THE DEXAMETHASONE SUPPRESSION TEST IN DEPRESSION – A SINGAPORE STUDY

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ABSTRACT

The Dexamethasone Suppression Test (DST) has been evaluated as a biological marker in psychiatry especially in depressive illness. A study on the DST involving 20 patients in Tan Tock Seng Hospital, Singapore, who fulfilled the Research Diagnostic Criteria for major depressive disorder and with 21 healthy controls was carried out. Two out of the 20 patients had abnormal DST responses.

Keywords: dexamethasone suppression test, depression

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Biological markers in depression are those altered biological functions present in depressed patients. They can indicate either a diagnostic entity or a specific brain process such as a circadian rhythm, or the function of a neuroreceptor (1). The Dexamethasone Suppression Test (DST), which is a state marker, has been reported to yield abnormal results in some depressed patients and with recovery from depression, the result becomes normal (2). It is one biological test that has been extensively evaluated for clinical use in psychiatry. Pathophysiologic changes at central nervous system level may be reflected in the DST (3).

The American Psychiatric Association (APA) Task Force on Laboratory Tests in Psychiatry has reviewed the sensitivity of the DST (2). It is thought to be positive (i.e. non-suppression of cortisol) in major depression in the range of about 40% to 50%. The specificity (true negative outcome) of DST in normal control subjects is above 90%, but it varies from less than 70% to more than 90% in other psychiatric conditions.

Singapore is an island republic with a population of about 2.6 million people, who are of mixed ethnic groups, predominantly Chinese, Malay and Indian. Tan Tock Seng Hospital is a large general hospital in Singapore and has a 26-bedded inpatient unit for psychiatric patients. We carried out a study using the DST in 20 depressed inpatients there, attempting to determine its sensitivity in local patients and present the findings as follows:-

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METHOD

Patient Criteria

In-patients with the diagnosis of primary major depressive disorder, between the ages of 24 to 55 years, were selected, and their diagnosis checked against the criteria according to Spitzer et al, Research Diagnostic Criteria 3rd Edition (RDC) 1978 (4).

Their diagnosis according to ICD-9 criteria was also noted.

All of the patients selected were receiving medication (antidepressants and anxiolytics). 21 volunteers were chosen as controls. They were free of significant physical disease and psychiatric disorder. None had electroconvulsive therapy.

Severity of Depression

This was rated using the Beck Inventory which is a self-rating questionnaire (5). This consists of 21 groups of items, each group containing items of graded severity of depression with a maximum score of 60.

DST Procedure

1.0 mg of dexamethasone in tablet form was taken by the patient at 11 pm. On the day after, blood samples for the determination of plasma cortisol concentration were drawn at 4 pm and 11 pm. A baseline level had been taken at 8 am the day prior to the test. The test was carried out within a week of admission in most of the patients.

For the controls the same dosage of dexamethasone was administered but only the cortisol level at 4 pm was taken.

The result is positive (abnormal) when there is an elevated plasma concentration of cortisol at either 4 pm or 11 pm of more than 5 ug/dl.

The technique used in measuring the cortisol was radioimmunoassay.

RESULTS

Twenty-two patients were entered into the study. Two were eliminated because they had alcohol dependence

