DEXAMETHASONE SUPPRESSION TEST IN DEPRESSION

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SUMMARY

Baseline plasma cortisol levels and response to dexamethasone in a group of twenty-five patients with major depressive disorder (MDD) and a control group of twenty-five patients with psychiatric diagnoses other than MDD were estimated. The results of our study show that dexamethasone suppression test (DST) is a useful diagnostic aid in MDD with melancholia with a sensitivity of 46% and specificity of 96%. Nonsuppression to DST is a marker of the state of melancholia and is not influenced by any other demographic or clinical variable. In our study a 4 p.m. sample alone identified all the DST positive patients. MDD with melancholia showed significantly higher percentage of cortisol hypersecretion and all non-suppressors were hypersecretors.

The function of adrenal cortex in depression is the most thoroughly studied aspect of clinical psychoendocrinology. Disturbance in the activity of Hypothalamo-pituitary-adrenal (HPA) axis has been the subject of extensive research. The importance of the study of the HPA axis is due to the supposed relationship between life stress and depression and the clinical association between depression and diseases of the Pituitary-Adrenal system. It is now well accepted that in patients with depression the baseline plasma cortisol level is elevated and also there is disturbance in the circadian rhythms of cortisol secretion (Carroll et al 1976, Schelless et al 1980). The abnormal escape from suppression with dexamethasone has been an area of particular interest. Carroll et al (1981) standardised the procedure for dexamethasone suppression test (DST). In their study DST identified patients with melancholia, a subtype of major depressive disorder (MDD) defined in DSM III (APA 1980), with a sensitivity of 67% and a specificity of 96%. Non-suppression was found to be a marker of the state of melancholia and was not influenced by other factors such as age, sex, frequency of episodes, duration of illness, severity of depression or psychotropic drugs, provided factors which can produce false negative and false positive results are eliminated. The diagnostic usefulness of DST in depression has been supported by the reports of Targum et al (1982) Mendlewicz et al (1982) Evans et al (1983) and Schatzberg et al (1983). But several other workers Spar et al (1982), Coppen et al (1983), Hallstrom et al (1983) and Berger et al (1984) questioned the diagnostic validity of DST by discussing several methodological problems in the earlier studies.

The present work is designed to study the HPA axis dysfunction, by measuring the baseline plasma cortisol levels and studying the response to dexamethasone in patients with MDD. The procedure was based on the procedure described by Carroll et al (1981).

Material and Methods

25 patients (15 males and 10 females) who fulfilled the criteria in DSM III (APA 1980) for MDD were included in the experimental group. The control group consisted of 25 patients (14 males and 11 females) with psychiatric diagnosis other than MDD based on DSM III criteria.

Exclusion Criteria:

Organic brain syndromes and any major
Results

Analysis of demographic data showed no significant difference between the two groups regarding sex distribution, marital status and socioeconomic status. There was statistically significant difference in the mean age between the experimental and control groups (Mean Age in MDD Group 40.59 ± 13.54; Control Group 25.64 ± 9.52; P < 0.001).

There was no significant difference in non-suppression when MDD group as a whole was compared with the control group. But within the MDD group, only patients with melancholia showed non-suppression and this was statistically significant in comparison with MDD without melancholia. The sensitivity of DST for diagnosis of melancholia in comparison with the control group was 46.15% and specificity was 96%. Non-suppression did not have any correlation with other factors like past history of affective illness, duration of present episode and unipolar or bipolar nature of the illness (Table 1 & 2).

Non-suppression was also not influenced by the severity of depression as measured on Hamilton's Rating Scale for depression. Even though there was statistically significant difference in mean age between the experimental and control groups, there was no difference between suppressors and non-suppressors in the age distribution (Table 3).

Non-suppression was observed in all the age groups (one patient in 21-30 years group; two patients in 31 to 40 years group; two patients in 51 to 60 years group and one in 61 to 70 years group) thereby showing that age was not the influencing factor.

There was no statistically significant difference between the MDD and control groups regarding pre-dexamethasone cortisol level. But within the group of MDD significantly higher percentage of patients with melancholia were hypersecretors (Table 4).
Table 1
Plasma cortisol levels of different diagnostic group showing the number of patients in each level

| CORTISOL VALUES | PRE DEXAMETHASONE | POST DEXAMETHASONE |
|-----------------|-------------------|-------------------|
|                 | 11 P.M.           | 4 P.M.            | 11 P.M.           |
|                 | Non              | Non              | Non              |
| m ug/dl         | C (n=25)         | M (n=12)         | M (n=13)         | C (n=25)         | M (n=12)         | M (n=13)         | C (n=25)         | M (n=12)         | M (n=13)         |
|Criterion for hypersecretion & Non-suppression ≥ 5 μg/dl |                    |                   |                   |                    |                   |                   |                    |                   |                   |
| ≥ 1             | -                 | 1                 | -                 | 8                  | 8                  | 1                 |
| ≥ 2             | 2                 | 1                 | 1                 | 13                 | 8                  | 3                 | 14                 | 4                  | 7                 |
| ≥ 3             | 3                 | 4                 | 1                 | 8                  | 4                  | 3                 | 2                  | -                  | 4                 |
| ≥ 4             | 12                | 6                 | -                 | 2                  | -                  | 1                 | 1                  | -                  | -                 |
| ≥ 5             | 3                 | 1                 | 1                 | -                  | -                  | 4                 | -                  | -                  | -                 |
| ≥ 6             | 3                 | -                 | 3                 | -                  | -                  | 1                 | -                  | -                  | -                 |
| ≥ 7             | 1                 | -                 | -                 | -                  | -                  | -                 | -                  | -                  | -                 |
| ≥ 8             | -                 | -                 | 1                 | -                  | -                  | -                 | -                  | -                  | -                 |
| ≥ 9             | -                 | -                 | 2                 | 1                  | -                  | 1                 | -                  | -                  | -                 |
| ≥ 10            | 1                 | -                 | 3                 | -                  | -                  | -                 | -                  | -                  | -                 |
| ≥ 11            | -                 | -                 | 1                 | -                  | -                  | -                 | -                  | -                  | -                 |

