The Relation between Short Course Oral Contraceptive Consumption and Cerebral Vein Thrombosis in Ramadan

Morteza Saidee[1], Mohsen Froghipoor[2], Payam Sasannejad [2],Ali Mellat Ardakani[3],Mohmoud Reza Azarpazhooh[1]

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Abstract

Introduction: There is a tendency in Muslim women to postpone their menstrual period with short course oral contraceptive (OC) consumption during Ramadan as well as Hajj Ceremony. Driven by many anecdotal reports regarding stroke, particularly cerebral Vein thrombosis (CVT) in Ramadan, this research was designed to investigate the incidence of CVT and its temporal relation with Ramadan.

Methods: This study was conducted between September 2006 and October 2007 and included 2 consecutive Ramadans. All patients with definite diagnosis of CVT in Ghaem Hospital of Mashhad were registered. We assessed all of the possible causes of CVT and analyzed the temporal aspect of CVT occurrence.

Results: 24 cases with CVT (5 males and 19 females) were recruited during study period. 11 cases were admitted during Ramadan months which was significantly higher than all the other 11 months (P value=0.00035 , χ^2= 17.1). There seems to be no underlying disorders for CVT in Ramadan except OC consumption.

Conclusion: The higher incidences of CVT in Ramadan may be related to OC consumption. Although we could not identify any risk factors such as hypercoagulopathy state in these cases, it is still possible to implicate an unknown genetic background which can result in CVT in special scenarios such as OC consumption. We need to consider fasting situation, dehydration and physical stress in Ramadan as probable cofactors for CVT.

Keywords: Cerebral Vein thrombosis, Oral contraceptive, Ramadan

[1] *Assistant Professor of Neurology, Department of Neurology, Ghaem Medical Center, Mashhad University of Medical Science (MUMS), Mashhad, Iran.*
[2] *Assistant Professor of Neurology, Department of Neurology, Ghaem Medical Center, MUMS*
[3] *Resident of Neurology, Department of Neurology, Ghaem Medical Center, MUMS*

Introduction

Oral contraceptive (OC) consumption is one of the most popular ways of birth control in the world. Shortly after the introduction of the first generation of the OC some adverse vascular effects were reported.[1] Several studies have clearly shown the relation between OC and cerebrovascular, cardiovascular, as well as peripheral vascular diseases.[2-6] The recent studies which dealt with newer generations of OC could not prove any higher rate of vascular disorders except CVT and deep vein thrombosis (DVT).[7] This fact might be explained by the changes in the drug's composition, more appropriate consumption manner of the drug and better consideration of relative and absolute contraindication of OC. Although the real mechanism of venous thrombosis has not been identified yet, there is evidence that it may result from hypercogulopathy disorders such as Factor V Leiden deficiency.[8-12]

Most of the studies in the field of OC side effects assessed the safety of the long term OC consumption.[13] However, assessing the safety of short course OC consumption is important in the Muslim community.[14] Based on the Islamic principles, there are some restrictions for women in menstrual period which prohibits them from entering particular places in holy cities of Mecca and Medina and disallows their fasting for the rest of the month. Therefore, driven by their strong desire to fulfill their religious duties, they use different types of OC in order to postpone menstruation. There is plenty of anecdotal report of stroke and CVT in young women with history of short course OC consumption in Hajj and Ramadan and thus, we aimed this study to evaluate the incidence of CVT and its possible relation with OC consumption in Ramadan.

Methods

This study was conducted between September 2006 (Ramadan 1427 in Islamic Calendar) and October 2007 (Ramadan 1428) and included 2 consecutive Ramadans. We extended the study period for 12 months, and this study will come to end at 2008. We registered all patients with definite diagnosis of CVT in Ghaem Hospital of Mashhad, which is the most important referral center of neurology in the north east of Iran. CVT was diagnosed based on the clinical presentations and neuroimaging findings including brain CT scan with or without contrast, Brain MRI, MR-Venography, temporal bone CT scan and in some cases four-vessel brain angiography.

