

# Increased Thrombophilic Predisposition In Premenopausal Females With Chronic Migraine

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## Background

- Female migraineurs aged <45 years are at increased risk of cardiovascular diseases (CVD);
- The pathophysiological mechanisms linking migraine and CVD might include a procoagulant status;
- Inherited thrombophilic factors have been generally emphasized;

*however*

- Endothelial dysfunction in migraine may well be responsible for an acquired prothrombotic state due to a loss of anticoagulant properties.

## Aim

To explore the thrombophilic potential of patients with migraine using a novel standardized assay for globally screening the patient thrombophilic state in a large, unselected, carefully clinically characterized population of episodic and chronic migraineurs.

## Methods

We evaluated the thrombophilic state of 550 patients (M/F: 108/442 females, aged 47.13 yrs) affected by episodic (n=413) or chronic migraine (n=137) using an assay investigating activated protein C (APC)-dependent thrombin generation [HemosIL ThromboPath (ThP)] used as a global thrombophilic screening tool, owing to a 95% sensitivity to protein C pathway abnormalities (acquired and/or inherited).

## Results

- APC functionality was impaired in migraineurs versus healthy controls (Fig. 1);
- Female sex and attack frequency were both associated to a thrombophilic condition in migraineurs (Table);
- None of the tested variables associated with APC function in the male cohort;
- Pre-menopausal status (Fig. 2), high attack frequency (Fig. 3) and use of OC/HRT (Table) were all independent predictors of impaired APC functionality in females.

## Stepwise multiple regression analysis of variables associated with thrombophilic predisposition in migraineurs

Dependent Variable	Explanatory Variable	Overall population (n=550)		Female patients (n=448)	
		Regression coefficient (SE)	p	Regression coefficient (SE)	p
ThromboPath	Sex, F/M	-0.118 (0.047)	0.011	-----	---
	Frequency	-0.100 (0.048)	0.036	-0.123 (0.054)	0.023
	Age	0.082 (0.049)	0.097	0.118 (0.055)	0.033
	OC or HRT	-----	---	-0.153 (0.052)	0.004

## Conclusions

- Migraineurs show an impairment of APC functionality correlating with female sex, young age and *near-daily* chronic migraine, but not other factors affecting pro-coagulant status ((cardiovascular risk factors, overt cardiovascular disease, or concomitant medications, ecc);
- Premenopausal *near-daily* chronic migraineurs are in a prothrombotic condition possibly due to an imbalance of the PC pathway, which might increase the ischemic risk especially when OC are being used;
- A possible link between inflammation and pro-coagulant switch could be involved;
- In these patients, we suggest to in depth assess concomitant vascular risk factors, carefully ponder oral contraceptive use, improve the use of aspirin as abortive agent, prevent the overuse of analgesics known to increase the ischemic risk and favor the prophylactic use of medications improving endothelial function such as sartans or statins.

