

POST DEXAMETHASONE PLASMA CORTISOL LEVELS IN DEPRESSIVES TREATED WITH IMIPRAMINE AND ELECTROCONVULSIVE THERAPY⁵

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SUMMARY

Sixty patients of endogenous depression and thirty normal controls were studied to find out the relationship of post dexamethasone plasma cortisol levels (PDPC) and clinical improvement of endogenous depression in patients treated with electroconvulsive therapy and imipramine. The PDPC levels in both the group of patients showed significant decrease with clinical improvement (Pre and post treatment PDPC values of ECT group was 20.7 ug/dl and 13.6 ug/dl while it was 17.9 ug/dl and 12.7 ug/dl respectively for the Imipramine group). A significant correlation was also found between PDPC and severity of illness ($p < 0.001$) in the both groups which indicates that PDPC levels is independent of treatment modality used.

The last quarter of the century has seen biological psychiatry growing from its infancy to a adolescence. Among the many theories propounded about the neuro-biological mechanisms in major functional psychoses, Dexamethasone Suppression Test (DST) has emerged to be the most promising one. The pioneer in this field was B. J. Carroll (1982) who along with M. Feinberg, M. Steiner and co-workers had done much to standardise the test for use in psychiatry.

DST has been called as laboratory marker of endogenous depressed state (Carroll et al., 1980). Response to DST is non suppressive during melancholia and suppressive during euthymia (Carroll, 1972). Newer studies have suggested that DST might serve as an ancillary

index to predict clinical response and outcome of depression (Carroll et al., 1968). The DST tends to normalize as depression subsides (Carroll, 1982 ; Greden et al., 1980) and may even normalize well before clinical improvement which may have a predictive value for good treatment response.

Coryell (1982) has predicted good ECT response when an abnormal DST was found at discharge. However, it was also suggested that ECT may be affecting hypothalamic structures which invalidate its use as response predictor (Grunhams et al., 1983).

The PDPC levels have been used in monitoring of antidepressant treatment (Greden et al., 1983). However, as the issue is still controversial regarding the

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utilisation of a uniform procedure for the measurement of PDPC and its use in depressives treated with ECT and antidepressant drugs, we had planned a prospective study with the following aims :

1. To assess the relationship of post dexamethasone plasma cortisol levels and severity of depression in endogenous depressives.

2. To study the effect of treatment (ECT and Imipramine) and clinical response on PDPC.

Material and Methods

The study was performed on an open parallel design. The patients were randomly assigned for treatment to either drugs or ECT. The patients of the experimental group comprised of 60 patients (drawn from the inpatient, Department of Psychiatry, K. G's. Medical College, Lucknow) diagnosed as Manic Depressive Psychosis Depression (ICD-9, WHO) and fulfilling the Research Diagnostic Criteria for major depression (Spitzer et al., 1978). The patients were between the age of 17-55 years and were evaluated on a preset selection criteria. The control group consisted of 30 normal subjects having no medical or psychiatric illness and matched for age and sex with the experimental group. They were evaluated clinically as well as on Cornell Medical Index (Broadman et al., 1949) to rule out psychiatric illness. The control group was taken to compare its values with that of depressives.

The patients were evaluated on screening schedule, semistructured proforma, Research Diagnostic Criteria and Hamilton Rating Scale for depression (HRSD) (Hamilton, 1960) at the commencement of the study. An informed consent was also obtained from each patient and control. These patients were kept under observation for 7 days (as a washout period of any drug taken) and those patients whose

HRS-D score was 17 or more on 7th day (day 0) were only included in the study.

The patients of ECT group were given biweekly direct ECT's (direct ECT's were given to exclude the effect of drugs used in anaesthesia) upto a maximum of 10 treatments. However, the treatment was stopped when HRS-D levels fell to 5 or less. No extra medication was given apart from nitrazepam on SOS basis. The patients of the antidepressant group received a fixed dose of Imipramine, 75 mg/day initially which was increased to 225 mg/day within a week. The drug was stopped when HRS-D fell to 5 or less.

Weekly estimations of HRS-D and PDPC was done in both the groups. PDPC estimations was done by giving 1 mg of dexamethasone to the patient at 11 P. M. followed by sampling of blood at 4 P.M. on the following day. The plasma was separated and PDPC levels estimated by spectrophotometric method (Mattingly, 1962). PDPC and HRS-D was estimated on Day 0 and thereafter every week on day 7, 14, 21, 28 and 35 or stopped earlier when HRS-D score fell to 5 or less. Only one point PDPC was done on the control group.

Results

Sixty depressed and thirty controls were compared for PDPC values. The mean PDPC values of the depressed patients (pre treatment) was 18.2 ± 6.2 $\mu\text{g/dl}$ (range 10.5-39.6) as compared to 11.9 ± 4.2 $\mu\text{g/dl}$ (range 7.2-19.5) that of controls. There was a significantly higher PDPC values in depressed patients as compared to the controls. Thirty seven out of sixty patients had their first episode of depression while the rest had two or more episodes.

