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REVIEW PAPER ON ANKYLOSING SPONDYLITIS AND THE IMPLICATIONS OF NSAIDS USE ON RENAL FUNCTION

Ganguluri Sekhar Vijay[1], Naga Subrahmanyam S*[2], Ravi Prakash Degala[2], Panchadi Anusha[3], Devu Surya Tejaswini[3], Meruva Swathi[3]

[1]IV/VI Pharma-D, Koringa College of Pharmacy, Korangi-533461, Tallarevu Mandal, Kakinada District, Andhra Pradesh, India.

[2]Associate Professor, Department of Pharmacy Practice, Koringa College of Pharmacy, Korangi-533461, Tallarevu Mandal, Kakinada District, Andhra Pradesh, India.

[3]Assistant Professor, Department of Pharmacy Practice, Koringa College of Pharmacy, Korangi-533461, Tallarevu Mandal, Kakinada District, Andhra Pradesh, India.

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Abstract

Background: Ankylosing spondylitis (AS), a type of axial spondyloarthritis, is a chronic inflammatory condition primarily affecting the spine and pelvis. It can lead to spinal fusion, reducing flexibility and potentially causing a hunched posture and compromised respiratory function1. AS is categorized into radiographic ankylosing spondylitis (visible on X-ray) and nonradiographic axial spondyloarthritis (detected through symptoms and other diagnostic methods).Objective: This study examines the safety and impact of nonsteroidal anti-inflammatory drugs (NSAIDs) on renal function in patients with ankylosing spondylitis and evaluates the efficacy and risks associated with various treatment options. Methods: We reviewed the effects of NSAIDs on renal health, particularly focusing on the potential for renal impairment and the influence of NSAIDs' COX-1and COX-2 selectivity. Data were analyzed from multiple sources including population-based studies and clinical trials2. Additionally, the impact of tumor necrosis factor (TNF) inhibitors and interleukin-17 (IL-17) inhibitors on renal function was assessed in patients with preexisting renal risks. Results: NSAIDs are effective in managing AS symptoms but can pose risks to renal function, particularly in patients with preexisting conditions such as older age, reduced renal function, or comorbidities. The study found that while NSAIDs generally do not cause significant renal deterioration in the broader AS population, they can exacerbate renal issues in susceptible individuals. The analysis also highlighted differences in the renal safety profiles of COX-2 selective inhibitors versus non-selective NSAIDs, with COX-2 inhibitors showing fewer adverse renal effects5.Conclusion: The findings suggest that while NSAIDs are effective for AS management, their use requires careful consideration of the patient's renal status and risk factors. In patients with existing renal impairment or other risk factors, alternative therapies or more stringent monitoring may be necessary. Further research is needed to refine guidelines for NSAID use in AS, especially regarding long-term renal safety and the comparative efficacy of newer biologic treatments.

Keywords: NSAIDS, Ankylosing spondylitis, renal function, glomerular filtration rate, tumor necrosis factor.

***Corresponding Author**
Naga subrahmanyam S

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Introduction

Ankylosing Spondylitis (AS), also known as axial spondyloarthritis, is a chronic inflammatory disease primarily affecting the spine and pelvis. It can lead to the fusion of vertebrae, resulting in decreased spinal flexibility and a hunched posture. The condition can also impact rib mobility, making deep breathing difficult. There are two types of axial spondyloarthritis7: ankylosing spondylitis, detectable through X-ray imaging, and nonradiographic axial spondyloarthritis, identified through clinical symptoms and other diagnostic tests when X-rays are inconclusive. When GFR falls below 20% of normal, a condition known as chronic renal disease is prevalent. Glomerulonephritis, hypertension, and diabetes mellitus are the three main contributors to chronic kidney disease.

The glomerular filtration, selective reabsorption, and tubular secretion are all significantly impacted. Water reabsorption is greatly hampered, and GFR and filtrate amounts are markedly reduced. This can result in up to 10 liters of urine being generated daily.

The most commonly recommended pharmaceuticals for treating illnesses like arthritis are nonsteroidal anti-inflammatory drugs, or NSAIDs (pronounced en-saids). Most people are familiar with over-the-counter, non-prescription NSAIDs like aspirin, ibuprofen, and naproxen. NSAIDs do more for you than only ease pain. They also aid in lowering fevers and inflammation. They stop blood from clotting, which is advantageous in certain situations but not in others. For instance, several NSAIDS, particularly aspirin, may be preventive against heart disease because they lower the clotting action. You might, however, bruise more readily. NSAIDs may raise your chance of experiencing nausea or stomach ulcers. They might also obstruct renal function. NSAID users over 65 need to use extra caution when taking them. Inform your physician of any additional medications you are taking as well. NSAIDs have the potential to exacerbate or neutralise the effects of some drugs. The longer you take NSAIDs, the greater the chance and intensity of side effects.

