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Research Article

Short-term Treatment with Biologicals in Ankylosing Spondylitis

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Abstract: The treatment option for early diagnosed Ankylosing Spondylitis (AS) is becoming more defined with the availability of biologicals. Among the biologicals, the anti tumour necrosis factor (TNF)-α agents have been found to be working well for Ankylosing Spondylitis. There are two such agents currently available—Infliximab and Etanercept. As there are no clear recommendations over the duration of usage of such biological we adopted a protocol of using it for three months, constituting 14 weekly doses of Etanercept subcutaneously in 19 patients. In our study, majority of the patients were found to be responding as early as the 3rd week and they sustained the effect even after stopping the medication. No adverse reaction was noted in our study. In conclusion, Ankylosing Spondylitis (AS) is a progressive condition which, if diagnosed early can be effectively treated. The biologicals, Infliximab and Etanercept have been proven to be effective in controlling the disease if instituted early. In our observation we have found that a short-term treatment of three months is effective in majority of cases. However a long-term follow up is required to see whether the relief is sustainable or whether re-medication has to be instituted.
Keywords: Ankylosing Spondylitis, Biological, Etanercept, Infliximab.

INTRODUCTION

Ankylosing Spondylitis is a chronic disease characterized by axial skeletal ankylosis, inflammation at the insertions of tendons (enthesitis), and sometimes peripheral arthritis. The disease results in persistent pain and disability similar to, and sometimes worse than rheumatoid arthritis [1]. Many patients continue to have inflammatory symptoms for a very long time after the diagnosis [2-4]. There is no specific treatment to slow the progression of disease in axial AS [5].

Tumour necrosis factor (TN-α) may play a part in the pathogenesis of AS and other forms of spondyloarthropathies [6]. Studies have demonstrated the efficacy of anti–TNF-α agents for the treatment of other inflammatory arthritides. The efficacy of etanercept, a dimeric fusion protein of the human 75-kD (p75) tumour necrosis factor receptor linked to the Fc portion of human IgG_1 for the treatment of ankylosing spondylitis has been earlier recorded [7]. However, there are no clear recommendations over the duration of usage. At our institution, which is a tertiary referral centre, we adopted the protocol of treatment for three months and analysed the outcome in 19 patients.

MATERIALS AND METHODS

Our centre being the referral centre all the patients in this study were referred from smaller hospitals. All the patients were seen by rheumatologists and treated initially with Disease Modifying Anti-Rheumatic Drugs (DMARDS). We had 19 patients across the period from March 2013 to May 2014. For these patients to be treated with these biologicals, they: have to meet the modified New York clinical criteria for definite Ankylosing Spondylitis [8]; have evidence of active spondylitis despite accepted treatments; and be at least 18 years old. Active spondylitis was defined as the presence of inflammatory back pain (stiffness and pain that worsened with rest, and improved with exercise), morning stiffness for at least 45 minutes, and at least moderate disease activity as assessed by the patient and the physician. Patients were excluded if they had a spondylitis other than Ankylosing Spondylitis, clinical deformity or radiographic evidence of complete spinal ankylosis; a history of recurrent infections or cancer; or a serious liver, renal, hematologic, or neurologic disorder. All patients were given weekly injections of 50mg of Etanercept subcutaneously for a period of three months comprising 14 doses. Patients continued to take drugs that had already been prescribed for Ankylosing Spondylitis. Laboratory investigations including HLA-B27 test and radiological screenings were done. Physical examination included assessment of tenderness, assessment of joint pain, and joint stiffness including range of movement [9]. Of the 19 patients, 15 were male patients and the remaining four were female patients.

RESULTS

All the 19 patients continued the treatment of 14 weeks (3 months) and followed-up for the next three months subsequently. The assessment was done clinically & radiologically. Among the 19 patients 13 had axial symptoms; five had peripheral joint symptoms, and one had both (see Table 1). The duration of symptoms ranged from six months to three years. The patients were assessed every week prior to the next dose of injections. Among the 19 patients 16 patients showed improvements as early as the third week from the initial dose and continued to show further improvement. Of the remaining three patients, one had delayed response that started from the fifth week. Of the two patients who did not show significant improvement, one patient discontinued after six weeks of treatment. The other remaining patient did not improve significantly even after the completion of three months of treatment. All the 16 patients who completed 14 doses (3 months) showed near-total relief from the symptoms and they were continued with other DMARDs which they were taking. There were no serious adverse events or withdrawals because of adverse events.

