psoriatic arthritis patients were on methotrexate (MTX) alone, two patients were on leflunomide alone. The AOSD patient was on MTX and prednisolone. Table 2 shows different rheumatic diseases and different drug regimens used for them.

Table 2: Different rheumatic diseases and different drug regimens used for them

Drug regimen	No. of patients
Rheumatoid arthritis patients	(n=10)
Methotrexate (MTX) alone	4
MTX+ Hydroxychloroquine (HCQ)	1
Prednisolone + MTX+ HCQ	2
Leflunomide alone	2
Prednisolone + Leflunomide	1
Ankylosing spondylitis	Total n=16
NSAID	9
Salazopyrine	2
Prednisolone + Salazopyrine	1
MTX	1
Infliximab	2
NSAID + Salazopyrine	1
Psoriatic arthritis patients	Total n=4
Leflunomide alone	2
MTX alone	2
AOSD patient	1
Prednisolone + MTX	1

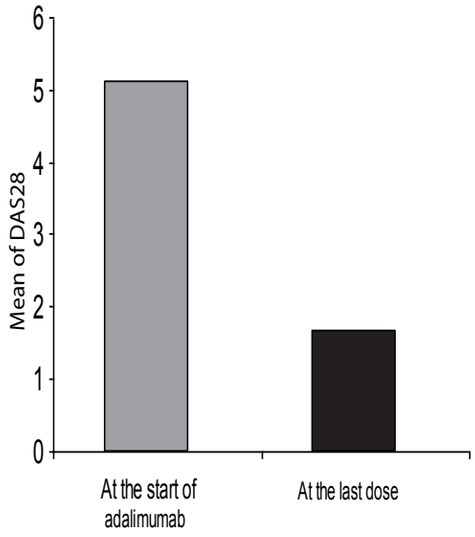
The mean of DAS28 before starting adalimumab for RA patients was 4.06±SD1.18 and the mean of DAS28 at the last dose was 2.7±SD0.81. P-value=0.0135, this difference was considered to be statistically significant (Figure 1).

Figure 1: The difference between DAS28 at the start and at the last dose of adalimumab (P-value=0.0135)



The mean of BASDAI before using adalimumab was 5.13±SD1.63 and the mean of BASDAI at the last dose was 1.656±SD1.49. P value<0.0001, this difference is considered to be extremely statistically significant (Figure 2).

Figure 2: The difference between BASDAI at the start and at the last dose of adalimumab. (P-value=0.0001)



PsA patients had moderate disease activity (mean of DAPsA=20±SD1.6) and became (mean of DAPsA=6±SD1.2) which means low disease activity (P value <0.02). AOSD patients showed significant improvement clinically and ESR dropped from 53 at the start to 12 at the last dose. Regarding side effects of adalimumab, one female RA patient developed hypersensitivity reaction at the first dose of adalimumab and one male AS patient had hypersensitivity reaction 9 months after starting it.

Discussion

Adalimumab is effective and well-tolerated in RA patients who had previously been treated with infliximab and/or etanercept[4]. All measures of the disease activity indicated that patients who had been intolerant of prior TNF-antagonist therapy achieved response rates similar to TNF- antagonist-naïve patients. Clinically meaningful improvement in patients with no response to prior TNF-antagonist treatment were demonstrated during adalimumab treatment, with 59% of patients who had no response to infliximab and in 41% of patients who had no response to etanercept achieving an ACR20 response at week 12[4].

In our study, we started adalimumab for two AS patients, after failure of response to infliximab. Both of them showed a good response to adalimumab which measured by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). BASDAI consists of six questions measuring the severity of fatigue, spinal pain, peripheral joint pain, tenderness, and stiffness on a visual analogue scale (VAS) (0-10). More than 50% improvement in BASDAI is considered clinically relevant[5]. The Assessment in Ankylosing Spondylitis international working group criteria or ASAS20 response criteria are now used more often[6]. An ASAS20 responder is defined as a patient experiencing improvement of at least 20% and an absolute improvement of at least 1 unit (on a 0-10 scale) compared with the baseline in at least three of the following four domains: patient's global assessment of disease activity as assessed by a VAS; patient assessment of pain represented by a total back pain score as assessed by VAS; patient function as assessed by Bath Ankylosing Spondylitis Function Index (BASFI) score (VAS)[7]; and inflammation, represented by the mean of the severity and duration of the morning stiffness as assessed by questions five and six of the BASDAI score (VAS).

Adalimumab has been used successfully in some patients with AOSD[8]. Adalimumab was effective in treating a patient with AOSD who failed to respond to etanercept[9]. It was also prescribed after infliximab to a patient with AOSD to treat chronic arthritis without further out come details[10]. In this study, adalimumab was given to one patient with AOSD and showed a good response clinically and her inflammatory markers decreased to normal. Regarding side effects in our patients, apart from hypersensitivity reactions, no other side effects were recorded.

Conclusion

During the three years of follow up of our rheumatic diseased patients on adalimumab, we noticed a significant improvement in disease activity scores with minimal side effects.

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