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**A Comparative study for Evaluation of Different
Doses of Oral Flecainide and Sotalol as Combination
for Termination of Atrial Fibrillation**

**A Thesis Submitted to the Department of Clinical Pharmacy and
the Committee of Post Graduate Studies of the College of
Pharmacy – University of Baghdad as Partial Fulfillment of the
Requirements for the Philosophy Degree in Clinical Pharmacy**

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ABSTRACT

Background: Oral combination of flecainide and sotalol for termination of atrial fibrillation was not described, only in very small number of case reports. Combining antiarrhythmic drugs orally may allow for lower doses of each drug, reduce potential risk of unwanted side effects and maintaining the same or, due to synergism between these drugs, may improve their antiarrhythmic potential.

Aims of the study: Evaluation the efficacy of Flecainide- Sotalol combination ; used orally for termination of atrial fibrillation and estimate the effective dose in the combinations through measuring of percentage and time of conversion, of atrial fibrillation to sinus rhythm and evaluation the effect of these combinations on ECG data ;that include P, PR, QRS, QTc intervals & heart rate; in comparison with amiodarone intravenous group and oral combination of flecainide 100mg plus metoprolol 50mg; in order to find out if there are any significant differences in the electrophysiological effects produced by flecainide sotalol combinations. Finally; evaluating new created mathematic relationship called combined risk ratio to evaluate patient rhythm stability and the risk of proarrhythmia.

Patients and methods: single blinded prospected clinical trial conducted by participation of One hundred and six (106) hemodynamically stable patients, (age 56.3 ± 13 years, range 18-90 years) have highly symptomatic episodes of atrial fibrillation lasting ≤ 48 hours; were randomly allocated to groups (by simple randomization); each group received the recommended treatment as follow: **Group1 (N=28):** Intravenous amiodarone as bolus then maintenance, the remaining groups treated by combination therapy used as single oral dose as fellow **Group2 (N=17):** Flecainide 100mg - metaprolol tartrate 50 mg. **Group3 (N=21):** Flecainide 100mg - Sotalol 80

mg. **Group4 (N=21):** Flecainide 100mg - Sotalol 120 mg. **Group5 (N=19):** Flecainide 150mg - Sotalol 80 mg.

Results: Groups 3, 4, 5 when compared with group 1 & 2:

- 1- Had significantly (at $p < 0.05$) higher conversions rate at 8 and 24 hours; except group 3 was significant as compared with group 1 only after 24hours.
- 2- Had significantly shorter (at $p < 0.05$) conversion time;
- 3- Had no significant differences (at $p < 0.05$) in QTc interval and P wave duration after treatment.
- 4- Had only significant shorter (at $p < 0.05$) QRS, PR and slower heart rate as compared with group2.
- 5- Group 4 had significantly greatest declining (at $p < 0.05$) in heart rate after treatment, highest percentage of patients having **combined Risk Ratio (CRR) ≤ 1** and Significantly lowest mean value as compared with other groups.
- 6- Time required to restore sinus rhythm; in this study, was significantly correlated (at $p < 0.05$) with changes in QRS, QTc, Heart rates, combined risk ratios, PR intervals and episodes duration before starting treatment. Thus estimation of likelihood and time required for conversion to sinus rhythm is difficult and cannot be predicted from one study parameter.

Conclusions: flecainide- sotalol combinations characterized by higher conversion rate and shorter conversion time than amiodarone and flecainide – metoprolol combination (flecainide 100mg plus sotalol 120 mg oral combination is most efficient) and their effects on ECG data during treatment was not significantly different from intravenous amiodarone which is widely used for managing patients with atrial fibrillation in CCU.