All patients were evaluated for CVT risk factors including past history or family history of venous thrombosis, hypercogulopathy state, collagen vascular disorders, infectious disorders,

complicated otitis, cancer, past history of trauma, drug abuse and history of migraine. History of short and long-term consumption of OC, and the type of OC based on the estradiol component were taken into account. The common contraceptive pills in Iran are "Low-Dose" OC (LD, 35µg ethynil-estradiol and 0.3 µg nervogesterone) and "High-Dose" OC (HD, 50 µg ethynil-estradiol and 0.5 µg nervogesterone).

We perfectly complied with all ethical issues in this research. We did not interfere with patients' management and the patients' data was collected and saved in numerical codes which was solely used for scientific purposes. Data was analyzed using SPSS version 11.5, Chi-square (goodness of fit) test was used and P value less than 0.05 considered significant.

Results

This is an ongoing study and we reported the result of first year in this paper. 24 cases with definite diagnosis of CVT (5 males and 19 females) were recruited during the study period. 11 cases were admitted in Ramadan months which is significantly higher than all the reminding 11 months($P=0.00035$, $\chi^2= 17.1$).

As displayed in table 1, all the patients in Ramadan were women and there seemed to be no underlying disorders except OC consumption. 10 cases had used LD and one had history of HD consumption. The superior sagittal sinus either with or without lateral sinuses was the most common site of injuries. Venous infarct with or without parenchymal hemorrhage was reported in 9 cases. One patient died in hospital and 2 were discharged with significant disability (Modified Rankin scale≥3).

13 cases were admitted in months other than Ramadan. 5 cases were men and 8 were women. 9 cases presented with definite risk factors for CVT (2 cases with hypercogulopathy states, 4 with complicated otitis or mastoiditis, 1 with history of drug abuse, 1 pregnant woman and 1 case with history of severe dehydration). Super sagittal sinus (with or without lateral sinuses) was still the most frequent site of injuries. Imaging abnormalities were less frequent than in cases with CVT in Ramadan (6/13 Vs 9/11 respectively). All of the patients were discharged without significant disabilities. Seizure and focal neurologic deficits were more common in the group with CVT in Ramadan.

Discussion

Cardiovascular, cerebrovascular as well as peripheral vascular disorders are possible major side effects of OC.[2-6] While several studies have evaluated the safety of long-term OC consumption, there is scant data regarding safety of short-term OC consumption.[13] Most of the studies pointed to the venous thrombosis as the most considerable side effect which might stem from a genetic background of hypercoagulopathic

disorders.[8-12] However, the safety and the real mechanism of vascular events, particularly in newer generation of OC, is still a matter of debate.

The result of this study clearly showed the higher incidence of CVT in Ramadan (P=0.00035). We could not detect any risk factors in this group except OC consumption. The major causes for CVT should be multifactorial. Although we could not identify any hypercogulopathic disorders, there might be a genetic background condition which could possibly be exaggerated upon OC consumption. We also need to consider some predisposing factors in Ramadan such as dehydration, tiredness and rigors of fasting. On the other hand, continuous consumption of tablets for more than a month, which deviates from the conventional manners, can also affect the vascular conditions due to hormonal changes.

Even though our sample size was not large enough to allow precise discussion of distribution of injuries and symptoms of CVT, it seems that the conditions of those with CVT in Ramadan were more severe in terms of clinical presentations and final outcome (table 1).

Table1: The CVT details in Ramadan months compared to the other months

		PATIENT WITH CVT* IN RAMADAN N=11	PATIENT WITH CVT NOT IN RAMADAN N=13
Gender : (M/F)		-/11	5/8
Age (Years): (M/F)		-/38	28/36
Underlying disorders		-	9
History of OC** Consumption	Short term	11	0
	Long term	0	3
Type of OC	LD***	10	3
	HD*****	1	0
Clinical features	Headache	11	13
	Seizure	11	4
	Focal Neurologic Deficit	10	4
Site of sinus involvement	Superior Sagittal Sinus	10	11
	Right Lateral Sinus	5	5
	Left Lateral Sinus	4	4
Type of brain injury(imaging abnormalities)	Venous Infarct	2	5
	Parenchymal hemorrhage	5	5
	Subarachnoidal hemorrhage	4	1
Mortality and morbidity		3	0