C = Controls
M = Melancholic MDD Patients
Non M = Non Melancholic MDD Patients

Table 2
Non-suppression in the Groups

| Subject Group | No. | No. of Non-suppressors | Percentage of Non-suppressors | Statistical Significance |
|---------------|-----|------------------------|-------------------------------|--------------------------|
| MDD Group     | 25  | 6                      | 24                            | NS                       |
| Control Group | 25  | 1                      | 4                             | NS                       |
| Melancholics  | 13  | 6                      | 46.15                         | P < .01                  |
| Non-melancholics | 12 | 0                      | 0                             | NS                       |
| Unipolar      | 21  | 5                      | 23.8                          | NS                       |
| Bipolar       | 4   | 1                      | 25                            | NS                       |
| Post History of Affective Illness | | | | |
| Present       | 10  | 2                      | 10                            | NS                       |
| Absent        | 15  | 4                      | 26.66                         | NS                       |
| Duration of Illness | | | | |
| < 6 months    | 18  | 4                      | 22.22                         | NS                       |
| > 6 months    | 7   | 2                      | 28.5                          | NS                       |
Table 3
Demographic Data & HDS Score

| Subject Group   | No. | M   | F   | M  | S | D/W | L  | M | U | Age | HDS Score |
|-----------------|-----|-----|-----|----|---|-----|----|---|---|-----|-----------|
| Non Suppressors | 6   | 4   | 2   | 1  | 1 |     | 2  | 3 | 1 | 45.5| 36.8      |
| Suppressors     | 7   | 4   | 3   | 5  | 1 | 1    | 3  | 3 | 1 | 47  | 33.3      |

Statistical Significance: NS NS NS NS NS

Table 4
Hypersecretors in the Groups
(Based on Pre-Dexamethasone 4 P.M. Cortisol Levels)

| Subject Group                | No | Hypersecretors | Significance |
|------------------------------|----|---------------|-------------|
| MDD Group                    | 25 | 14            | NS          |
| Control Group                | 25 | 8             |             |
| MDD with Melancholia         | 13 | 11            |             |
| MDD without Melancholia      | 12 | 1             | P < .001    |
| Non-suppressors              | 6  | 6             |             |
| Suppressors                  | 7  | 5             | NS          |

Criterion for Hypersecretion - Baseline Plasma Cortisol Value of ≥ 5 μg/dl

Discussion

Results of the present study indicate that non-suppression to DST is a state marker of melancholia and is not influenced by any of the demographic factors and other clinical variables. This finding is in agreement with the reports of other workers (Carroll et al 1981, Mendlewicz et al 1982, Schatzberg et al 1983, Targum et al 1982).

Even though there is some agreement regarding the diagnostic usefulness of DST in melancholia, the predictive value of the test varied in different studies. The variability has been attributed to diagnostic criteria used for sample selection, dose of dexamethasone administered, timing of the sample, method of estimation of plasma cortisol and the criterion value taken for non-suppression. The influence of different methods of estimation on the results has been discussed by Maruta (1982), Fang (1982) and Meltzer and Fang (1983).

Strokes et al (1984) argued that age and gender may affect the result and Berger et al (1984) discussed that stress of hospital admission and psychotropic drugs are some of the factors influencing non-suppression. The results of present study do not support the above possibility. Non-suppression was found both in outpatients and inpatients and also in patients on psychotropic drugs and those without.

It is widely discussed that weight loss is a significant factor influencing non-suppression. But Coppin et al (1984) in their study of two groups - Depression with weight loss and depression without weight loss does not necessarily result in an abnormal DST result. They have shown non-suppression was seen in 73% of depressive with
weight loss and in 61% of depressive without weight loss.

Carroll et al. (1981) suggested that two samples taken at 4 p.m. and 11 p.m. increase the sensitivity of the test. In our study the 4 p.m. sample alone identified all the positive results. This indicates that DST can be done with the 4 p.m. sample alone without loss of sensitivity or specificity. The importance of this finding is regarding the cost of the procedure and also in administration for outpatients.

In conclusion the results of our study show that DST is a laboratory test useful for the diagnosis of melancholia. But the results should be interpreted with caution considering the small sample size. Further research along with the other tests of neuroendocrine battery may prove useful in identification of specific diagnostic tests for depressive illness.

It may be interesting to see the treatment responses in relation to DST and Brown et al. (1980) have reported better response in a significantly higher percentage of non-suppressors compared to suppressors. A project regarding treatment response is under current investigation by the authors.

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