

## THE DEXAMETHASONE SUPPRESSION TEST IN ENDOGENOUS DEPRESSION<sup>1</sup>

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### SUMMARY

In 34 patients of endogenous depression and 30 normal controls, the dexamethasone suppression test (DST) had a sensitivity of 67.6%, a specificity of 93.3% and a positive predictive power of 92%, which compares favourably with other diagnostic tests in clinical medicine. DST nonsuppressors were significantly more depressed as compared to DST suppressors, had a higher incidence of suicidal attempts and past and family history of depression, needed electroconvulsive therapy more often, but showed a better response to therapy. Though the claim of the DST being a specific biological marker for endogenous depression remains controversial, it is an useful investigative tool for the diagnosis and treatment of endogenous depression.

Depression is one of the most frequent illness in psychiatric practice. However, due to disagreements about the nosological classification the diagnosis of depressive disorders remain confusing. The practical consequences of this diagnostic uncertainty are that some patients with endogenous depression do not receive effective somatic therapies, while patients with nonendogenous depression may be treated inappropriately. It is obvious that an objective laboratory test for the diagnosis of endogenous depression would be extremely useful.

Hypothalamus-pituitary-adrenal (HPA) axis dysregulation in depression has been widely studied with the DST during the past few years. Some investigators have hailed the DST as a diagnostic test for endogenous depression (Carroll et al., 1981) though others have refuted these claims (Berger et al., 1984). In view of the conflicting results the present study was undertaken to evaluate the DST in endogenous depression in an Indian setting.

### MATERIAL AND METHOD

The sample consisted of 34 male inpatients in a large service hospital with the

diagnosis of Manic-depressive psychosis—Depressed type (ICD-9). Severity of depression was assessed by the Hamilton rating scale for depression (HRSD). Patients with a minimum HRSD score of 21 were only included in the study. Thirty healthy volunteers from staff members, matching closely in age with the patients, and screened thoroughly to exclude any psychiatric illness, constituted the control sample. All the subjects were free of drugs known to interfere with the DST for atleast one month (Carroll, 1983). There was no evidence of any physical illness, particularly pointing to endocrinopathy. Those with a history of alcoholism, drug addiction, excessive ingestion of coffee (more than 4 cups/day) or recent weight loss were excluded. All subjects gave informed consent. Details of past and family history were obtained from the patient, his relatives, if available, and records of previous hospitalisation.

All patients were kept drug free for three days after hospitalisation while they were investigated and got acclimatised to the hospital milieu. On the fourth day, 1 mg of dexamethasone was administered orally at 11 PM under observation of nursing staff.

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Blood samples were collected at 4 PM & 11 PM the next day for estimation of plasma cortisol by radioimmunoassay. DST non-suppression was defined as a post-dexamethasone plasma cortisol (PDPC) level in any one sample, equal to or greater than 5  $\mu\text{g}/\text{dl}$ . The clinical investigators had no knowledge of the DST results till the discharge of the patients. The laboratory technician estimating the plasma cortisol level was unaware of the clinical details of the subjects.

All patients were treated with imipramine hydrochloride (Dose range 150-225 mg/day in divided doses). To start with they were put on 75 mg of imipramine hydrochloride and the dose was gradually increased, depending on the clinical response. Severely depressed patients with active suicidal rumination, in addition to antidepressants, also received ECTs (4-6). Outcome of treatment was assessed by repeating the HRSD every 7 days. Clinical recovery was defined as a HRSD score of 5 or less. Statistical analysis was performed using the students 't' test

and Chi square test (with Yates correction where applicable). Predictive power of the DST were calculated as per Baldessarini et al. (1983).

## RESULTS

DST nonsuppression occurred in 23 patients and 2 of the normal controls. Thus the DST had a sensitivity of 67.6%, a specificity of 93.3% and a positive predictive power of 92% which compares favourably with other diagnostic tests in clinical medicine (Carroll, 1982). Depressed patients did not differ significantly from the normal controls in respect of age. The mean score of the depressed patients on the HRSD was 28.4. The mean PDPC level of the patients was significantly higher than those of the controls both at 4 PM (5.51  $\mu\text{g}/\text{dl}$  versus 2.4  $\mu\text{g}/\text{dl}$ ) and 11 PM (3.84  $\mu\text{g}/\text{dl}$  versus 1.3  $\mu\text{g}/\text{dl}$ ) (Table I).

DST nonsuppressors and suppressors did not differ in respect of mean age. However, DST nonsuppressors as a group were significantly more depressed compared to DST

TABLE I. Clinical and laboratory characteristics of normal controls, depressed patients and DST nonsuppressors & suppressors

Subjects	N	Mean age in years (range)	Mean HRSD score ( $\pm$ SD)	Mean PDPC levels in $\mu\text{g}/\text{dl}$ ( $\pm$ SD) at	
				4 PM	11 PM
Normal Controls <sup>a</sup>	30	34.1** (19-48)	2.2* (1.5)	2.4* (1.4)	1.3* (0.8)
Depressed patients <sup>b</sup>	34	34.7** (19-47)	28.4* (4.69)	5.51* (2.93)	3.84* (2.24)
DST non-suppressors <sup>c</sup>	23	35.4** (19-47)	29.7‡ (3.28)	6.48‡ (2.05)	4.8‡ (1.23)
DST suppressors <sup>d</sup>	11	33.3** (23-43)	26.2‡ (3.33)	3.4‡ (1.12)	1.8‡ (0.51)