*: Cerebral Vein Thrombosis **: Oral Contraceptive ***: Low Dose Oral Contraceptive ****: High Dose Oral Contraceptive

There were some limitations in our study. We could not recruit a sufficiently large sample population which is generally due to the low incidence of CVT. Therefore we extended the study period to include two consecutive Ramadans so as to incorporate more cases. On the other hand we extended the study period for another 12 months and will report the final result after the Ramadan 2008. We only managed to evaluate the common causes of hypercoagulopathic disorders such as factor V Leiden deficiency, Pr C and S deficiency, anti thrombin III deficiency and collagen vascular disorders, but failed to perform a more thorough genetics study.

Conclusion

Short-term OC consumption may lead to serious vascular disorders such as CVT and thus, should be prescribed with utmost caution. A multicenter study with a larger sample size and more comprehensive investigation of possible causes is highly recommended. The authors wish to thank Dr. Habib Allah Esmaili for his valued assistance in statistical analysis of the project.

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رابطه بین مصرف کوتاه مدت قرص های ضد بارداری و پیدایش ترومبوز وریدی در ماه مبارک رمضان

دکتر مرتضی سعیدی، دکتر محسن فروغی پور، دکتر پیام ساسان نژاد، دکتر علی ملت اردکانی، دکتر محمودرضا آذرپژوه

فصلنامه علوم مغزواعصاب ایران، سال هفتم، شماره۲۳، پاییز ۱۳۸۷ ، ۲۶۰-۲۶۵

چکیده:

زمینه و هدف: در طی ایام حج و ماه مبارک رمضان زنان مسلمان تمایل به استفاده از قرص های ضد بارداری و در نتیجه تعویق دوره عادت ماهانه دارند. با در نظر گرفتن گزارشات موردی از سکته های مغزی بویژه ترومبوز وریدی مغزی در ماه رمضان این مطالعه جهت تعیین رابطه بین مصرف کوتاه مدت قرص های ضد بارداری و ترومبوز وریدی در ماه مبارک رمضان طراحی شد.

روش بررسی: این مطالعه در حد فاصل سپتامبر ۲۰۰۶ تا اکتبر ۲۰۰۷ انجام گرفته و شامل ۲ ماه رمضان بود. تمام بیماران با تشخیص قطعی ترومبوز وریدی مغزی در مرکز پزشکی قائم عج مشهد تحت بررسی قرار گرفتند. تمام علل احتمالی ترومبوز وریدی و رابطه زمانی وقوع کسالت بررسی و تجزیه و تحلیل شد.

یافته‌ها: ۲۴ بیمار با تشخیص قطعی ترومبوز وریدی مغزی (۵ مرد و ۱۹ زن) در طی دوره مطالعه تشخیص داده شدند. ۱۱ بیمار در ماه مبارک دچار عارضه شدند که این میزان به طور معنی داری بیشتر از ۱۱ ماه دیگر بود (χ^2 =۱۷/۱) (P = ۰/۰۰۰۳۵) .

نتیجه‌گیری: میزان بیشتر ترومبوز وریدی در رمضان می تواند مربوط به مصرف کوتاه مدت قرص های ضد بارداری باشد. هرچند که در این گروه بیماران هیچ عامل طر آفرینی جهت ترومبوز وریدی از جمله بیش انعقادی پیدا نشد، هنوز این احتمال مطرح است که یک عامل زمینه‌ای ژنتیک وجود داشته باشد که در شرایط خاص مانند مصرف قرص ضدبارداری منجر به ترومبوز وریدی مغزی شود. لازم است برخی عوامل احتمالی زمینه ساز دیگر در ماه مبارک شامل شرایط روزه داری، دهیدراتاسیون، استرس فیزیکی نیز مد نظر قرار گیرد.

واژگان کلیدی: ترومبوز وریدی مغز، قرص‌های ضد بارداری، رمضان