Abstract
1.0 ABSTRACT

The present study was designed to evaluate the interaction of angiotensin converting enzyme inhibitors (ACEIs) enalapril and lisinopril, and concomitantly administered diclofenac sodium in non-diabetic and diabetic hypertensive arthritic patients. The study was conducted in a total of 148 patients who were divided into eight different groups based on the underlying diseases and the treatment regimen. The parameters studied included demographic profile of the patients viz. age, sex, height, weight, risk factors involved and underlying diseases, physical parameters like systolic blood pressure (SBP), diastolic blood pressure (DBP) and biochemical parameters viz. insulin sensitivity and urinary albumin excretion rate (in diabetic patients only), platelet aggregation, renal function, serum electrolytes, lipid profile and hepatic function.

The blood pressure control with enalapril as well as lisinopril was reduced by simultaneously administered diclofenac sodium in non-diabetic and diabetic patients when compared with the patients receiving either of the ACEIs alone. Insulin sensitivity and urinary albumin excretion rate were also reduced by diclofenac sodium treatment in diabetic patients receiving either enalapril or lisinopril. Further, concomitant treatment with diclofenac sodium along with either of the ACEIs showed significant reduction in platelet aggregatory effect of the former when compared with patients receiving ACEIs alone.

Serum electrolytes were found altered in patients receiving the combination treatment with diclofenac sodium and ACEIs. Significant lowering of serum sodium levels was observed in both non-diabetic and diabetic patients receiving either of the ACEIs alone and also those patients receiving diclofenac sodium-ACEI combination. Whereas serum potassium level increased in non-diabetic as well as diabetic patients receiving diclofenac sodium in combination with either of the ACEIs.

Renal function of these patients was studied in terms of serum creatinine and blood urea nitrogen (BUN) levels. Serum creatinine levels increased
significantly in non-diabetic patients receiving combination of diclofenac sodium and ACEIs. The BUN levels were also significantly raised in both non-diabetic and diabetic patients receiving the combination. However, these findings were not clinically significant.

Lipid profile was studied in terms of serum cholesterol, serum triglyceride, serum low density lipoprotein (LDL), serum high density lipoprotein (HDL), serum cholesterol/HDL ratio and serum LDL/HDL ratio. Combined treatment with diclofenac sodium and lisinopril effectively reduced serum cholesterol levels when compared with patients receiving only lisinopril treatment. Serum triglyceride levels were reduced significantly in both non-diabetic and diabetic patients receiving diclofenac sodium and enalapril combination. Reduction in serum triglyceride levels were found to be significant in diabetic patients receiving the combination of diclofenac sodium and lismopril. Serum LDL levels reduced significantly in diabetic patients receiving enalapril-diclofenac sodium combination. Concomitant treatment with diclofenac sodium and either of the ACEIs showed significant rise in serum HDL levels. Besides, serum LDL/HDL and serum cholesterol/HDL ratios decreased significantly upon treatment with either of the ACEIs combined with diclofenac sodium.

Hepatic function was studied in terms of serum glutamate oxaloacetate transaminase (SGOT) and serum glutamate pyruvate transaminase (SGPT) activities There was no clinically significant change observed in activity of these enzymes in any of the treatment groups.

In the light of these observations it can be concluded that concomitant administration of diclofenac sodium with ACEIs (enalapril / lisinopril) has beneficial effect on lipid profile, insulin sensitivity, and platelet aggregation. On the other hand, the antihypertensive efficacy of the ACEIs and renal function of the patients may be adversely affected by inclusion of diclofenac sodium in the therapy with ACEI. Although hepatic function was not affected by ACEIs or by the combination of
diclofenac sodium with ACEI to the extent of clinical significance, periodic monitoring of hepatic function may be indicated on the basis of earlier reports of hepatotoxicity with ACEIs. Serum potassium and serum sodium levels were also altered without demonstrating any clinical symptoms. However, close monitoring of the patients for any signs and symptoms of hyponatremia and/or hyperkalemia in the light of our observations on the effect of ACEIs-diclofenac sodium combination on serum electrolytes. It can also be suggested that blood pressure and renal function may be closely monitored in hypertensive arthritic patients (with or without diabetes mellitus) receiving NSAID and ACEI combination.