Note : While comparing a versus b and c versus d

\*indicates significance at 0.1%  $p < 0.001$

‡indicates significance at 1.0%  $p < 0.01$

‡indicates significance at 5%  $p < 0.05\%$

\*\* indicates comparison not significantly different.

suppressors (Table I) and had a higher incidence of suicidal attempts (4 versus 1), past history of depression (6 versus 2) and family history of depressive illness (4 versus 0). Treatment with ECT, in addition to antidepressants, was required by 78.3% (n=18) of nonsuppressors as compared to 45.4% (n=5) of suppressors. A satisfactory response to therapy was obtained in 82.6% (n=19) of nonsuppressors compared to 63.6% (n=7) of suppressors.

## DISCUSSION

The mean PDPC levels of the depressed patients was significantly higher as compared to the controls both at 4 PM and 11 PM. Moreover, the mean PDPC levels of the patients at 4 PM was higher than the levels at 11 PM (Table I). These observations confirm the findings of Halbreich et al. (1985) and suggest that despite the plasma cortisol hypersecretion, the circadian rhythm of plasma cortisol secretion is maintained in the depressed patients.

The high sensitivity of the DST for endogenous depression in the present study (67.6%), though in agreement with some reports (Carroll et al., 1981; Targum et al., 1982), contrasts with the low sensitivity of 25% & 30% reported by Meltzer et al. (1982) and Peselow et al. (1983), which could be due to variations in the DST procedure employed and inclusion of more patients with mild depression HRSD score > 16.

In agreement with a number of studies (Carroll et al., 1981; Bowie & Beaini., 1985), in our study also the DST had a specificity of 93.3% for endogenous depression. This observation, however, contrasts with the low specificity of 53% & 56% reported by Meltzer et al. (1982) and Berger et al. (1984) who concluded that the DST is not specific for endogenous depression and explained DST nonsuppression on the basis of confounding intervening variables such as the stress of hospitalisation, withdrawal of psy-

choactive drugs, weight loss, alcohol withdrawal and so on. However, despite eliminating these factors, we found a higher specificity of the DST for endogenous depression.

In the present study conducted at a general psychiatric ward with a prevalence of 53.1% of endogenous depression the DST had a positive predictive power of 92%, which is in agreement with a number of studies and proves the usefulness of the DST in the diagnosis of endogenous depression. However, the predictive power of the DST varies tremendously depending upon the prevalence, and can increase from 29% to 92% with no change other than increased prevalence of endogenous depression (Shapiro & Lehman., 1983). Unless this is appreciated, the performance of the DST can be very disappointing. The results of the DST can be improved by screening patients to increase artificially the prevalence of endogenous depression and improving specificity by controlling the factors known to produce false-positive results. Just as physicians do not use routine ECGs to screen for myocardial infarction, psychiatrists should not use the DST to screen psychiatric patients for endogenous depression. Thorough clinical assessment must always precede any laboratory testing which is aimed at confirming a tentative diagnosis.

DST nonsuppressors were significantly more depressed as compared to DST suppressors (Table I), which is consistent with the findings of Whiteford et al. (1986) and also explains why DST nonsuppressors required treatment with ECT more often. The HPA disruption therefore appears to be explained by the severity of depression. On the other hand, Levy and Stern (1987) failed to find a significant relation between the severity of depression and DST nonsuppression. Thus further investigations are warranted.

A strong association between suicidal behaviour and abnormal DST results has been observed and it has been suggested that

the tendency of endogenously depressed patients to attempt suicide is exacerbated by an underlying neurobiological disorder reflected by limbic HPA axis dysregulation (Carroll, 1982; Targum et al., 1983). In our study also, of the five patients who gave a history of suicidal behaviour four were DST nonsuppressors.

A family history of depressive illness was given by only four patients, but interestingly all were DST nonsuppressors. Though the number is small, this finding is consistent with the view that among patients with endogenous depression, abnormal DSTs are significantly associated with a family history of depression (Carroll, 1982).

A pretreatment abnormal DST result appears to predict a favourable response to therapy, as is evident from the fact that 82.6% of nonsuppressors showed a good response to therapy, compared to 63.6% of suppressors. Likewise, Arana et al. (1985) after reviewing eight studies involving 819 patients concluded that 75.5% of DST nonsuppressors responded satisfactorily to treatment compared to 64.4% of suppressors.

DST nonsuppression is claimed to be a biological marker for endogenous depression comparable to serum acid phosphatase levels in prostatic carcinoma, implying that the cause of the abnormal test reflects the cause of the disease. This claim is premature because, as yet, there is no evidence for a pathological process occurring in endogenous depression for which DST nonsuppression is a 'marker'. Attempts to explain nonsuppression as an indicator of cholinergic hypoactivity or of noradrenergic hyperactivity in the hypothalamus remain speculative (Carroll, 1982). Current evidence indicate that these explanations are considerable oversimplifications of the biochemical abnormality in endogenous depression. It is probable that the HPA axis hyperactivity is only a sign occurring in a subgroup of patients with endogenous depression. However, the ability

of the DST to identify this abnormality accurately makes the test useful in the diagnosis and management of patients having endogenous depression.

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