7.0 CONCLUSIONS

- The present study demonstrates that aspirin adversely interacts with ACE inhibitor in hypertensive rats.

- High doses of aspirin interact potentially adversely than low doses. This was evident from higher mortality rate in hypertensive rats and complete reversal of cardio-renal protective effect of ACE inhibitor by high-dose aspirin.

- Although low dose aspirin produced little mortality; moderate and variable toxic effects were observed on pathological examination of cardiac muscle fiber and renal tissue of rats receiving ACE inhibitor simultaneously.

- The concomitant administration of aspirin and ACE inhibitor in normal rats caused no toxicity indicating that the combination is potentially hazardous in degenerative conditions like hypertension or congestive heart failure.

- Angiotensin receptor blocker (ARB), telmisartan showed only moderate reduction in systolic blood pressure with only moderate protective effect on myocardium and kidney of L-NAME treated rats. However, it caused significant regression of vascular hypertrophy. Aspirin did not interfere with blood pressure lowering effect or vascular remodeling of telmisartan but abolished the cardioprotective effect of telmisartan.

- The COX-2 inhibitor rofecoxib, is cardio-toxic, interferes with cardio-renal protection of ACE inhibitor and causes destabilization of blood pressure. We propose that the cardiotoxic and nephrotoxic property is shared by all other COX-2 inhibitors, which should be prescribed with caution only in patients for which these drugs have proven efficacy and should be contraindicated in patients of cardiovascular and renal diseases.

- The role of sodium hydrogen exchange in the etiology and pathogenesis of human hypertension should be explored and the possibility of sodium hydrogen exchange inhibitors as antihypertensives should be further investigated.
The acute administration of aspirin caused myocardial depressant effect in patients of advanced congestive heart failure indicating the detrimental effect of aspirin on the clinical status of such patients.

Whether a patient on ischemic heart disease on an ACE inhibitor should be placed on aspirin may rest on the severity of heart failure. The more severe the heart failure, the more likely an appreciable interaction between aspirin and ACE inhibitor will occur. Therefore, therapy with alternative agents such as warfarin or clopidogrel which do not interfere with prostaglandin system is recommended.

FUTURE DIRECTIONS

Aspirin has been shown to reduce cardiovascular morbidity and mortality in patients with preexisting vascular disease. However, there is variability in the way individuals respond. Persistent normal platelet function despite therapy referred to as "aspirin resistance" is associated with an increased risk of major cardiovascular events. Although formal diagnostic criteria and a validated method of measurement are lacking, aspirin resistance may affect between 5% and 45% of population. Given the prevalence of cardiovascular disease, the potential impact of aspirin resistance is large. Currently there are many unanswered questions regarding the biological mechanism, diagnosis, population prevalence, clinical relevance, and optimal therapeutic intervention for aspirin resistance. Polymorphism in COX gene has been described which modify response to aspirin. In addition, many patients for secondary prevention of cardiovascular events are prescribed low-dose enteric coated formulations for aspirin which may provide inadequate drug bioavailability and incomplete inhibition of platelet COX activity. Further epidemiological studies can be done to address these questions to predict increased risk of future atherosclerotic events in patients receiving aspirin.