

**EFFECT OF CLEXANE ON  
DETERMINING PREGNANCY  
OUTCOME IN PATIENTS WITH HIGH  
RISK OF DEVELOPING  
ANTIPHOSPHOLIPID ANTIBODIES**

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# Our Aim of this study

- ◆ To evaluate the effect of empirical Clexane administration on pregnancy outcome in patients with high risk of developing antiphospholipid antibodies and devise the optimum effective dose and timing of administration.

- ◆ Phospholipid antibodies, lupus anticoagulant, and cardiolipin antibodies are associated with recurrent miscarriage, thrombosis, and thrombocytopenia (Harris 1987).

- ◆ Fifteen per cent of women with a history of recurrent miscarriage (three or more consecutive losses of pregnancy) have persistently positive results for phospholipid antibodies (Rai et al 1995).

- ◆ These women have a rate of fetal loss of 90% when no specific treatment is given during pregnancy (Rai et al 1997).

- ◆ Many women with antiphospholipid syndrome who attend recurrent miscarriage clinics have antiphospholipid antibodies as the sole identifiable pathologic abnormality, and the antibodies are often present at a low level. (Birdsall 1992)

- ◆ There are 6 reported randomized controlled trials. Kutteh 1996  
[Laskin et al 1997, Cowchock et al 1997, Silver et al 1993, Rai et al 1997, Cowchock et al 1992.]

- ◆ A major concern with the published trials is that women with divergent clinical presentations have been grouped together and not stratified by clinical presentation or by antibody type or level. Kutteh 1996;

- ◆ The authors of the recent consensus statement on the antiphospholipid antibody syndrome pointed out the need for stratification in future studies to address the various patient subgroups that make up the population with antiphospholipid syndrome. (Piette 1999)

- ◆ Therapies from these trials suggests that women with antiphospholipid syndrome should be treated with aspirin and heparin throughout pregnancy.

- ◆ Screening for antiphospholipid antibodies is a subject to widespread interlaboratory variation.
- ◆ The performance of these assays is one of the most controversial issues in laboratory, for several reasons : sensitivity to preanalytical variables fluctuating titres over time , variety of assays used to detect same antibody.

# Possible pathogenesis

- ◆ PRL and IGFB -1 were found to be significantly decreased after exposure of endometrial stromal cells to monoclonal anticardiolipin Antibody ID2 (Mak et al 2002)
- ◆ Trophoblast function is as well affected by antiphospholipid antibodies increasing placental apoptosis and impairing trophoblastic invasion

# Patients and methods

- ◆ This study included 50 pregnant females aged 24-32 years with high risk of developing antiphospholipid antibodies. All patients were tested for anticardiolipin antibodies, lupus anticoagulant, thrombophilia and proteins C & S before conception and showed normal levels.

# Inclusion Criteria

- ◆ History of missed abortion.
- ◆ History of previous IUFD.
- ◆ History of recurrent PIH with IUGR,
- ◆ ICSI patients with history of missed abortion in previous trial.

# Exclusion criteria

- ◆ All with anticardiolipin antibody +ve patients (IgG/IgM)
- ◆ All with lupus anticoagulant level above 42
- ◆ +ve thrombophilia, or anomalies of protein C or S.

*Group I (Control group):*

25 patients were given empirical low dose Aspirin 100mg/day starting from the day of diagnosis of pregnancy

## *Group II (Clexane treated group)*

The other 25 patients were given empirical Clexane 40mg/day starting from the verification of healthy intrauterine pregnancy by U/S, in addition to low dose Aspirin as in Group I.

- ◆ All Patients were followed up every week from the 20th week of pregnancy by U/S Doppler examination and were terminated between 32-36 weeks according to the presence of alarming signs as diminished liquor, PIH or adverse Umbilical artery Doppler

- ◆ We used the RI for measuring the Umbilical artery blood flow.

## Neonatal outcome evaluation included:

- ◆ Pregnancy duration.
- ◆ Birth Weight.
- ◆ Admission to NICU (Neonatal Intensive Care Unit).
- ◆ The incidence of Intracranial Hemorrhage, Mortality and Stillbirth.

- ◆ Data was gathered and the results were statistically evaluated using the student-t test and p-value for comparison between the two group.
- ◆ Also the relative risk and relative risk reduction was evaluated for group II.

# Comparison between outcome parameters

	Group I	Group II
<b>Pregnancy Duration</b>	32±3.59 wks	35±1.67 wks*
<b>UA Doppler (RI)</b>	0.63±0.14	0.56±0.09*
<b>Birth Weight</b>	2455±213 gm	2537±190 gm
<b>Intracranial Hge.</b>	3 cases (12%)	2 cases (8%)
<b>Admission to NICU</b>	10 cases (40%)	3 cases (12%)*

*\*Statistically significant difference*

	Relative Risk	Relative Risk reduction
Intracranial Hge	0.67	33%
Admision to NICU	0.3	70%

# Conclusion

- ◆ The results of this study suggests that prophylactic Clexane at a dose of 40mg daily appears to enhance pregnancy course and outcome for patients with high risk of developing antiphospholipid antibodies during pregnancy.

- ◆ Further studies may be required to optimize the dose of Clexane and decide whether it should be increased empirically or in patients who develop antiphospholipid antibody reactions during pregnancy.

- ◆ Low molecular weight heparin prolonged pregnancy duration, improved neonatal outcome (reduced incidence of intracranial haemorrhage)

- ◆ Larger scale study is definitely needed for determining beneficial effects of LMWH ( decreasing complications of PIH, beating prematurity) as well as Hazards (?? PROM, long term affection of Bone integrity) and adequate dosage(??individualized)

◆ Developing new laboratory cut off values regarding antiphospholipid Antibodies ( positivity at lower levels ).

??????? Atypical Antiphospholipid Syndrome!!!!!!!!!!

THANK YOU ALL