Relapses in bipolar patients: changes in social rhythm?

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Abstract

The Ramadan month represents a valuable opportunity to test the hypothesis that the course of the illness of bipolar patients can be disrupted by the change in social rhythm which usually occurs during this month. The objectives of this study were to follow up the mood state and blood lithium level of fasting Muslim bipolar patients who had been on lithium therapy for at least 3 months, and were clinically stable before being included in the study. Twenty bipolar patients were enrolled during the month of Ramadan in 1997. Diagnosis of bipolar disorder was according to ICD-10 criteria. Patients were assessed during the week before Ramadan, the second and the fourth weeks of the fasting month and the first week after its end, with the Hamilton Depression and Bech–Rafaelsen scales. The plasma concentration of lithium was also assessed. The main finding of the study was that 45% of the patients relapsed, 70% during the second week and the remaining patients at the end of Ramadan. These relapses were not related to plasma concentration of lithium. Most of the relapses were manic (71.4%). Patients who did not relapse had insomnia and anxiety during the second and third weeks of the study. Side-effects of lithium increased and were observed in 48% of the sample, mostly dryness of the mouth with thirst and tremor. The result of this pilot study indicates that the Ramadan month may disrupt the mood state of bipolar patients. More studies are needed to confirm this observation and to evaluate the validity of the Ramadan model to study the impact of social rhythms on bipolar patients.

Introduction

Fasting during the month of Ramadan represents one of the five pillars of Islam. All adult Muslims around the world are required to comply with this religious obligation every year. During Ramadan month, people fasting abstain from eating, drinking and having sexual intercourse from sunrise to sunset. Sick or travelling people, as well as breast-feeding or menstruating women, are temporarily exempt from complying with this obligation. After the condition that precluded fasting resolves, individuals have to complete 1 month of fasting, even though the Ramadan month is over.

Ramadan occurs in the ninth month of the lunar calendar, lasting between 29 and 30 days. The lunar calendar does not correspond to the Gregorian one; therefore, Ramadan can occur in all seasons, varying from year to year. The cycle of the sun marks the beginning and the end of fasting. Its duration varies depending on the season: approx. 18 h in the summer to approx. 12 h during winter. Daily routine is markedly changed during the Ramadan month. It also varies depending on the geographic situation, the socio-economic level and the specific habits of each country. In Morocco, during this month, Muslims take 2–3 meals during the night (between sunset and sunrise). The first one, called ‘ftour’, is taken immediately after sunset; the second one is taken 1–3 h later and represents dinner. The last meal, ‘shour’, is taken between ½ and 1 h before sunrise. This third meal is recommended by religion.

The obligation to eat only during the night leads to an important change in the rhythm of life that especially affects sleep and eating schedules as well as the alternation of rest and activity. In Morocco, sleep duration during Ramadan has been found to be shorter, delayed in the 24-h cycle and interspersed because of the last meal. Several studies (Ehlers et al., 1993, 1988; Frank et al., 1994) have linked circadian rhythm disturbances to mood disorders. Social rhythm plays an important role in phase resetting of circadian rhythms in human subjects (Aschoff et al., 1971, Weyer, 1975, 1988). These social rhythms, which are the most important circadian ones (‘zeitgebers’) for human subjects include physical components such as daylight and darkness. The schedule of eating, sleeping
and exercising can also act as possible zeitgebers that maintain circadian rhythm (Aschoff, 1981). In this respect, Ramadan month represents an ‘experimental opportunity’ to study the effect of disruption in social rhythms of bipolar patients.

The objectives of this study were to follow up the mood state and the blood lithium concentration of the Muslim fasting bipolar patients who were receiving lithium therapy for at least 3 months and were clinically stable before being included in the study.

