

Effect of Fasting in Patients Taking Acenocoumarol

A. Chachi^{1*}, S. Jourani¹, A. Benbahia¹, M. Eljamili¹, S. Elkarimi¹, D. Benzarouel¹, M. Elhattaoui¹

¹Cardiology Department, MOHAMMED VI University hospital, Marrakech, Morocco

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*Corresponding author: A. Chachi

Cardiology Department, MOHAMMED VI University hospital, Marrakech, Morocco

Abstract

Original Research Article

Anticoagulation with acenocoumarol is influenced by dietary changes but the effect of fasting on acenocoumarol therapy is unknown. **Objectives:** To study changes in international normalized ratio (INR) and the percentage of time within therapeutic range (%TTR) before and during Ramadan. **Methods/Patients:** In this prospective study, weekly INR readings were taken from participating patients during two study periods: before and during Ramadan. Readings were blinded to patients and their primary physicians except for when pre-set study endpoints were reached. Results: Among 128 participating patients, mean INR increased by 0.25 ($P = 0.006$) during Ramadan from the pre-Ramadan month. There was no significant difference ($P = 0,02$) in mean INR between the non-Ramadan months. No bleeding or thrombotic events were recorded. **Conclusion:** Fasting significantly increases the mean INR of medically stable patients taking acenocoumarol and the likelihood of having an INR above therapeutic targets.

Keywords: Fasting, Ramadan, Acenocoumarol, international normalized ratio.

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INTRODUCTION

Ramadan, is observed by approximately 400 million Muslims all over the world [1]. During Ramadan, Muslims abstain from food and drink from dawn until sunset. While a significant number of patients with heart disease insist on fasting despite the physician's medical advice, physicians do not always know how to advise such patients regarding fasting during Ramadan. Several studies have been published on the effects of fasting in healthy adults, but little is known on the clinical problems during the fast of Ramadan [1, 2]. Only few have studied the metabolic implications of Ramadan fasting [3, 4]. The aim of this study was to assess the impact of fasting during Ramadan on the clinical status of patients with cardiac disease, and to evaluate the effects of fasting on their biochemical profiles.

METHODS

To study the effects of fasting Ramadan on cardiac patients, 148 patients seen in the cardiac outpatient clinic with intention to fast were studied. Patients were recruited to the study during the 3 days prior to the onset of Ramadan. Detailed clinical and biochemical assessments were performed within 3 days

before the start of Ramadan and then on the 28th day of Ramadan. Fasting blood was taken for full blood count (EDTA 4.5 ml tube, Beckman Coulter Gen-S automated analyzer), erythrocyte sedimentation rate (ESR) (EDTA 4.5 ml tube, Westergen method), prothrombin time (PT), partial thromboplastin time (PTT) (citrate blood 4.5 ml tube, Dade-Behring analyzer). The blood was drawn between 12 and 2 o'clock p.m. The patients were advised to take their medications regularly and adjustment to once or twice daily drugs was made.

Statistical analysis

All values are expressed as mean standard deviation. Continuous variables are compared with 2 tailed t-test. Categorical variables are compared using the chi-square test. The p value 0.05 was considered significant.

RESULTS

A total of 128 patients consented to participate in this study. Patient demographics, indications for acenocoumarol and prescribed INR targets are shown in Table 1. Among this cohort, most patients suffered from atrial fibrillation (84,3%), venous thromboembolism (9,4%) and had an INR target of 2.0–3.0 (93,75%). The INR readings of the 128 patients who completed the

study were used for analysis of the study endpoints. The results of the primary outcome are shown in Table 2. Mean INR readings increased by 0.25 (2.43 vs. 2.68, $P = 0.006$) during Ramadan when compared with pre Ramadan. Across the two periods, the %TTR during Ramadan was lower compared with the non-Ramadan

periods although this was not statistically significant (pre-Ramadan, 79.69%; Ramadan, 69.56%, $p=0.02$).

No thrombotic or bleeding events were reported during the study period. There were also no complications arising from the weekly finger-prick monitoring of INR.

Table 1: Patients demographics

Study population (N=128)	
Mean age, years	54.1 (23-81)
Sex (%)	
Male	64 (50)
Female	64 (50)
Indication (%)	
Atrial fibrillation (Afib)	108 (84.3)
Venous Thromboembolism (VTE)	12 (9.4)
Mechanical valve replacement (MVR)	8 (6.3)
Treatment duration prescribed (%)	
6 months	4 (3.1)
9 months	4 (3.1)
12 months	0 (0.0)
Long term	120 (93.8)
INR target (%)	
2.0–3.0	120 (93.75%)
2.5–3.5	8 (6.3)

Table 2: Results of the primary outcome

	Pre-ramadan	Ramadan	
Mean INR	2.43	2.68	$P=0.006$
Mean TTR	79.69%	69.5%	$P=0.02$

DISCUSSION

The significant increase in mean INR during Ramadan when compared with non-Ramadan periods is attributable to the effect of fasting and the consequential changes to dietary patterns and timing of food intake. Ramadan is associated with sleep deprivation as a result of long periods of praying and dehydration due to daytime withdrawal of fluids [5]. In terms of metabolic changes, it has been shown that fasting during Ramadan resulted in a temporary reduction in body weight, blood glucose and high-density lipoprotein and an increase in low-density lipoprotein levels [6]. These physical and mental stress factors during the Ramadan period are possible reasons for the increase in INR, which has been demonstrated in animal studies [7]. As a result of the fewer number of meals taken each day and changes to dietary content, the amount of dietary vitamin K obtained from food may also be reduced. Multiple factors are therefore present during Ramadan that may directly or indirectly reduce the synthesis of clotting factors, resulting in the increase in INR. The return of the mean INR to baseline after Ramadan lends further

credence to the suggestion that the effect of fasting on INR is not incidental.

CONCLUSION

In conclusion, fasting during Ramadan significantly increases the mean INR of Muslim patients taking acenocoumarol and the likelihood of having an INR above therapeutic targets. For patients maintained at the higher end of INR target ranges or at increased risk of bleeding, clinicians will need to be aware of this effect and consider more intensive monitoring or preventive dosage adjustments.

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