When mean PDPC was compared in the male and female depressives it was found to be statistically non significant. The mean PDPC levels of the depressed

TABLE—Mean PDPC levels in ECT and Imipramine group ($\mu\text{g}/\text{dl}$)

	ECT group		Imipramine group	
	Improved (N=23)	Non improved (N=7)	Improved (N=19)	Non improved (N=11)
<i>Pre treatment</i>				
Mean	20.7	13.1	17.9	13.7
s.d.	6.2	1.8	5.5	1.5
range	10.8–39.6	10.9–21.4	10.5–27.3	11.1–19.2
<i>Post treatment</i>				
Mean	13.6	11.3	12.7	11.8
s.d.	2.6	0.6	4.1	0.8
range	8.2–18.8	9.1–14.2	7.1–20.8	8.7–12.8
t	7.45	2.3	5.13	2.6
p	<0.001	N.S.	<0.001	N.S.

patients at the beginning was 18.2 ± 6.2 $\mu\text{g}/\text{dl}$ (micro gram per decilitre) (range 10.5–39.6) with the corresponding HRS-D of 27.4 ± 9.0 (range 19–36). There was significant correlation found between PDPC levels and severity of illness, i.e. the PDPC tends to increase with increasing severity of illness ($r: 0.71$; $p > 0.001$).

The mean PDPC levels in the patients treated with ECT and those treated with Imipramine were found to change significantly on clinical improvement in their depressive status. Thus pre and post treatment PDPC values in the ECT treated group was 20.7 $\mu\text{g}/\text{dl}$ and 13.6 $\mu\text{g}/\text{dl}$ respectively. There was a significant decrease in the mean PDPC from 17.9 $\mu\text{g}/\text{dl}$ to 12.7 $\mu\text{g}/\text{dl}$ in the Imipramine group (Table).

No significant difference was found in the PDPC values of MDP-depressed type and MDP-circular currently depressed. 76.7% patients improved with ECT's while 63.3% showed improvement with antidepressant drugs. The patients on ECT showed quick recovery (50%

improved within three weeks) as compared to patients on Imipramine (37% improved within three weeks). This shows that patients on ECT tend to respond faster than on pharmacotherapy. Another finding was the significant decrease of plasma cortisol levels in the improved group.

Discussion

The DST has been primarily investigated as an aid in diagnosing endogenous depression, yet its major clinical use has been as a predictor of treatment response. It is commonly held that as abnormal DST predicts response to somatic therapies. Gitlin and Garner (1986) reviewed 16 published reports and found that DST predicted response to somatic therapies in only 6 of them.

No difference could be detected in overall therapeutic improvement between those patients with a normal or abnormal DST respectively based on 5 $\mu\text{g}/\text{dl}$ cortisol cut off point used by Coppen *et al.* (1985). However, when

they increased the cut off point to 10 $\mu\text{g}/\text{dl}$ it was found that patients having PDPC more than 10 $\mu\text{g}/\text{dl}$ responded significantly better than those who had a normal DST response. This was found to be independent of the treatment modality used. Our findings are in agreement with the above study. The patients of the improved group had a higher mean PDPC as compared to the patients of the non improved group (The patients of the improved group had mean PDPC of 20.7 and 17.9 $\mu\text{g}/\text{dl}$ in the ECT and Imipramine group respectively whereas the non improved had 13.1 and 13.7 $\mu\text{g}/\text{dl}$ in these two groups).

The PDPC levels in the present sample was found to be significantly higher in depressed patients as compared to normal controls ($p < 0.001$). This is in agreement with McClure (1966), Carpenter and Bunney (1971), Carroll (1978), Verghese et al. (1973). However, Shopsin and Gershon (1971) could not find any difference in PDPC levels in the depressives and controls.

Several studies (McClure, 1966 ; Coppen, 1967 and Sethi and Sethi, 1971) have reported that higher plasma cortisol levels were found during heightened state depression thus indicating the increased of secretion of plasma cortisol in severe depressives. Similar findings were observed in the present study when a significant correlation was found between PDPC levels and severity of depression . However, this is not universally accepted and some authors (Carroll and Davies, 1970 and Verghese et al., 1973) had presented contradictory reports.

Patients of the ECT treated group as well as, imipramine treated group showed significant improvement (Table) and a significant decrease in PDPC values. This goes on to prove that PDPC is independent of the treatment modality used.

As Galen and Gambino (1975) stated, "the monitoring of treatment is one of the most persuasive reasons for ordering a laboratory test", DST is all set to fulfil the above requirement in the years to come.

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