Table I

Table Of Results

No	Sex	Age	Race	ICD-9 Diagnosis	Beck Inventory Score	Cortisol (ug/dl)			DST Status
						Baseline	4 pm	11 pm	
1	M	31	Chinese	Endogenous Depression	19	10.1	1.1	0.6	Suppressor
2	F	49	Chinese	Endogenous Depression	28	22.2	1.5	2.1	Suppressor
3	M	49	Chinese	Endogenous Depression	10	16.3	20.3	4.4	Non-Suppressor
4	M	27	Chinese	Endogenous Depression	19	9.2	2.4	1.5	Suppressor
5	M	23	Indian	Endogenous Depression	29	14.8	0.9	0.7	Suppressor
6	M	52	Chinese	Endogenous Depression	19	17.3	1.6	1.3	Suppressor
7	F	28	Chinese	Neurotic Depression	8	Not Done	2.4	6.9	Non-Suppressor
8	F	34	Chinese	Neurotic Depression	10	10.8	0.6	0.8	Suppressor
9	F	43	Chinese	Endogenous Depression	13	18.4	2.1	1.4	Suppressor
10	F	50	Indian	Endogenous Depression	15	23.4	1.1	1.0	Suppressor
11	M	44	Malay	Endogenous Depression	4	14.9	1.4	1.2	Suppressor
12	F	40	Chinese	Endogenous Depression	22	9.7	1.6	2.0	Suppressor
13	M	53	Chinese	Endogenous Depression	11	16.6	0.9	0.8	Suppressor
14	F	42	Chinese	Neurotic Depression	17	7.9	1.0	0.8	Suppressor
15	M	42	Malay	Neurotic Depression	44	8.8	0.7	0.7	Suppressor
16	F	35	Chinese	Endogenous Depression	14	17.8	0.9	0.8	Suppressor
17	F	30	Chinese	Neurotic Depression	12	6.9	0.7	0.5	Suppressor
18	F	25	Chinese	Endogenous Depression	22	12.1	1.1	1.4	Suppressor
19	F	28	Chinese	Endogenous Depression	34	9.8	0.5	0.5	Suppressor
20	F	52	Chinese	Neurotic Depression	34	3.2	0.3	0.3	Suppressor

prior to their depressive illness, leaving 20 who were selected (See Table I).

Of these there were 8 males and 12 females. Their ages ranged from 23 to 53 years, with a mean age of 38.9 (S.D. 10.1). Sixteen were Chinese, 2 Malay and 2 were Indian. In terms of diagnosis according to ICD-9 criteria, 14 of them were suffering from endogenous depression and 6 of them from neurotic depression. The Beck Inventory scores ranged from 4 to 44, with a mean score of 19.2 (S.D. 10.2).

The mean pre-dexamethasone (baseline) cortisol level was 13.2 ug/dl (S.D. 5.4). The post-dexamethasone cortisol levels at 4 pm ranged from 0.3 to 20.3 ug/dl with a mean value of 2.2 (S.D. 4.3). The cortisol levels at 11 pm ranged from 0.3 to 6.9 ug/dl with a mean value of 1.5 (S.D. 1.6).

Only 2 showed an abnormal DST response (non-suppression), giving a sensitivity rate of 10% in this group of depressed patients.One of them had a post-dexamethasone of 20.3 ug/dl (4 pm) and was diagnosed as endogenous depression. The other had a post-dexamethasone cortisol level of 6.9 ug/dl (11 pm) and was diagnosed as neurotic depression. The correlation between the cortisol levels of the 20 patients at 4 pm and 11 pm show T = 2.584, df = 18 and the difference in values were statistically significant (p less than 0.01).

Twenty-one healthy volunteers acted as controls that were matched for age and sex. There were 11 males and 10 females with mean age of 31.0 (S.D. 8.8) and of these 10 were Chinese, 7 were Malay and 4 were Indian. The mean post-dexamethasone cortisol level at 4 p.m. was 1.6 ug/dl (S.D. 1.5). One of the controls showed non-suppression with a level of 8.0 ug/dl giving an abnormal response rate of 4.8%. The difference between the 4 p.m. cortisol values of the patient group compared to the control group was statistically not significant.

DISCUSSION

The WHO Collaborative Study (1987) on DST in depression, with 13 participating centres, showed results that had post-dexamethasone plasma cortisol concentrations that were higher among depressive patients meeting RDC criteria than among normal controls (6). There was much variation among the centres with the highest mean post-dexamethasone plasma cortisol concentration (116.5 ug/dl) and the lowest mean (22.5 ug/dl). This variation among the centres was also present in the percentage of abnormal responses (71% to 15%) among the patients.

Our study showed a low percentage of abnormal responders and also a low mean cortisol concentration. In terms of absolute values, the highest post-dexamethasone cortisol level of 20.3 ug/dl in our study was even lower than the lowest mean level of 22.5 ug/dl in the WHO collaborative study. What may be some of the reasons for this low response rate and low post-dexamethasone cortisol levels?

