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Research Article

A Study on Tofacitinib in Patients with Spondyloarthritis:-Retrospective Analysis

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ABSTRACT

Ankylosing spondylitis (AS), now referred to as axial spondyloarthritis (axSpA), is a complicated inflammatory rheumatic illness that mostly affects the spine and sacroiliac joints. These conditions are classified as axial (ax Spa) or peripheral based on the main afflicted body parts. Axial spondyloarthritis (axSpA) is an inflammatory disease that primarily affects the axial enthuses and joints, especially the fibro-cartilaginous bone. The Assessment of Spondylo Arthritis International Society i.e., ASAS classification was done based on a history of chronic back pain of unknown origin and a possible diagnosis of SpA. Clinical data including gender, age, duration of back pain, clinical history, laboratory tests, and imaging results, were presented to the experts in the format of 'paper patients'. In terms of imaging, information about sacroiliitis on plain radio graphs was provided according to the modified New York criteria. Depending on variables like study population or data source, case definition, ascertainment technique, geographic region, and recent studies, prevalence estimates for AS in the general population vary from 9 to 30 per 10,000. Risk elements for individuals developing AS encompass HLA-B-27-Seropositivity, Sex, Family History & Acquired/Frequent GI Infections. Factors involved in Ankylosing Spondylitis Pathogenesis are HLA-B-27, ERAP 1&2, genetic factors & environmental factors. The main indicators and symptoms of spondyloarthritis include persistent pain and stiffness in the affected joints and spine. The modified New York criteria of 1984 were used to determine AS like reduced chest expansion in comparison to age and sex-appropriate norms & more than grade 2 bilateral sacroiliitis. Reducing disease activity and controlling joint damage are the primary objectives of managing SpA, as these measures enhance patients' quality of life while maintaining their autonomy, functional abilities, and social engagement. Pharmacological therapy includes NSAID, corticosteroids, and biological DMARD'S .Non-pharmacological therapy includes exercise therapy and educating patients

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regarding their condition. To facitinib, a new selective immunosuppressant of the Janus kinase inhibitor class used for patients who have moderate-severe spondyloarthritis.itis an oral synthetic small molecule that targets the JAK protein and acts intracellular by competitively and reversibly inhibiting it. Many essential functions are mediated by JAK pathways. In addition to influencing the innate responses and hemopoiesis, they are involved in cell division, proliferation, survival, and migration.. Tyrosine kinase 2 (TYK2) is one of four proteins in the JAK family. The others are JAK1, JAK2, and JAK3. Some chemicals that may activate these proteins include cytokines, growth hormone, erythropoietin, and interleukins and interferons, which are hormone-producing compounds. Certain cytokine receptors are specific to each tyrosine kinase protein. A cytokine's binding to a cytokine receptor causes the receptor-associated JAKs to become activated. The related JAK receptor proteins then phosphorylate the intracellular receptor, turning it into a binding site for STAT1-7 proteins. Once JAK-receptor kinases attach to their respective receptors, they phosphorylate STAT proteins. Upon dissociation from the receptor subunit, the phosphorylated STAT proteins undergo dimerization. They then relocate into the cell nucleus, where they affect gene transcription and fuel additional inflammation. To facitinib has been found to be efficacious in patients with spondyloarthropathy in case reports and case series earlier. A recent RCT [Quote-article]has also shown its efficacy resulting in the addition of a drug into the treatment armamentarium.