Pathophysiology

Ankylosing Spondylitis (AS), involves progressive inflammation of the axial skeleton, primarily affecting the sacroiliac joints and vertebrae. The inflammatory process can lead to new bone formation, which gradually bridges gaps between vertebrae and may eventually result in their fusion. This fusion causes the loss of spinal mobility and a characteristic hunched posture.

Symptoms

Early symptoms of Ankylosing Spondylitis include:

Back Pain and Stiffness: Predominantly in the lower back and hips, worsened by inactivity and often most severe in the morning.

Neck Pain and Fatigue: Common as the disease progresses.

Joint Involvement: Most commonly affects the sacroiliac joint, lower back vertebrae, tendinous and ligamentous attachments, cartilage between the breastbone and ribs, and sometimes the hip and shoulder joints.Symptoms may fluctuate, with periods of worsening, improvement, or stabilization.

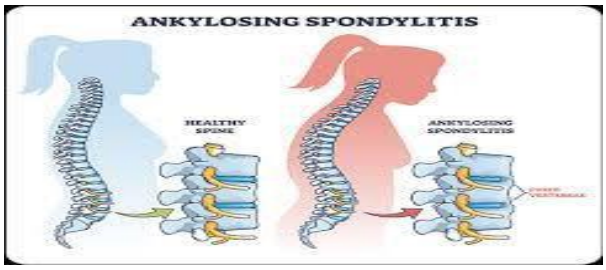

Figure - 1: Ankylosing Spondylitis

Treatment:

NSAIDS: Nonsteroidal anti-inflammatory drugs are the primary treatment for relieving inflammation, pain, and stiffness in AS. Common NSAIDs include:

Ibuprofen (e.g., Advil, Motrin), 50mg/kg/day. Naproxen (e.g., Aleve), 250mg-500mg OD/BD/TID. Diclofenac,75mg adult/0.1mg pediatric 50mg adult/0.3mg pediatric 100mgadult/0.5mgpediatricKetoprofen,50mg>adult,0.5-0.25mg/kg>pediatric,Aspirin,1200-1500mg/TID.

Biologic Agents: For patients who do not respond adequately to NSAIDs, biologic drugs targeting specific inflammatory pathways are used:

Tumor Necrosis Factor (TNF) Blockers: Adalimumab (Humira),80mg-IV-2Consecutivedays, Certolizumabpegol (Cimzia),400 mg initally/200mg in week 2 and 4-SC. Etanercept (Enbrel), 50mg-IV-Twice per week for 3 months Golimumab (Simponi), 200 mg week 0,100 mg week 2,100 mg maintenance therapy every4weeks-SC. Infliximab (Remicade)5mg/kg-IV-6weeks. Interleukin-17 (IL-17) Inhibitors: Secukinuma (Cosentyx), Ixekizumab (Taltz) Janus Kinase (JAK) Inhibitors:Tofacitinib (Xeljanz), Upadacitinib (Rinvoq) cox-2 selective inhibitor: meloxicam -15mg adult, 0.125mg/kg-7.5mg/day <pediatric. Celecoxib-200mg>adult, 10-40 mcg/ kg/ day>pediatric.

NSAIDS Safety and Renal Function

NSAIDs are commonly prescribed to manage AS symptoms. However, their use raises concern about renal safety. NSAIDs work by inhibiting cyclooxygenase (COX) enzymes, reducing prostaglandin synthesis, which in turn can impair renal hemodynamics. Prostaglandins, specifically PGE2 and PGI2, maintain glomerular filtration and renal blood flow by vasodilating the afferent arterioles. Inhibition of these prostaglandins by NSAIDs can lead to vasoconstriction, potentially causing renal injury.

Key Points from Recent Studies

1. Channeling Bias: There may be a selection bias where patients with better renal function are prescribed higher doses of NSAIDs. This could mask the true renal risks associated with NSAID use.

2. Age and Renal Function: Older age and preexisting renal impairment significantly increase the risk of NSAID-induced renal deterioration. Younger patients with AS generally show a lower incidence of renal function decline.

3. Cumulative NSAID Dose: Long-term NSAID use and the cumulative dose might be more relevant in assessing renal risk than the intensity of use alone.

4. COX-2 Selectivity: Recent analyses suggest that COX-2 selective inhibitors (e.g., celecoxib) may have a more favorable renal safety profile compared to non-selective NSAIDs (e.g., ibuprofen, naproxen), though this remains under investigation.

Conclusion

Ankylosing spondylitis is a chronic inflammatory condition that primarily affects the spine and pelvis, leading to potential fusion of vertebrae and impaired mobility. NSAIDs are a cornerstone of treatment for managing pain and inflammation. However, they can negatively impact renal function, particularly in patients

with preexisting risk factors such as advanced age, impaired renal function, and comorbidities. Careful monitoring and judicious use of NSAIDs are recommended, with consideration given to the choice of medication and the patient's overall health status. Further research is needed to fully understand the long-term renal risks associated with NSAID use in Ankylosing spondylitis and to refine treatment strategies to balance efficacy and safety.

Author Contribution

All authors contributed equally.

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