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Evaluation of dexamethasone suppression test in fibromyalgia patients with or without depression

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Summary

Objective: While in most healthy persons dexamethasone administration suppresses cortisol synthesis from the adrenal cortex, such suppression is not usually observed in patients with depression. We set out to investigate whether the dexamethasone suppression test (DST) reveals any neurobiological relationship between fibromyalgia (FM) and depression related to the hypothalamic-pituitary-adrenal (HPA) axis.

Method: To discover a relationship between depression and FM we performed the DST in 20 FM patients with depression, 26 FM patients without depression and 20 healthy subjects serving as a control group.

Results: Compared with the control group the cortisol level was found to be significantly higher in response to the DST in FM patients with depression (p = 0.03; z: –2.165), but not in those without depression (p = 0.153; z: –1.429). The cortisol level was not found to be statistically significant when patients with FM without depression were compared with the control group (p = 0.249; z: –1.152). In 7 FM patients with depression the DST failed to suppress cortisol; this was statistically significant compared with FM patients without depression (p = 0.014) and the control group (p = 0.008). Among FM patients without depression cortisol was not suppressed in one case. Cortisol was suppressed in all the controls. There was no statistically significant difference in cortisol suppression between FM patients without depression and the control group (p = 1.00).

Conclusion: Our findings show that the DST reveals no neurobiological relationship between FM and depression related to the HPA axis.

Key words: fibromyalgia; depression; dexamethasone suppression test

Introduction

Fibromyalgia (FM) is a chronic musculoskeletal syndrome involving tenderness in certain parts of the body and diffuse pain. Patients may also display weakness, sleep disturbance, morning stiffness, headache, irritable bowel syndrome, Raynaud's phenomenon-like state, anxiety, depression, tachycardia and dyspnoea [1, 2]. 80–90% of patients are women and FM is more commonly seen between the ages of 30 and 60 years [2, 3]. The cause of FM is not known. Central, peripheral and immunological theories are most frequently aired in discussions of aetiology [1].

It is known that most patients with FM also have depressive symptoms and depressive patients suffering from pain are not uncommon. Some investigators have therefore suggested a possible connection between FM and depression. The first

Abbreviations:

DST	dexamethasone suppression test
FM	fibromyalgia
HPA	hypothalamic-pituitary-adrenal
NSAIDs	non-steroidal anti-inflammatory drugs
RIA	radioimmunoassay

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pointer to such a connection is that most patients with FM exhibit depressive symptoms such as fatigue, sleep disturbances and anxiety [4]. Second, phenomenological similarities exist between chronic pain syndrome, which has been claimed to be related to depression, and FM [5, 6]. Finally, an increased prevalence of depression has been found in patients with FM, and bipolar illness has been diagnosed more frequently in close relatives of these patients [7]. Similarities in patients with FM and depression [8] raise the possibility of a neuoroendocrine relationship between these two disorders.

Previous studies have clearly established that cortisol is not suppressed in response to the dexamethasone suppression test (DST) in 40–60% of patients with depression, and dexamethasone administration suppresses cortisol secretion from the adrenal glands in healthy persons [9, 10]. We tested the hypothesis that, if there is a neurobiological connection between FM and depression, FM patients without depression should, like depressive patients, fail to suppress cortisol. For this purpose we evaluated response to the DST in patients with FM with or without depression, and also in a group of healthy controls.

Methods

We diagnosed FM on the basis of the American College of Rheumatology 1990 criteria [2]. All the FM patients and the control group were evaluated by a psychiatrist who was unaware of the study. Patients with depression who fulfilled the criteria of DSM-IV [11] and had a score of 16 [12] or more were included in the study on the strength of the 17–item Hamilton Depression Rating Scale [13]. Twenty-six FM patients without depression, 20 FM patients with depression and 20 healthy subjects were included in the study. All the patients were evaluated on an in-patient basis and the healthy volunteers were from our hospital staff. Subjects receiving hormones or drugs likely to affect the DST and with any disease other than FM were excluded from the study. Depressive patients who had suicidal ideation and psychotic features were also excluded. Of patients with FM and depression, 8 were taking non-steroidal anti-inflammatory drugs (NSAIDs), 11 were on antidepressant medication (6 amitriptyline, 2 imipramine, 2 venlafaxine and 1 paroxetine). One patient was taking both an NSAID and an antidepressant. Of patients with FM without depression, 11 were taking an NSAID and 15 an antidepressant (7 amitriptyline, 5 sertraline and 3 venlafaxine). None of the subjects in the control group was taking medication. NSAIDs and antidepressant drugs were discontinued in all patients 5 days prior to the DST.

