VOLUME-7, ISSUE-7, JULY-2018 • PRINT ISSN No 2277 - 8160

Original Research Paper

Rehabilitation Science

PROLACTIN LEVELS BEFORE AND AFTER ELECTROCONVULSIVE THERAPY AND ITS CORELATION WITH CLINICAL IMPROVEMENT IN PSYCHOPATHALOGY

Dr.Shalini Bijali	DNB Resident, Institute of Mental Health Amritsar.
Dr D. Ram	Professor and Director, Central Institute of Psychiatry, Ranchi.
Dr. S.K. Munda	Assistant Professor of psychiatry, Central Institute of Psychiatry, Ranchi.
Dr. Vikalp Wasnik*	Assistant Professor of Psychiatry, Raipur Institute of Medical Sciences *Corresponding Author

ABSTRACT

BACKGROUND: It is a well-known fact that prolactin increases after Electroconvulsive Therapy (ECT), but in later studies it was found that the amount of prolactin rise after each ECT gradually declines on successive ECT. Many studies have found that there is a correlation between this prolactin drop and improvement in psychopathology. But the results found were inconsistent and only limited to depression.

AIM: To see the serum prolactin changes during a course of ECT in patients suffering from BPAD mania and to assess whether any correlation exists between these changes and improvement in psychopathology.

METHORD: 20 inpatients meeting diagnostic criteria for BPAD mania as per ICD-10 who were planned to receive ECT were taken as cases and 20 BPAD mania patients not receiving ECT were taken as controls. Blood for prolactin and psychopathology on YMRS assessed three times in each case. First at baseline, second after 1st ECT and third after last ECT. Similarly controls were assessed at baseline and after three weeks for prolactin and psychopathology.

RESULTS: In patients who received ECT, serum prolactin levels were significantly raised after 1st ECT (mean 78.65) compared to baseline (mean 54.02). Prolactin level significantly decreased after a course of ECT (mean 67.22). There was no significant correlation between prolactin changes and in YMRS score.

CONCLUSION: There is no significant correlation between prolactin changes during a course of ECT and improvement in psychopathology in BPAD mania patients suggesting the prolactin rise may be an epiphenomenon to ECT rather than reflection of therapeutic process.

KEYWORDS : Prolactin, ECT, Bipolar Disorder.

INTRODUCTION

Prolactin secretion is affected by a large variety of stimuli provided by the external and the internal environment. The most important physiological stimuli that elevate pituitary prolactin secretion are suckling, stress, and increased levels of ovarian steroids, primarily estrogen (Tucker, 1981). Such stimuli are detected by hypothalamus which releases various prolactin releasing factor (PRF) and prolactin-inhibiting factors (PIF). Observations that drugs affecting catecholamine metabolism alter prolactin secretion (Arey, Kanyicska, & Freeman, 1991; Coppola, Leonardi, Lippmann, Perrine, & Ringler, 1965) and the dopamine is present in high concentration in both the median eminence and the hypophysial stalk blood led to the conclusion that dopamine is the major physiological hypothalamic PIF. Prolactin levels are also increased immediately after seizures, both spontaneous and those induced by electroconvulsive therapy (ECT) (Abrams & Swartz, 1985a; Deakin, Ferrier, Crow, Johnstone, & Lawler, 1983; Ohman, Balldin, Walinder, Wallin, & Abrahamsson, 1976). This prolactin release is transient and the prolactin level reaches back to normal within one to two hours. Around 75-96% of the prolactin released 15 minutes after the seizures and 88-99% completed by 20 minutes (C. M. Swartz, 1985b).The increases in plasma prolactin (PRL) during electroconvulsive therapy (ECT), as a reflection of cerebral stimulation, have been much studied with the prospective to obtain information about its neurobiological mode of action, especially on neurotransmitter systems that may be involved, the most probable candidates being serotonin and dopamine. An attenuation of the prolactin response to ECT has been found after pre-treatment with the non-selective serotonin antagonist methysergide, a drug that also possesses dopamine receptor agonistic activity as well. A total blockade of the prolactin increases by ECT has been reported by Ziset al.1992(A. ZIS, MCGARVEY, CLARK, LAM, & ADAMS, 1992), when the dopamine receptor antagonist metoclopramide, which is also a 5-HT3 receptor antagonist, was given intravenously 30 min before ECT in five patients. The drug causes a substantial elevation of plasma PRL to a mean of 196ng/ml, and the application of the electrical stimulus did not cause any further increases. The authors conclude that seizure-induced PRL increases occur only when some degree of dopaminergic inhibitory tone on the pituitary lactotroph is operative. The prolactin release by ECT can be caused just by a transient increase in serotonergic activity, and/or a transient inhibition of dopaminergic input in the hypothalamus- pituitary axis.

