ORIGINAL RESEARCH PAPER

Volume-8 | Issue-4 | April-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

SHORT TERM EFFICACY AND SAFETY OF BIOLOGICAL THERAPIES IN RHEUMATOLOGICAL ILLNESS- A SINGLE CENTRE STUDY

Rheumatology

Hema Murugesan* Assistant Professor Of Rheumatology, Stanley Medical College, Chennai-1
*Corresponding Author

Dr Ganesan Rajan Associate Professor Of Medicine, Stanley Medical College, Chennai-1

KEYWORDS

BACKGROUND

Inflammatory rheumatic diseases, such as rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis and Juvenile idiopathic arthritis(JIA) are treated with various conventional disease-modifying antirheumatic drugs (DMARDs). Conventional DMARDs used are methotrexate, leflunomide, azathioprine hydroxychloroquine and sulfasalazine. They are used as mono or combination therapies to reduce joint damage and preserve joint function. Biologic DMARDS, are the agents, made from living cells, approved for the treatment of inflammatory rheumatic diseases. Biologic therapies approved for use in inflammatory joint diseases are Tumour Necrosis Factor inhibitors, T-cell modulators and B-cell depletors, IL- 6 inhibitors and JAK inhibitors. All immuno-modulating therapies have potential side effects also. In this study, we present our experience with biological therapies in our institution.

Abbrevations - SO-JIA-systemic onset juvenile idiopathic arthritis, MTX-methotrexate, HbsAg-Hepatitis B virus, HIV-Human immunodeficiency virus, DMARDS-Disease modifying anti rheumatic drugs, BASDAI-Bath ankylosing spondylitis disease activity index, ACR-American college of rheumatology

MATERIALS AND METHODS

To study the short term efficacy and side effects of biologic DMARDS used at Government Stanley Medical College ,Chennai, Tamilnadu .

Patients attending rheumatology outpatient department from November 2016 to December 2018 were chosen. Patients included were ankylosing spondylitis, rheumatoid arthritis, juvenile idiopathic arthritis satisfying the inclusion criteria. This is prospective observational study.

Inclusion criteria

1. Ankylosing spondylitis with BASDAI score >4, active disease >4 weeks and non steroidal anti-inflammatory drug failure in 4 weeks
2. Juvenile idiopathic(systemic) arthritis patients with inadequate response to NSAIDS and systemic steroids with elevated acute phase reactants.
3. Rheumatoid arthritis with combination DMARDS failure (methotrexate+sulphasalzine+ chloroquine), DAS 28>4.8.

Inj Etanercept, Inj Tocilizumab, Inj Rituximab, Inj Infiliximab were the biologicals used. Inj Etanercept and Infiliximab was used in Ankylosing spondylitis patients, Inj Rituximab was used in Rheumatoid arthritis patients and Inj Tocilizumab in SO-JIA patients. Inj Etanercept 50 mg sc weekly for 12 weeks, Inj Infiliximab 200 mg IV 0, 2 and 4 weeks, Inj Rituximab 1gm IV two doses 0 and 15 days apart, inj Tocilizumab 8mg/kg monthly IV for 6months were the dosage used.

Patients with chronic infections, tuberculosis, HIV, HbsAg, HCV, pregnancy, cardiac failure class NYHA III and IV were excluded from the study.

Patients were screened for tuberculosis by mantoux test, xray chest and CT chest. HBsAg , HCV and HIV infections were tested by appropriate methods.

RESULTS :

Out of 55(49 males and 6 females) patients with ankylosing spondylitis , 20 were started on inj Etanercept 50 mg/week for12 weeks and 35 patients received inj infiliximab 200mg, 3doses on day 0,2 and 6 weeks. All these patients had BASDAI ranging from 4.5-6 with mean of 4.65(SD 0.415). BASFI ranging from 4 to 7 .

Out of 20 patients on Inj Etanercept, in 16 patients BASDAI reduced to 50% and the ACR 20 response was achieved in 80% of the patients. One patient had injection site reaction which resolved spontaneously and did not recur. None of the patients had serious adverse reaction. Out of 35 patients who received Inj Infiliximab , 50% BASDAI reduction and ACR 20 response was achieved in 31 patients (88.57%). None of these patients had infusion reaction and serious adverse events .These patients were continued on tab methotrexate 10mg /week. None of them were on NSAIDS during the therapy.

10 patients with SO-JIA received Injection Tocilizumab. These patients had a mean ESR of 55mm/hr, CRP >10mg/L and recurrent episodes of fever with a disease duration of more than 2 years. Dose given was 8mg per kg as monthly infusion, 6 doses. After 2nd dose one patient had elevated liver parameters and pneumonia, hence drug was withheld. Remaining 9patients ESR and CRP decreased significantly by 50% at end of the 4th dose. ACR 30 response was achieved in 7 patients(77.7%). At the end of 3 months, none of these patients had flare of systemic symptoms in between the doses. All these patients received low dose prednisolone 5mg and tab methotrexate 10mg/week.

Inj Rituximab was given to 10 RA patients. Females were more than males. All were seropositive rheumatoid patients with mean DAS score of 5.11(SD 0.215) and the mean disease duration was 3 years. They had a significant decrease in ESR, tender joint and swollen joint count after 2 doses. Mean DAS score reduced to 3.6 after 1 month with significant improvement in DAS score of >1.5. All these patients received tab prednisolone 5mg and Tab methotrexate 10mg/week as baseline. One patient developed herpes zoster after 2 dose and was treated, one patient developed pruritis which was treated with anti-histamines. None of the patients developed infusion reaction and serious adverse events.