INTRODUCTION

Ankylosing spondylitis (AS), now referred to as axial spondyloarthritis (axSpA), is a complicated inflammatory rheumatic illness that mostly affects the spine and sacroiliac joints. These conditions are classified as axial (ax Spa) or peripheral based on the main afflicted body parts. Axial spondyloarthritis (axSpA) is an inflammatory disease that primarily affects the axial enthuses and joints, especially the fibro-cartilaginous bone. The Assessment of Spondylo Arthritis International Society i.e., ASAS classification was done based on a history of chronic back pain of unknown origin and a possible diagnosis of SpA. Clinical data including gender, age, duration of back pain, clinical history, laboratory tests, and imaging results, were presented to the experts in the format of 'paper patients'. In terms of imaging, information about sacroiliitis on plain radio graphs was provided according to the modified New York criteria. Depending on variables like study population or data source, case definition, ascertainment technique, geographic region, and recent studies, prevalence estimates for AS in the general population vary from 9 to 30 per 10,000. Risk elements for individuals developing AS encompass HLA-B-27-Seropositivity, Sex, Family History & Acquired/Frequent GI Infections. Factors involved in Ankylosing Spondylitis Pathogenesis are HLA-B-27, ERAP 1&2, genetic factors & environmental factors. The main indicators and symptoms of spondyloarthritis include persistent pain and stiffness in the affected joints and spine. The modified New York criteria of 1984 were used to determine AS like reduced chest expansion in comparison to age and sex-appropriate norms & more than grade 2 bilateral sacroiliitis. Reducing disease activity and controlling joint damage are the primary objectives of managing SpA, as these measures enhance patients' quality of life while maintaining their autonomy, functional abilities, and social engagement. Pharmacological therapy includes NSAID, corticosteroids, and biological DMARD'S. Non-pharmacological therapy includes exercise therapy and educating patients regarding their condition. To facitinib, a new selective immunosuppressant of the Janus kinase inhibitor class used for patients who have moderate-severe spondyloarthritis.itis an oral synthetic small molecule that targets the JAK protein and acts intracellular by competitively and reversibly inhibiting it. Many essential functions are mediated by JAK pathways. In addition to influencing the innate responses and hemopoiesis, they are involved in cell division, proliferation, survival, and migration. Tyrosine kinase 2 (TYK2) is one of four proteins in the JAK family. The

others are JAK1, JAK2, and JAK3. Some chemicals that may activate these proteins include cytokines, growth hormone, erythropoietin, and interleukins and interferons, which are hormone-producing compounds. Certain cytokine receptors are specific to each tyrosine kinase protein. A cytokine's binding to a cytokine receptor causes the receptor-associated JAKs to become activated. The related JAK receptor proteins then phosphorylate the intracellular receptor, turning it into a binding site for STAT1-7 proteins. Once JAK-receptor kinases attach to their respective receptors, they phosphorylate STAT proteins. Upon dissociation from the receptor subunit, the phosphorylated STAT proteins undergo dimerization. They then relocate into the cell nucleus, where they affect gene transcription and fuel additional inflammation. To facitinib has been found to be efficacious in patients with spondyloarthropathy in case reports and case series earlier. A recent RCT [Quote-article]has also shown its efficacy resulting in the addition of a drug into the treatment armamentarium.

AIM & OBJECTIVES:-

The Main Aim and Objectives of this study are to assess the safety, efficacy ,and tolerability of generic to facitinib and to assess the quality of life of SpA patients on to facitinib.

METHODOLOGY

All the relevant and necessary data will be collected from patient records, Lab reports, Prescriptions, and communicating with health care Professionals.

METHODS AND COLLECTION OF DATA:-

This single-center study was conducted in the Department of Rheumatology, KIMS, Hyderabad between July to December. Data will be collected from the Out-Patients (OP) Department of Rheumatology, KRISHNA INSTITUTE OF MEDICAL SCIENCES (KIMS) HOSPITAL, SECUNDRABAD.

STUDY SITE:-

This study was conducted in the Out-Patient Department of Clinical Immunology and Rheumatology, Krishna Institute of Medical Sciences [KIMS] Hospital, Secundrabad."

STUDY DESIGN:-

This is a RETROSPECTIVE, SINGLE ARM, and OBSERVATIONAL STUDY. The institutional ethics committee must provide its permission before this research may begin. strict adherence to patient and prescriber confidentiality is guaranteed. Prior to conducting the research, approval will be sought from the department head.