Methods

Subjects were recruited from the outpatient clinic population under treatment for bipolar disorder at the University Psychiatric Centre, Casablanca, Morocco. Five months before the beginning of Ramadan 1417 (Hegirian calendar, corresponding to January 1997), the investigators started to screen potential patients for enrolment. Forty bipolar patients were screened, 20 patients were eligible and were included. They were of both genders, aged 18 and over and had bipolar disorder according to ICD-10 criteria (World Health Organization, 1992). They had to fast during the month of Ramadan. Their mood had to be stable for at least 3 months, under lithium therapy associated with or without neuroleptics and/or other mood stabilizers. They gave informed consent to participate in the study and committed themselves to be available during the duration of the study for clinical and biological testing. Out of the 20 patients, 11 were female. The mean age was 32.10 $\pm$ 7.72 yr (range 21–57 yr). 6 patients (30%) were unemployed, 11 (55%) were single, 6 (30%) married and 3 (15%) divorced. The socioeconomic level (defined by the monthly income of the patient) was considered low in 4 (20%) of cases, medium in 12 (60%) and high in 4 (20%). Substance use was found in 8 (40%) of the cases [cigarettes ($n = 8$), alcohol ($n = 6$) and cannabis ($n = 2$)]. In 13 cases (65%), patients had one or more first- and second-degree relatives with psychiatric illness. The mean duration of illness was 7.9 $\pm$ 4.0 yr (range 3–16 yr). Relapse was defined as a manic or depressive episode, which was severe enough to necessitate hospitalization or at least psychiatric intervention in the outpatient clinic during the course of the illness. The mean number of relapses prior to the study was 3.45 $\pm$ 0.76 (range 2–5). Eighteen patients were bipolar type I; of these, 4 had only manic episodes in their antecedents and 14 depressive and manic episodes. Two patients were bipolar type II.

The mean duration of lithium therapy was 26 $\pm$ 20 months (range 3–60 months). Two weeks before the beginning of the study, all the patients were asked to take their lithium once daily at 09:00 hours. Six patients were taking other mood stabilizers (carbamazepine), in association with lithium and 14 were receiving concomitant neuroleptic treatment (mean daily dose was $255 \pm 147$ chlorpromazine equivalents). Regarding side-effects, at the beginning of the study 1 patient complained of a sensation of thirst and 2 had tremor.

When the fasting month starts, people abruptly switch from their usual lifestyle to a different one, changing their food intake rhythm, as well as the duration and rhythm of sleep. This is also true at the end of Ramadan. Thus, at the beginning and at the end of the month, the individual has to adapt to new conditions. Ratings were conducted 1 wk before the beginning of the Ramadan month (W1), during the second (W2) and the fourth (W3) weeks of fasting and during the first week after Ramadan month ended (W4).

At the first assessment, subjects completed a questionnaire administered by a clinician. This included questions about socio-demographic variables, clinical data (date of onset of the disorder, number, date and type of relapses during the course of the illness), substance use (cigarettes, alcohol, hashish) and psychotropic medication history. During each visit, a somatic examination was performed in order to check for symptoms of hypothyroidism, tremor and other neurological side-effects.

To assess manic symptoms, the Bech–Rafaelsen Scale (Bech et al., 1979) was used, and for depressive symptoms, the 21-item Hamilton Depression Scale (HDS) (Hamilton, 1960). The investigators recorded their global clinical impression of the patient’s mood state during each consultation. Blood lithium level was assessed 4 times during the study. Patients who stopped fasting were considered dropouts from the study. Statistical analysis was performed using Epi-Info, v.6, with the $\chi^2$ test for categorical variables and analysis of variance (ANOVA) for continuous variables.

Results

During W1, 20 patients were evaluated. During W2, 17 patients (1 patient dropped out of the study for a social reason, 2 others had a manic relapse and stopped fasting, the first one was followed in an ambulatory way and the second had to be hospitalized). During W3, 15 patients were evaluated (2 patients had depressive relapses and were excluded because they stopped fasting). During W4, 14 patients were evaluated (1 patient stopped fasting because she had a lung sarcoidosis and had to take no salt, which contraindicated lithium therapy). The mean blood level of lithium for the 20 patients was $0.46 \pm 0.16$ mequiv./l during W1. In W2, for the 17 remaining patients, it was $0.55 \pm 0.22$ mequiv./l. In W3, for the 15 remaining patients, it was $0.51 \pm 0.18$ mequiv./l. In W4, for the 14 remaining patients, it was $0.44 \pm 0.17$ mequiv./l.
Figure 1. Evolution of the blood lithium level.