Few studies which showed a significant negative association between the PRL surge and clinical response, with responders demonstrating a decrease in their Prolactin surge as the ECT course progressed. This diminution in the PRL surge could not be fully explained by a decrease in the relative electrical dose above threshold that responders received, secondary to ECT-induced increases in seizure threshold over the treatment course (SACKEIM, DECINA, PORTNOY, NEELEY, & MALITZ, 1987). The lack of a positive association between the PRL surge and clinical response suggests that the mechanisms or pathways responsible for the PRL release are not essential to the therapeutic effects of ECT. These findings argue against the theory of hypothalamic mediation of the therapeutic effects of ECT. The prolactin changes occurring immediately after the ECT may reflect the underlying changes of neurotransmitter after the seizure and thus may have a clinical relevance (C. SWARTZ & ABRAMS, 1984). Studies done in melancholic patients showed that higher post ictal prolactin was associated with the slower improvement and requirement of more number of ECTs, indicating depressive patient's larger pool of prolactin in pituitary was more resistant to treatment (Abrams & Swartz, 1985b). Accordingly a single patient who showed no elevation in prolactin after any ECT recovered from depressive stupor within an hour after ECT (C. M. Swartz, 1985b).

According to the present neurophysiological hypotheses for depression, ECT modulates the responsivity of central neurotransmitter systems. Serotonergic responsively was assessed by measuring the prolactin responses to I.V. administration of the clomipramine, serotonin uptake inhibitor and dopaminergic responsivity by measuring the prolactin responses to the dopamine

receptor blocker haloperidol, administered intramuscularly. The prolactin responses to CMI were significantly blunted in the patient group compared to the control group and remained unaltered at the end of the ECT course, although the depressive symptomatology was substantially reduced. Concluding that the therapeutic effect of ECT in depression is not a result of modifications in central serotonergic or dopaminergic responsivity, as revealed by the neuroendocrine challenge tests. The prolactin and cortisol responses to the electrical stimulus were the same during the first and the last ECT of the course. The lack of changes implicates that the release of the hormones during ECT are caused mechanisms that are not connected to psychopathology. Among the four major dopaminergic pathways, tuberoinfundibular pathway is constrained to the hypothalamus and regulates some functions of the anterior pituitary through the release of dopamine into the portal vessels. The tuberoinfundibular system is confined to the hypothalamus, which is currently not amenable to accurate in vivo volumetric image analysis but widened third ventricle may reflect loss of tissue from this structures (Bhadoria et al., 2003). A meta-analysis demonstrated significant enlargement and dilation of the anterior portion of the third ventricle compared to controls in BPAD patients (KEMPTON, GEDDES, ETTINGER, WILLIAMS, & GRASBY, 2008). This reflects the abnormal involvement of hypothalamic- tuberoinfundibular pathway suggesting as a source of dopamine imbalance in BPAD.

ECT being the effective treatment option in Bipolar patients, currently in mania, and has improved considerably in the last decades, the crucial neurobiological mechanisms contributing to the therapeutic efficacy in are still under investigation Explanations for the mechanism of ECT tend to be similar to those used to explain the therapeutic actions of the psychoactive drugs, that is by alteration of neurotransmitters. There are very few studies conducted, assessing the role of post ECT prolactin levels with respect to psychopathology in bipolar mania patients. The hypothesis proposed for depressive disorders were applied to the manic disorder and the correlation was studied. As the seizures induced by ECT is important its therapeutic action and also induced seizures results in release of prolactin from hypothalamus, it was assumed that the amount of prolactin released may reflect the stimulation of hypothalamus, and hence can be co-related with the psychopathology (Abrams & Swartz, 1985b). This prolactin release was observed to drop significantly from first ECT to the last ECT. But one study conducted in mania patient showed no relationship of this drop of prolactin with psychopathology (CHAUDHRY et al., 2000).

However, it is still not fully understood whether the changes, which were found at different neuroendocrine or neurohormonal levels caused by ECT, are epiphenomenal to the seizure, or a reflection of on-going therapeutic processes.