STUDY PERIOD:-

This study is conducted for 06 Months.

SAMPLE SIZE:-

A Sufficient number of patients will be enrolled to ensure a study population of at least 100 adult patients with spondyloarthritis. Data will be recorded from recruited patients.

INCLUSION CRITERIA:-

1. ≥18 years of age
2. Patients who had active disease despite the use of csDMARDS (methotrexate and sulfasalazine
3. Patients who are willing to give their consent.

EXCLUSION CRITERIA:-

1. Current/prior treatment with targeted synthetic disease-modifying anti-rheumatic drugs & current DMARDs treatment.
2. Psoriatic arthritis
3. Enteropathic arthritis
4. Juvenile spondyloarthropathy
5. Evidence of active, latent, or inadequately treated tuberculosis infection.

SOURCE OF DATA:-

All essential and useful Data was gathered from Out-Patient Department patient records, Lab reports,and Medications. Communicated with Healthcare Professionals.

ETHICAL CONSIDERATIONS:-

It will be decided by an institutional human ethics commission. The research will ensure that all participants provide written informed permission before being included in the study. The anonymity of the participants will also be preserved, and only individuals who are willing to sign the informed consent will be included.

INSTITUTIONAL REVIEW BOARD:-

The Scientific Review Board's Ethics committee examined and approved the study's protocol and associated informed consent form (ICF) before participants gave their informed consent. The Ethics Committee gave their stamp of approval to the study's protocol and ICF.

INFORMED CONSENT FORM:-

Patients were informed of the study's aim, methods, possible risks, and their rights in a way that was easy them to understand before they were recruited. After listening to the lecture and reviewing the Informed Consent Form carefully, all patients consented to the procedure in writing.

STATISTICAL ANALYSIS:-

The data was analyzed using appropriate statistical procedures Or Methods, such as the Paired "T" Test, in order to meet the study's purpose .A paired samplest-testis used to compare the means of two samples when each observation in one sample can be paired with an observation in the other sample.

PROPOSED PLAN OF WORK:-

- Preparation and evaluation of the literature review
- Preparation of Protocol
- Getting approval from ethical committee
- Selection of subjects for the study will be done based on assessment of the inclusion and exclusion criteria for obtaining patient consent form
- Patient demographic data, disease duration and symptoms, co-morbid conditions, the medication details, investigations and all other required data will be collected based all the required data will be collected based on ASDAS- ESR, BASDAI, BASFI,ASQOL Scorings
- Study conducted by the safety and efficacy of the TOFACITINIB as per designed protocol and data will be collected in questionnaire form.
- Follow up all the patients after 16 weeks (4 Months)
- Safety and efficacy of TOFACITINIB drug will be observed after administration of the drug
- The obtained data will be compiled and analyzed using suitable statistical methods
- Results
- Conclusion
- Report
- A Thesis will be Prepared and submitted