Table 1: Clinical details of patients with duration of treatment

Sl.No	Sex	Age	Duration of treatment	Clinical Details of the Patient	Laboratory
1	M	29	14 weeks	Pain & stiffness in the back	HLA-B27 positive
2	M	30	14 weeks	Pain Sacro-Iliac Joints bilateral, back stiffness	HLA-B27 positive
3	M	40	14 weeks	Pain & stiffness in the back	HLA-B27 positive
4	M	39	14 weeks	Pain & stiffness in the back	HLA-B27 negative
5	M	37	14 weeks	Pain in both hip joints	HLA-B27 positive
6	M	25	14 weeks	Pain in Rt Hip Joint.	HLA-B27 positive
7	M	29	14 weeks	Pain & stiffness in the back	HLA-B27 positive
8	M	23	14 weeks	Pain & stiffness in the back	HLA-B27 positive
9	M	33	14 weeks	Pain in both hip joints	HLA-B27 negative
10	M	39	6 weeks, discontinued	Pain & stiffness in the back	HLA-B27 negative.
11	M	25	14 weeks	Pain in Lt Hip Joint, stiffness in the back	HLA-B27 positive
12	M	28	14 weeks	Pain & stiffness in the back	HLA-B27 positive
13	M	27	14 weeks	Pain Sacro-Iliac Joints -bilateral	HLA-B27 positive
14	M	19	14 weeks	Pain in Lt Hip Joint.	HLA-B27 positive
15	M	28	14 weeks	Pain & stiffness in the back	HLA-B27 positive
16	F	45	14 weeks	Pain in both hip joints, stiffness in the back	HLA-B27 positive
17	F	26	14 weeks	Pain & stiffness in the back	HLA-B27 negative
18	F	36	14 weeks	Pain in Rt Hip Joint.	HLA-B27 negative
19	F	25	14 weeks	Pain & stiffness in the back	HLA-B27 positive

DISCUSSION

Among the Spondyloarthrides (SpA), Ankylosing Spondyloartopathies is the most common one and has the most severe course [10]. Researchers have only recently started to investigate the burden of this disease—both personal and economic, in patients who have it.

SpA in general, and AS especially, is more prevalent than was previously thought and have a clear socio-economic impact on society. Against this background, it is becoming increasingly clear that more effective therapies are needed, although there is a role for intensive physiotherapy, as was recently shown [11]. Previously, the treatment comprised non-steroidal anti-inflammatory drugs (NSAIDs), Disease-modifying anti-rheumatic Drugs (DMARDs), Corticosteroids, bisphosphonates, radiation therapy & thalidomide [10]. Among the NSAIDs, Indomethacin & Phenylbutazone were effective. Among DMARDs sulfasalazine worked well especially for peripheral joint AS [9, 12]. Today there are two main biologic agents targeting TNF-α: the chimeric monoclonal IgG_1 antibody infliximab with human constant and murine variable regions and the recombinant 75-kD TNF receptor IgG_1 fusion protein etanercept.

In the study conducted by Jennifer D. Gormen and Kenneth E [7], and in other reported studies, Etanercept has been found to be effective in the management of AS if the treatment is instituted early in the disease. However the duration of treatment is still not well defined. The cost of the treatment is a concern in a developing country like India. This has largely limited the accessibility of biologicals in the management of AS. However in our institute, the injection Etanercept was available for the eligible referred patients from smaller hospitals. We have been using the drug from 2012 and have observed that it worked well when used in the early stages of the disease. According to what we observed, when the drug worked it started showing response as early as third week, which was sustained with further treatment. We adopted a protocol of treatment as a period of three months, in which all the patients were given 14 doses of Etanercept, (Embrel) 50 mg subcutaneously. The marked reduction in stiffness,

pain, and functional limitations with Etanercept therapy is particularly promising, since these are the primary problems reported by patients with Ankylosing Spondylitis and are among the leading causes of disability [7]. The patients were followed with NSAIDs, DMARDs & physiotherapy for the next three months. As per this study, no patient has been re-instituted with the biological treatment for relapse so far. However, owing to the prolonged duration of the disease, a long-term follow up of these patients is required to recommend this short duration of treatment. This may be considered the limitation in our study.

CONCLUSION

Ankylosing Spondylitis starts early and lasts long resulting in crippling of the patient if unchecked. Early diagnosis holds the key to treating the disease. The time-tested medications like NSAIDs, DMARDs along with physiotherapy helps in some cases. Biologicals like Infliximab and Etanercept have proved to be promising in controlling the disease if advocated early and when patient fails to respond to conventional drugs. If the patient responds to these biologicals, it can be given for short period and observed further. However the duration of such treatment has to be well-defined to benefit the patient. More studies in this regard are perhaps needed to come to a logical conclusion.

Abbreviations used

AS = Ankylosing Spondylitis, DMARD = Disease-Modifying Antirheumatic Drug, HLA = Human Leukocyte Antigen, NSAID = Nonsteroidal Anti-Inflammatory Drug, SpA = Spondyloarthritis, TNF = tumor necrosis factor

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