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NSAIDs and Renal function in Rheumatoid Arthritis

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ABSTRACT
Non-steroidal anti-inflammatory drugs(NSAIDs) are of the most commonly prescribed drugs in Rheumatoid Arthritis(RA).Their use carries a high risk of gastrointestinal and renal side effects. It is often difficult to differentiate between damage due to disease activity and that due to drugs (NSAIDs) used to treat rheumatoid arthritis. Although there are a number of parameters to study renal function, these cannot be applied to day to day practice and still remains research tools. In such a scenario, it is important to periodically monitor serum urea, serum creatinine and ESR, so as to pick up the earliest signs of inflammation and renal dysfunction in rheumatoid arthritis. For the above study 100 RA patients were enrolled, 50 being on NSAIDs. Elevated values i.e.S. urea (101.1%), S.creatinine (164.1%) and ESR (287%) was found in these subjects, which is statiscally significant. Treatment with Non-steroidal anti-inflammatory drugs (NSAIDs), showed decrease levels but it was not statistically significant. Hence, it is concluded from the above observation, that-raised levels of serum urea and serum creatinine is associated with rheumatoid arthritis and this in turn with variety of kidney disorders, principally due to chronic inflammation and drug exposure or toxicity.
Keywords- *Urea, Creatinine, RA, NSAIDs, ESR.*

1. INTRODUCTION

Death from renal failure is much more common in patients with Rheumatoid Arthritis (RA) than in the general population [1] and definite renal disease has been noted in no fewer than 72% of patients with RA coming to necropsy[2].The reported kidney disease prevalence in patients with rheumatoid arthritis ranges from 5%-50% based on studies of different designs [3,4] and the true prevalence of kidney disease remains unclear.

RA has been associated with a variety of kidney disorders principally due to chronic inflammation and drug exposure or toxicity.[5]

As treatment pattern for RA have changed over the years, the incidence of kidney disease may be altered. Agents such as gold salts and d-penicillin more commonly used in the past were linked directly to proteinuria and kidney disease [6 ,7].Cyclosporine therapy is associated with a dose related nephrotoxicity in patients with RA [8 ,9].More recently, biologic agents including tumor necrosis factor α inhibitor have emerged as effective treatment. A variety of case reports suggesting a link etanercept and glomerulonephritides indicate that kidney disease continues to be a disease and treatment related feature of RA [10] .Finally, long term maintenance anti-inflammatory therapy with non-steroidal anti-inflammatory drugs (NSAIDs) or

cyclooxygenase 2 inhibitors is a well recognized cause of kidney injury [11].

In the present study we have attempted to determine the frequency of serum biochemical abnormalities in rheumatoid disease and to provide explanations for some of the result obtained.

We have analysed serum urea, serum creatinine and ESR in patients of RA to assess---

(a) whether any change occur in the serum of RA patients on NSAIDs, as compared to RA patients without medication,

(b) And to assess the effect of NSAIDs in the normalization of these profiles.

MATERIAL AND METHODS

The study population was selected from the city of Allahabad (U.P).150 volunteers both male and female between 20-50 yrs of age were taken up for the proposed study. They were further classified into Control group-consisting of healthy males and females, Group-I-consisting of RA patients and Group-II-consisting of RA patients taking anti-inflammatory drugs i.e, NSAIDs.

For the parameters to be analysed, blood samples were drain from the anticubital vein avoiding venostasis. Serum was used to measure urea and creatinine and whole blood for ESR measurement.

Urea, creatinine and ESR were estimated by Diacetyi monoxime, Alkaline picrate and Wintrobe methods respectively.