Figure 2. Evolution of Hamilton Depression scores.

Figure 3. Evolution of Bech–Rafaelsen scores.

Discussion

The main finding of this study is that 45% of bipolar patients who were clinically stable on lithium therapy, relapsed during the Ramadan month. Seventy per cent of the relapses occurred during the second week of the fast (W2) and the remaining 30% at the end of Ramadan (W3). The relapses were not associated with a change of blood level of lithium, which remained within the therapeutic range (increasing slightly during Ramadan month, although not significantly, as compared to the levels before and after Ramadan). There were no problems of compliance in the group. Most of the relapses were of a manic type (77.7%, n = 7). Patients who did not relapse had mood disturbances during the second or the third weeks of Ramadan as shown by the rating scales. Side-effects of lithium increased and were mostly of neurological and gastrointestinal in nature.

Several chronobiological hypotheses have been pro-
posed in relation to mental disorders in general and affective illness, in particular. To explain features such as the diurnal fluctuation in mood and early morning awakening observed in depressed subjects, as well as the recurrent nature of mania and depression in bipolar subjects, several theories have been proposed. The various hypotheses include desynchronization (Halberg, 1968), phase advance (Goodwin et al., 1982; Wehr and Wirz-Justice, 1982), the two-process model of sleep regulation (Borbely and Wirz-Justice, 1982), biological rhythm amplitude reduction (Beersma et al., 1993, Czeisler et al., 1986; Schultz and Lund, 1983), dysregulation (Siever and Davis, 1985), dysrhythmia (Healy, 1987) and loss of appropriate entrainment (Von Zerssen et al., 1985). These theories have led to studies that have yielded a considerable amount of empirical data relating circadian rhythm disturbances to affective disorders.

Exogenous factors termed ‘zeitgebers’ have an influence on maintaining the cycle length or period of circadian rhythms. They synchronize circadian rhythms into stable period and phase relationships with the external day–night cycle. These zeitgebers include physical and social factors (Aschoff et al., 1975). Social rhythms such as the timing of eating, sleeping and exercising can also act as potential zeitgebers that maintain circadian timing (Aschoff, 1981). Abrupt change in these factors has the potential for disrupting normal circadian timing. The mechanism by which social rhythms participate in entrainment of biological rhythms is unknown.

In our study, 45% of bipolar patients who were under lithium therapy and clinically stable before the beginning of Ramadan, relapsed without a change in their lithium blood level. This result suggests that the change of social rhythm (change in timing of eating, duration and time of sleeping, cycle activity/rest) may have been associated with these relapses. The patients who did not relapse were also disrupted by the change of their usual social-life rhythm as was shown in their depression and manic symptom scores. Previous studies on sleep and vigilance during Ramadan (Ain Fares, 1989) have shown that decrease in sleep time and its fragmentation by one or several awakenings have a negative influence on cognitive functioning, such as a decrease in vigilance during the first week of fasting. Impairment generally diminished during the second and the third weeks of Ramadan, returning to baseline during the fourth week. Our study showed a similar pattern of evolution of affective symptoms. The increase in side-effects of lithium during Ramadan is probably due to the fact that people abstain from drinking, inducing a concentration of the plasma. These side-effects appeared during winter time. It is probable that they would be worse in summer time leading to an increase of the risk of intoxication by lithium.

This study had several limitations. The size of the sample was small, there was no control group and the renal function was not explored. One of the main limitations of the study was the fact that the level of blood lithium was low from the beginning of the study. Another one might have been the change of prescription of lithium from twice per day to once daily. This was a pilot study. More studies are needed to explore the effects of social factors on the mood state of bipolar patients. Such studies should use instruments specifically designed to measure the rhythmicity of daily life such as Social Rhythm Metric (Monk et al., 1990, 1991) and its relation to the mood state. Ramadan month offers a unique opportunity to assess the effect of change in the social zeitgebers on the mood state during 1 month each year in a fairly large number of bipolar patients.

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