Interferon alpha-associated depression in patients with Behçet's syndrome: a prospective controlled study

Sirs,
Interferon (IFN) is an immune-modulatory agent effective in the medical management of joint and eye involvement in Behçet's syndrome (BS) (1-3). It is also used to treat chronic hepatitis B and C infection, melanoma, hairy cell leukaemia, and chronic myelogenous leukaemia (4). However, its use is accompanied by several side effects such as flu-like syndrome and autoimmune disorders. Moreover, mood changes, depressive disorders and suicidal behaviour are frequently reported among patients with hepatitis C (4-6). In this study, we formally evaluated the psychiatric status of a group of BS patients in whom IFN was used at baseline and at week 12. As a control group we studied BS patients who used drugs other than IFN.

We studied BS patients who were seen between January 2012 and January 2014 at the Behçet's syndrome outpatient clinic at Cerrahpaşa Medical Faculty. Those with a history of psychiatric illness, who use illicit drugs/alcohol, or have parenchymal neurological involvement due to BS were not included in the study. All patients fulfilled the ISG criteria (7). Patients who started to use IFN for the first time (Group 1) and those who started to use drugs other than IFN (Group 2) were included in the study. Beck Depression Inventory (BDI) and Hospital Anxiety and Depression Scale (HADS) – both validated in Turkish – were used to measure status of depression at baseline and at week 12. We also analysed the answers given to question 9 in BDI which is specifically associated with suicide. These answers were tabulated as:

a. I don't have any thoughts of killing myself;
b. I have thoughts of killing myself but I would not carry them out;
c. I would like to kill myself;
d. I would kill myself If I had the chance.

Group 1 included 19 while Group 2 included 24 patients. Two patients in Group 1 were excluded within the first month due to the flu like syndrome. Two patients who were using anti-depressants and another with CNS parenchymal neurological involvement – all from Group 2 – were also excluded. We studied 17 (14 M, 3F) patients in Group 1 and 21 (13 M, 8 F) patients in Group 2. Eye disease was the main reason for IFN use (14/17) followed by joint involvement (3/17). The dose of IFN was 5 MU/day. During 12 weeks of follow-up, 6 patients used prednisolone (10 mg/day in 4 patients and 5 mg/day in the remaining 2) while 3 used colchicine in addition to IFN in

Group 1. Drugs that were started in Group 2, were azathioprine and cyclosporine combination (n=5), infliximab (n=2), methotrexate (n=1), azathioprine alone (n=6) and colchicine (n=7). Apart from these, 9 patients continued to use prednisolone at a dose of 10 mg/day in 6 and 5 mg/day in the remaining 3. Table I shows the socio-demographic and clinical characteristics. Socioeconomical and marital status were similar in both groups. Patients who used IFN were more likely to be male and more likely to have longer disease duration and eye disease. While both BDI and HADS scores increased significantly after 12 weeks of follow-up, among patients who used IFN, these scores did not change among patients who used other drugs (Table II). When we analysed 12 week answers to question no: 9 of BDI, we found that the patients either answered '*b*' (Group 1: 6/17, 35% *vs*. Group 2/21, 10%, *p*=0.053) or '*a*'. None in either Group answered '*c*' or '*d*'. This was also true for baseline answers ('*b*': 24% *vs*. 10%, respectively, *p*=0.24). This indicated that, the frequency of those with suicidal ideation increased only in the IFN group It has to be noted that the study is limited due to the small sample size. One explanation of this could be the early withdrawal of IFN due to side effects such as fever, myalgia and flu like syndrome.

In conclusion, we found that the depression scales increased among IFN users after 12 weeks of follow-up compared to those who used other drugs. Additionally, after 12 weeks of follow-up, the frequency of those with suicidal ideation increased only among the IFN users. A recent survey indicated that BS patients with major organ involvement have increased risk for depression and suicidal behaviour (8). Physicians should be cautious while using IFN in BS, since this drug may further increase this risk.

Table I. The socio-demographic and clinical characteristics in study patients.

	Interferon, n=17	Other drugs, n=21	*p*-value
Males/Females	14/3 (4.5)	13/8 (1.6)	0.282
Mean age	34.9 ± 7.4	34.3 ± 9.2	0.830
High school or university education	10 (59)	11 (52)	0.432
Married, n (%)	13 (76)	16 (76)	1.0
Disease duration, median [IQR]	5 [2.5–10]	2 [1–6.5]	0.064
Joint disease, n (%)	9 (53)	8 (38)	0.51
Vascular involvement, n (%)	6 (36)	7 (33)	1.0
Eye involvement, n (%)	14 (82)	11 (52)	0.08

IQR: interquartile range.

Table II. Depression scales at baseline and at week 12.

	Interferon, n=17			Other drugs, n=21		
	Baseline	Week 12	*p*-value	Baseline	Week 12	*p*-value
BDI, mean ± SD	11.4 ± 8.7	14.7 ± 9.0	0.05	10.9 ± 9.6	10.0 ± 8.0	0.39
HADS, mean ± SD	5.0 ± 4.5	7.1 ± 4.2	0.04	5.5 ± 4.2	5.3 ± 3.2	0.71

BDI: Beck Depression Inventory; HADS: Hospital Anxiety and Depression Scale.

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