STATISTICAL ANALYSIS

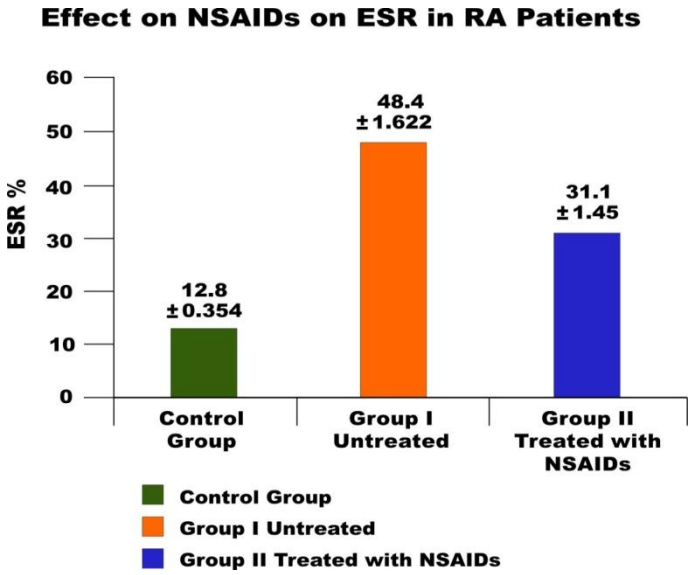
Values are expressed as mean±SD. The significance of mean difference between groups was analysed by student**'t'** test and distribution of probability 'p'.

OBSERVATION

Observation tables and graph of various parameters are tabulated as follows:

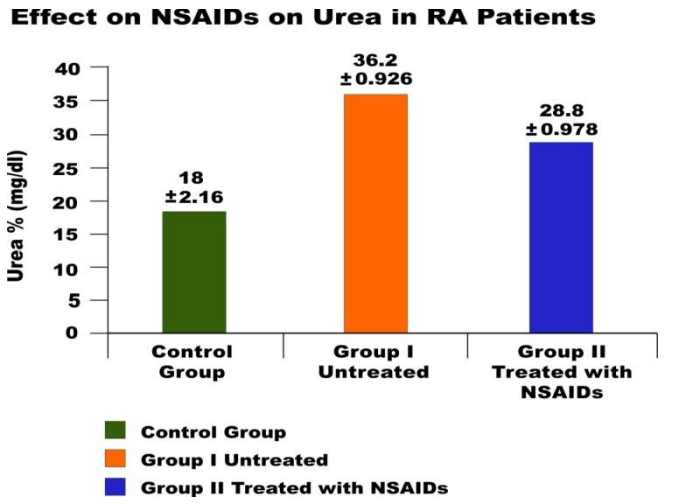
ESR Percentage (mg/dl)

PARTICULARS	*CONTROL GROUP*	*GROUP - I*	*GROUP –II*
Sample size	50	50	50
Mean	12.8	48.4	31.3
± S.D	0.354	1.622	1.45
% INC	-	287.0%	150.4%
% DEC	-	-	-
t- value	-	30.1	17.4
p- value	-	<0.001	<0.001



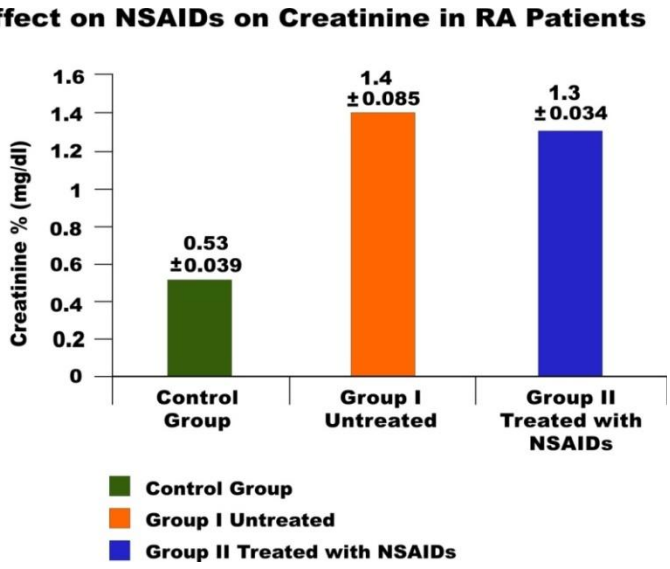
Urea Percentage (mg/dl)

PARTICULARS	*CONTROL GROUP*	*GROUP - I*	*GROUP –I*
Sample size	50	50	50
Mean	18	36.2	28.8
± S.D	2.16	0.926	0.978
% INC	-	101.1%	55.5%
% DEC	-	-	-
t- value	-	10.73	6.315
p- value	-	<0.01	<0.01



Creatinine Percentage (mg/dl)