The question of diagnosis and sub-classification is important as it is the most important source of divergent

findings concerning the DST (1). Caroll (1982) has consistently reported that dexamethasone resistance is seen almost exclusively among those depressed patients with a clinical diagnosis of endogenous depression or melancholia (7). However the use of RDC (Spitzer et al, 1978) to compare endogenous and non-endogenous depression has led to inconsistent findings. It is to be noted that the RDC definition of endogenous depression is based exclusively upon the recognition of symptoms and ignores the presence or absence of precipitating factors (4). The use of the Newcastle classification of endogenous depression (Carney et al, 1965) may be able to help differentiate the DST responses in sub-groups of depression (8). This English system uses symptoms together with an assessment of aetiological factors. In our patients, precipitating factors appeared to be important in the aetiology of their illness even in those diagnosed as suffering from endogenous depression.

Exclusion criteria must also be considered as the DST can be influenced significantly by drugs or metabolic factors unrelated to depression. Ideally, patients should be drug free, physically healthy and physiologically stable to ensure unambiguous interpretation of DST results (2). However this ideal is not easily attained. We found that 2 of the patients in this study started off with alcohol dependence before their depressive illness and had to be eliminated from the analysis of results.

The measurement of cortisol is also another source of variance (9). The 2 most common techniques used for determining plasma or serum cortisol levels are the competitive protein-binding assay (PBA) which is outdated, and various radioimmunoassays (RIA's) which is used in the Singapore General Hospital Nuclear Medicine Laboratory. Care is required to obtain precision and accuracy especially at relatively low concentrations of cortisol (4 to 10 ug/dl) which are critical in the use of DST in psychiatry. Each laboratory must define its own appropriate criterion level for cortisol. Because normal values are variable and because plasma cortisol concentrations close to 5 ug/dl are often not carefully standardised, the APA Task Force on Laboratory Tests in Psychiatry has advised that test results between 4 and 7 ug/dl should be interpreted cautiously (2). One of the patients had a cortisol value of 6.9 ug/dl which falls into this uncertain category. It is noted that one patient had a cortisol value more than 5 ug/dl at 4 pm while the other was at 11 pm. It is thought that by only taking a 4 pm blood sample, there is a modest loss of test sensitivity (2). In fact, in our study the difference in the cortisol values at 4 pm and 11 pm in the patient group was statistically significant.

In the WHO Collaborative Study on DST in depression (1987), it was apparent that abnormal responses might also vary from country to country (6). Normal controls are therefore necessary in such a local study. The 2 Asian cities that participated in the collaborative study, both Japanese (Nagasaki and Sapporo), out of the 13 centres involved, had depressed patients with a low mean post-dexamethasone plasma cortisol concentration. However the means for their control groups were also very low. It is thus inappropriate to set a universal cut-off point to define an abnormal DST response. The mean cortisol level of our control group was very low, 1.6 (±1.5), compared to that of the study in Nagasaki (13.5±1.0) and Sapporo (16.3±2.0) mg/dl.

This also leads to the question of whether a lower dosage of dexamethasone (0.5 mg) may be more useful in eliciting abnormal DST responses in depressives compared to normal controls. In a study by Sarai et al (1982), a low-dose dexamethasone suppression test resulted in all 9 of the patients with major depressive episodes showing non-suppression compared to the controls (9 other psychiatric patients and 1 normal subject) who had cortisol levels which were uniformly suppressed under 5 ug/dl (10). The possibility of a low-dose DST should be considered in the design of another study.

The rating of the severity of depression using the Beck's Inventory seemed to be inconsistent with clinical judgement in some of the cases. Although all of them fulfilled the RDC criteria for major depressive disorder, some of the scores were surprisingly low. The Beck's Inventory has not been validated on our local population and depressive symptoms may have been under-rated by the patients themselves for socio-cultural or other reasons. The Hamilton Rating Scale for Depression which is tester-rated may be more suitable for such a study (11).

In summary, our study showed a low abnormal DST response rate among depressed patients and also a low mean post-dexamethasone cortisol level. An important reason for this finding may be that there is a biological or physiological difference from patients in Western countries which have higher response rate or a higher mean post-dexamethasone cortisol level. In this regard, the control group in our study indicated that a lower cut-off point to define an abnormal DST response is needed for our population. A lower dosage of dexamethasone may be useful in eliciting abnormal DST responses.

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