For the DST all subjects received 1 mg dexamethasone orally at 11 pm under control on the 5th day of hospitalisation and blood samples were obtained on the following day at 4 pm and sent to the laboratory for measurement of plasma cortisol levels. Plasma cortisol levels were determined by radioimmunoassay (RIA) in our university laboratory (IMMULITE BIO DPC). A plasma cortisol level of 5 µg/dL or higher was considered to be non-suppressed.

Fisher's exact test, two-tailed, was used for non-parametric comparisons of the study groups, and Mann-Whitney U test was used for mean post-dexamethasone plasma cortisol levels between groups.

Results

There were 19 females and 1 male among the patients with FM and depression. The mean age and duration of disease were 42.4 ± 8.22 (32–61) and 4.6 ± 2.37 years respectively. In the group with FM without depression all the patients were female. The mean age was 40.8 ± 7.31 (29–57) years and the mean disease duration was 4.11 ± 1.9 years. In the control group all the patients were female, with a mean age of 39.5 ± 6.3 (30–48). Psychiatric evaluation of the control subjects was normal in all cases. Biochemical findings were in the normal range in all members of the three study groups. The characteristics of the study groups are presented in Table 1, the results of the DST in Table 2, and statistical analysis of the study groups in Table 3. Of 20 FM patients with depression, plasma cortisol was not suppressed in response to the DST in 7 patients (35%), and the average level was 6.61 ± 1.11 µg/dL. The mean cortisol level of the suppressed subgroup (n: 13) was 2.17 ± 0.63 µg/dL. The group of FM patients with depression showed a statistically significant difference from the FM patients without depression (p = 0.014) and the control group (p = 0.008) with regard to suppressors and non-suppressors, using two-tailed Fisher's exact test. In one FM patient (3.7%) without depression, plasma cortisol was not suppressed in response to DST; the plasma cortisol level was 5.8 µg/dL in this patient. Cortisol levels were suppressed in all healthy subjects of the control group. A 3.7% cortisol non-suppression rate in FM patients without depression was not statistically significant compared with the control group (p = 1.00). The average plasma cortisol level was found to be 3.72 ± 2.31 µg/dL in patients with FM and depression. This was not statistically significant compared with FM patients without depression (p = 0.153; z: –1.429), but statistically significant compared with the control group (p = 0.03; z: –2.165), whose plasma cortisol levels were found to be 2.49 ± 1.10 µg/dL and 2.11 ± 0.7 µg/dL respectively. Comparing the plasma cortisol levels of FM patients without depression and those in the control group in response to DST, there was no statistically significant difference (p = 0.249; z: –1.152).

Table 1
Characteristics of study groups.

Characteristic	Groups		
	FM without depression	FM with depression	Healthy control
N	26	20	20
Sex			
Male	–	1	–
Female	26	19	20
Age -yr	40.8 ± 7.31	42.4 ± 8.22	39.5 ± 6.3
(range)	(29–57)	(32–61)	(30–48)
Duration of disease -yr	4.11 ± 1.9	4.6 ± 2.37	–
NSAIDs usage	11	8	–
Antidepressant			
usage	15	11	–
Total	7	6	–
Amitriptyline	–	2	–
Imipramine	5	–	5
Sertralin	3	2	–
Venlafaxine	–	1	–
Paroxetine			

FM: fibromyalgia NSAIDs: non-steroidal anti-inflammatory drugs

Table 2
DST results in study groups.

Group	Cortisol level (µg/dL)		
	Mean	Nonsuppressive group	Suppressive group
FM without depression	2.49 ± 1.107 (n: 26)	5.8 (n: 1)	2.35 ± 0.89 (n: 25)
FM with depression	3.72 ± 2.31 (n: 20)	6.61 ± 1.11 (n: 7)	2.17 ± 0.63 (n: 13)
Healthy control	2.11 ± 0.7 (n: 20)	–	2.11 ± 0.7 (n: 20)

DST: dexamethasone suppression test FM: fibromyalgia

Table 3
Statistical analysis of study groups.