PARTICULARS	*CONTROL GROUP*	*GROUP - I*	*GROUP –II*
Sample size	50	50	50
Mean	.53	1.4	1.3
± S.D	.039	.085	.034
% INC	-	164.1%	145.2%
% DEC	-	-	-
t- value	-	14.5	25.6
p- value	-	<0.001	<0.001



RESULTS

Elevated Erythrocyte Sedimentation Rate (ESR) values were observed in both the groups. Untreated Group I showed 287.2% and treated Group-II showed 150.4% raised ESR ($p<0.001$). Raised ESR values besides being a marker for inflammation is also an indicator of an increased oxidant stress in both groups. The serum concentration of urea and creatinine were significantly higher ($p<0.01$) in untreated RA patients (Group I) than in healthy controls, which on treatment with NSAIDs (Group-II) showed a decrease in levels of the above parameters, but this decrease is not statistically significant.

DISCUSSION

We chose to study the effect of NSAIDs on kidney in RA patients, as it is the commonest inflammatory rheumatic disorder needing long term NSAIDs. Further, renal disease primarily due to RA is extremely rare. [12]

Studies on non steroidal anti-inflammatory drugs induced intestinal inflammation in humans by Bjarrason I, Zanelli G, Smith T. et al[13] showed that intestinal and colonic inflammation also occur commonly in patients with rheumatic diseases receiving NSAIDs. Such lesions may also lead to blood and protein loss from the gut.One of the early events in the normal inflammatory reaction is increased activation and migration of leucocytes into the inflamed area, to indicate the degree or severity of inflammation in the body; erythrocyte sedimentation rate (ESR) test is performed. A high "Sedimentation rate" means onset of inflammation. By periodic tests, a doctor can tell whether the inflammation in the joint is getting better or worse. In case of rheumatoid arthritis (RA) it is usually high.

Earlier findings concerning a high erythrocyte sedimentation rate by Carlson L.A. et al[14] may be partly an explanation of the infectious processes.

Barland P., Lipstein E.[15] in their article on "selection and use of laboratory tests in the rheumatic diseases", Considered Westergren erythrocyte sedimentation rate as markers of disease activity. They observed strong and consistent association between several indicators of inflammation in patients with rheumatoid arthritis, including clinical indicator, such as the disability score and the number of swollen joints, as well as biochemical markers of inflammation such as erythrocyte sedimentation rate (ESR).

These above studies, support our finding of increased ESR in RA patients which is statistically significant.

Serum creatinine is the most commonly used marker of renal insufficiency (RI). Creatinine clearance the other measure of

renal function is time consuming, often unreliable and not routinely practiced.[16]

Increased values of serum creatinine and serum urea in patients suffering rheumatoid arthritis ,which on treatment with NSAIDs showed decrease in the levels but not so significant, from our study ,is similar to the findings of Gastrointestinal toxicity with Celecoxib vs Non-steroidal Antinflammatory Drugs for Osteoarthritis and Rheumatoid Arthritis, by Fried E.Silverstein, MD et al showed that the overall incidence of renal adverse effects,and the incidence of increased creatinine and hypertension in particular, were significantly lower in patients receiving celecoxib than in those receiving NSAIDs.also ,significantly more patients receiving NSAIDs exhibited clinically significant elevations in serum creatinine and/or serum urea nitrogen levels than celecoxib.[17]

Further study on" Renal co-morbidity in patients with rheumatic diseases "by Anders and Vielhauer, showed that owing to high prevalence, RA and renal disease often coincide. The renal toxicity of antirheumatic drugs (for example, NSAIDs), secondary renal disease induced by the chronic inflammatory process and, potentially, renal manifestations of the primary disease process, however, are important differential diagnosis. They further showed that, elevated serum creatinine values were found in 19% of prevalent RA patients.[18]

NSAIDs (including cyclooxygenase-2 inhibitors) can cause acute deterioration of renal function, because renal blood flow is dependent on renal prostaglandin synthesis.[19,20]

CONCLUSION

Patients with rheumatic diseases must be routinely monitored by blood and urinary parameters, both. Ideally, patients with rheumatic diseases and renal comorbidity should be managed through close collaboration between a rheumatologist and a nephrologist.

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