DISCUSSION:-

This Single arm Observational Study was conducted in the Out-Patient Department of Clinical Immunology and Rheumatology, Krishna Institute of Medical Sciences [KIMS] Hospital, Secundrabad. The institutional ethics committee must provide its permission before this research begins. strict adherence to patient and prescriber confidentiality is guaranteed. Prior to conducting the research, approval will be sought from the department head. This study is conducted for 06 Months. A Sufficient number of patients were enrolled to ensure a study population of at least 100 adult patients with spondyloarthritis. Data will be recorded from recruited patients. The Inclusion of this Study includes Patients≥18 years of age, Patients who had active disease despite the use of csDMARDS (methotrexate and sulfasalazine), and Patients who are willing to give their consent and the Exclusion Criteria of this study include Current/prior treatment with targeted synthetic disease-modifying anti-rheumatic drugs & current bDMARDs treatment, Psoriatic arthritis, Enteropathic arthritis, Juvenile spondyloarthropathy and Evidence of active, latent or inadequately treated tuberculosis infection. According to the study's criteria, 100 patients from the rheumatology department at Krishna Institute of Medical Sciences (KIMS) were given Generic TOFACITINIB. The patients were assigned according to their demographic characteristics; There are a total 76 % males and 24% females. According to the Data Collected out of 100 patients, 29% of patients were found to be HLA-B27 Positive, and 71% were found to be HLA-B27 Negative & In a Total of 100 patients, 12 patients were on Prior 1 csDMARDs, 15 patients were on Prior 2 csDMARDs, 10 patients were on Prior 1 bDMARDs, 71 patients were not on prior treatment. This study has shown significant improvement compared to other studies which were conducted previously like Phase II and Phase III studies. ASDAS-ESR of 3.90which reduced to 1.9 after 16 weeks of follow-up[P-value <0.001], BASDAI of 4.9 which reduced to 2.5 after 16 weeks of follow-up[P-value <0.001]. BASFI of 4.4which is reduced to 2.9 after 16 weeks of follow-up[P-value <0.001].ASQOL of 13.0 which is reduced to 1.9 after 16 weeks of follow-up[P-value <0.001].These efficacy findings are consistent with those from the Phase II and Phase III studies of tofacitinib versus placebo in patients with AS. The safety profile of tofacitinib, including laboratory changes, in patients with AS in this study was consistent with the established safety profile of tofacitinib 5 mg two times per day across all clinical programs .Therefore in this single-arm observational study, patients with active AS had a rapid, sustained, and clinically meaningful response to tofacitinib 5 mg. In this study adverse events like respiratory tract infection were found in 10 patients out of 100[10%]Herpes zoster was detected in just 2 patients. There is a rise in ALT (54/100)[54%]and creatinine(52/100)[52%]. Weight gain is observed in 76/100[76%]There is a minor drop in Hb levels(14%). No deaths or documented cases of cancer, thromboembolic events, major cardiovascular events, or tuberculosis occurred in patients receiving to facitinib .Individuals with HLA-B27 are not very common. This suggests a favorable benefit-risk balance in patients with active AS treated with tofacitinib.

RESULTS:-

Based on the Data collected Out Of 100 Patients Baseline data showed that the mean value ASDAS-ESR of 3.90which reduced to 1.9 after 16 weeks of follow-up[P-value <0.001]. BASDAI of 4.9 which reduced to 2.5 after 16 weeks of follow-up[P-value <0.001]. BASFI of 4.4which is reduced to 2.9 after 16 weeks of follow-up[P-value

<0.001].ASQOLof 13.0 which is reduced to 1.9 after 16 weeks of follow-up[P-value <0.001]. According to the study's criteria, 100 patients from the rheumatology department at Krishna Institute of Medical Sciences (KIMS) were given Generic TOFACITINIB. The patients were assigned according to their demographic characteristics; There are a total 76 % males and 24% females. According to the Data Collected out of 100 patients, 29% of patients were found to be HLA-B27 Positive ,and 71% were found to be HLA-B27 Negative & In a Total of 100 patients, 12 patients were on Prior 1 csDMARDs, 15 patients were on Prior 2 csDMARDs, 10 patients were on Prior 1 bDMARDs, 71 patients were not on prior treatment. By using TOFACITINIB, there is a significant decrease in the level of ASDAS-ESR, BASDAI, BASFI, and ASQOL with a significance value of <0.05.

CONCLUSION:-

Finally, In this study, we concluded that the observed lack of response to prior NSAIDs and csDmard prompted a strategic decision to switch patients to TOFACITINIB. The observed enhancement in the patient's disease activity following 16 weeks of tofacitinib treatment suggests a positive therapeutic impact, highlighting the potential efficacy of this intervention in managing the respective medical condition. Further studies and long-term monitoring may provide additional insights into the sustained benefits of to facitinibin addressing the specific disease.

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