Groups	Statistical analysis			
	Z	p[a]	95% CI	p[b]
FM with depression vs. FM without depression	–1.429	0.153ns	0.83–33.41	0.014*
FM with depression vs. control	–2.165	0.03*	0.26–0.60	0.008**
FM without depression vs. control	–1.152	0.249ns	0.43–0.72	1.00[ns]

CI: confidence interval
FM: fibromyalgia
[a] Mann-Whitney U Test
[b] Fisher's exact test
ns non-significant
* significant
** very significant

Discussion

In our study the HPA axis hyperactivation commonly seen in cases with isolated depression was not observed in FM patients without depression and patients with FM and depression had a non-suppression ratio of 35% similar to the known non-suppression ratio of 40–60% in depressive patients [10]. This non-suppression ratio (35%) in the DST in patients with FM and depression may therefore be due to the presence of depression in these cases. Biogenic amines are incriminated in the aetiology of depression [14]. Since they are also involved in regulation of the neuroendocrine axis, functional deprivation of biogenic amines may cause depression along with dysregulation in the neuroendocrine axis [10]. In our study the 35% non-suppression rate in FM patients with depression may be related to the aetiopathogenesis of depression. Biogenic amines, which have been assigned an aetiological role in depression, are inadequate to explain all cases of depression but may account for a percentage of cases [15]. The non-suppression rate of 35% in our study may cover the cases of depression in which the aetiology is related to biogenic amines. The 65% suppression rate in

FM patients with depression may reflect the variations in the aetiology of depression.

There was a difference between the ratios of 3.7% in FM patients without depression and 0% in controls which was not statistically significant. The non-suppressive case among FM patients without depression was taking an NSAID before the DST. This association may therefore have been due to usage or abrupt cessation of NSAID. Although the effects of NSAIDs on the DST are unknown, current literature suggests that activation of peripheral nociceptive, somatosensory, and afferent fibres would lead to stimulation of both the catecholaminergic and CRH neuronal systems via ascending spinal pathways [16]. Abrupt cessation of this drug may have resulted in activation of the HPA axis due to increased perception of pain in this patient.

Regarding the mean cortisol values in the study groups, the higher mean cortisol value in the FM patients with depression compared with the other two groups was due to the 7 non-suppressor patients. This finding also supports the thesis that non-suppression of cortisol is related to depression.

In conclusion, a rate of 35% non-suppression of cortisol in FM patients with depression was similar to the rate in depressed patients *per se*. Our findings thus showed that the DST reveals no neurobiological relationship between FM and depression related to the HPA axis. Additionally, there is a possible common aetiological factor between FM and depression which needs to be explored in other fields of aetiopathogenesis.

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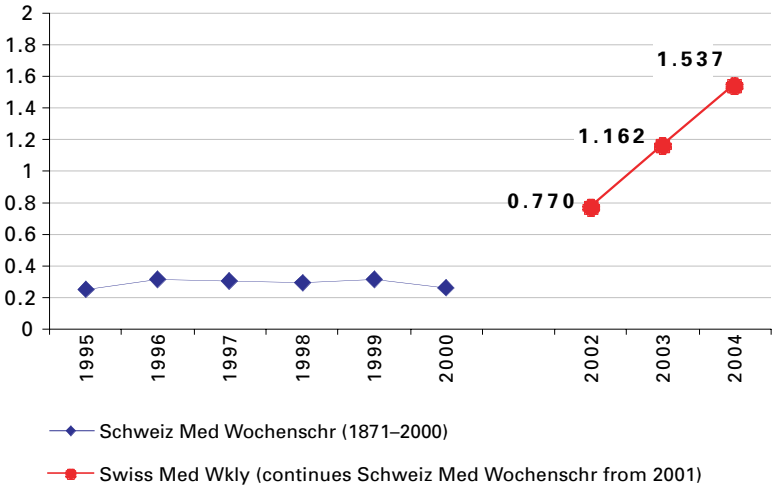

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