TABLE-1 RESULTS

INJ	No Of Patients		Dose	No Of Dose	Side Effects	ACR 20 (12 wks)	ACR30 (12wks)	Das Improve
	Male	Female						
Etanercept	19	1	50mg, SC, Weekly	12	1	80%	-	-
Infiliximab	30	5	200 mg, IV	3	NIL	88.57%	-	-
Tocilizumab	7	3	8mg/kg, iv	6	1	-	77.7%	
Rituximab	3	7	1GM, IV	2	2	80%	-	>1.5

DISCUSSION

The introduction of biological therapies has significantly modified the treatment armamentarium of inflammatory rheumatic diseases. Even though many molecules are available we have studied the agents

available in our government institute Stanley medical college.

Anti TNF α therapy

Tumour necrosis factor α , is a cytokine that mediates inflammatory activities in SpA. The two major anti-TNFα therapies that have been demonstrated efficacious in the treatment of ankylosing spondylitis are Infliximab, a chimeric monoclonal IgG1 antibody and Etanercept a 75 kDa IgG1 receptor fusion protein. TNF inhibitors produce substantial improvement in the symptoms of AS patients. It reduces the pain and inflammatory markers and improves their functional mobility. Patients treated with anti-TNF have shown sustained efficacy in many RCTs[1]. 113 AS patients treated with anti-TNF, In the Leeds cohort, 79% showed a sustained response to therapy, only 13% were non-responders and 8% changed their therapy due to adverse events (Coateset al.2008][2]. A similar response and toxicity has been documented in the Finnish national registry [Konttinenet al.2007)[3]. Infection risk is the long term worried complications of anti -TNF agents. But randomised control trials have shown that the risk is high only with long term therapies. In our study, AS patients were started on anti TNF; anti TNFs showed good clinical remission without side effects in 80% of the patients. The ACR response achieved in Inj Etanercept and Inj Infiximab didn't vary significantly, showing comparable efficacy. Male population were more than females in the AS cohort.

B cell therapy

Rituximab, a chimeric monoclonal antibody that targets the CD20 molecule expressed on the surface of B cells, are very well used in rheumatoid arthritis as B cell is the one of the pathogenetic factor in RA. In Dancer Trial 465 patients with active long-standing RA refractory to DMARDS received Inj Rituximab (two doses of 1,000 mg) along with Mtx[5,6]. At 24 weeks significant proportions of patients achieved moderate/good ACR20/50/70 responses. Rituximab has also been shown to halt radiological progression in multiple RCTs[4]. In our study 80% achieved ACR 20 response at the end of 3 months and there was significant improvement in DAS score without significant adverse events.

IL-6 inhibitors

In Asia, SO-JIA accounts for 50% of JIA cases. Tocilizumab is an humanised antihuman IL-6 receptor monoclonal antibody. It is an effective drug in patients with SO-JIA . In a Japanese trial where they studied the efficacy and safety of inj Tocilizumab significant ACR 30 and ACR 70 response was seen[7]. In our study 77% of patients achieved good clinical response at the end of 3 months Only very few side effects were noted in our study; none had serious adverse events with these agents.

CONCLUSIONS

Biological therapies are the real boon in the therapeutic basket of rheumatic diseases who are not responding to the conventional synthetic DMARDS. They can be used as short term therapy in controlling the disease activity in patients with high disease activity. It gives a good functional outcome and reduces the patients morbidity when used in the early stage. Increased risk of infection is noted in long term therapies only

REFERENCES

1. Laura C. Coates, Helena Marzo-Ortega,Alexander N. Bennett,and Paul Emery (2010)Anti-TNF Therapy in Ankylosing Spondylitis: Insights for the Clinician.
2. Coates LC1, Cawkwell LS, Ng NW, Bennett AN, Bryer DJ, Fraser AD, Emery P, Marzo-Ortega H(2008). Real life experience confirms sustained response to long-term biologics and switching in ankylosing spondylitis
3. Konttinen L1, Tuompo R, Uusitalo T, Luosujärvi R, Laiho K, Lähteenmäki J, Puurtinen-Vilkki M, Lanteri R, Kortelainen S, Karilainen H, Varjolahti-Lehtinen T, Nordström D; ROB-FIN Study Group. Anti-TNF therapy in the treatment of ankylosing spondylitis: the Finnish experience.
4. Chi Chiu Mok(2013) Rituximab for the treatment of rheumatoid arthritis: an update.
5. Mease PJ1, Revicki DA, Szechinski J, Greenwald M, Kivitz A, Barile-Fabris L, Kalsi J, Eames J, Leirisalo-Repo M. Improved health-related quality of life for patients with active rheumatoid arthritis receiving rituximab: Results of the Dose-Ranging Assessment: International Clinical Evaluation of Rituximab in Rheumatoid Arthritis (DANCER) Trial.
6. Emery P, Fleischmann R, Filipowicz-Sosnowska A, et al. DANCER Study Group The efficacy and safety of rituximab in patients with active rheumatoid arthritis despite methotrexate treatment: results of a phase IIB randomized, double-blind, placebo-controlled, dose-ranging trial. Arthritis Rheum. 2006;54(5):1390–1400
7. Shumpei Yokota ,Yasuhiko Itoh , Tomohiro Morio , Hideki Origasa1 Naokata Sumitomo Tocilizumab in systemic juvenile idiopathic arthritis in a real-world clinical setting: results from 1 year of postmarketing surveillance follow-up of 417 patients in Japan.