METHODOLOGY:

It was an open label study conducted at Central Institute of Psychiatry (C.I.P.), Ranchi, India. The study sample comprised of 20 patients aged between 18-60years admitted in CIP, fulfilling the diagnostic criteria for bipolar affective disorder current episode manic ICD-10 (DCR) planned for ECT. 20 age and sex, matched patients having diagnosis of bipolar affective disorder current episode manic, who are not receiving ECT, were taken as controls. Both the groups were kept on fixed dose of Haloperidol and Benzodiazepines when required. Females who were pregnant in the past one month or breast feeding and patients with major medical disorders were excluded. Study was started after taking informed consent from all the participants. Socio-demographic and clinical data was collected. Baseline severity of mania of both the study and the control group was obtained using Young's Mania Rating Scale (YMRS). 5ml blood from cubital vein was collected from each patient using all aseptic measures, for the measurement of baseline serum prolactin level. The study group was subjected to the ECT. 5ml venous blood was collected from the patients of study group after 15minutes of first ECT and again after a course of ECT. The severity of mania assessed after first ECT and after last ECT in study group using YMRS. In control group another sample of blood was taken after 3 weeks and YMRS was applied at the same time. The entire blood samples were assessed for serum prolactin levels using ELIZA method. ECT MACHINE- ECT machine used to give electrical stimulation to all patients was kept constant throughout the study. The spECTrum 5000 ECT machine was used with 4 individual parameter sets of pulse width, frequency, duration and current. The treatment dosage is set using the 4 knob beneath the LCD touch screen so that the user can easily see and choose the treatment option. During ECT sessions vitals were monitored using ECG arrangements connected to base unit. ECT machine had two electrodes placed over patient's temporal areas bilaterally.

RESULTS

Comparison of baseline prolactin levels with demographic variable like age and marital status, and with clinical variable like family history. Analysis showed higher baseline serum prolactin levels with mean prolactin value of 89.65ng/dl (with SD of 11.62) in females than males who showed mean baseline prolactin value of 42.44ng/dl (with SD of 12.59) Whereas marital status and family history showed no significant correlation with baseline serum prolactin levels (Table 1)

The Bipolar mania patients receiving ECT treatment had average age of 27.45 ± 6.91 years, the age of onset of illness was 19.6±4.03 years, average numbers of past manic episodes being 3.1±2.24, number of past depressive episodes being 0.50±0.88 and average number of total episodes of 3.6±2.41. On comparison there were no difference between two groups in respect to age of patient, age of onset of illness, and previous manic, depressive and total episodes. (Table 2)

Significant difference was noted in the serum prolactin level at baseline, after 15 minutes of 1st ECT and after a course of ECTs. Serum prolactin levels were significantly less at the baseline in comparison to serum prolactin level after 15 minutes of 1st ECT and after a course of ECTs. Serum prolactin level after 15 minutes of 1st ECT was significantly high compared to serum prolactin level after a course of ECTs and baseline (Table 3). The values of baseline prolactin and after antipsychotic treatment prolactin, in patients who did not receive ECT showed significant difference. Prolactin levels were significantly increased after 3 weeks coarse of antipsychotic. (T. Haloperidol- 10mg) (Table 4) correlation of the changes in prolactin 2 and prolactin 1 (prolactin surge after ECT) with number of ECT required to treat the patient, baseline YMRS and final YMRS and improvement in psychopathology in the form difference between the YMRS 3 AND YMRS1. Analysis shows no significant correlation between the prolactin surge seen after ECT and these parameters.(Table 5). Correlation of the changes in prolactin 2 and prolactin 3(prolactin drop after course of ECT) with number of ECT required to treat the patient, baseline YMRS and final YMRS and improvement in psychopathology in the form difference between the YMRS 3 AND YMRS1. Analysis shows no significant correlation between the prolactin drop seen after course of ECT and these parameters.(Table 6)

Table-1: Comparison of Baseline Serum Prolactin levels with demographic and clinical variable

VARIABLES		BASELINE PROLACTIN		Mann-whitney U test	P value
		(Mean±SD) N=40	Mean Rank		
SEX	Male	42.44±12.59	16.50	.000	.000
	Female	89.65±11.62	36.50		
Family History Of Bpad	Present	42.05±9.03	17.30	139.5	.182
	Absent	57.77±26.29	22.42		
Marital Status	Married	56.18±25.68	22.26	162.5	.316
	Unmarried	47.12±18.15	18.55		

Table-2: Comparison of Socio-demographic and clinical variables (continuous) between patients receiving ECT and those who are not receiving ECT

VARIABLES	Patients with ECT (Mean±SD) N=20	Patients without ECT (Mean±SD) N=20	t	Df	P
Age(in years)	27.45±6.91	28.9±6.92	-.66	38	.512
Age of onset (in years)	19.6±4.03	20.65±4.51	-.77	38	.442
No. Of Past manic episodes	3.1±2.24	3.05±1.82	.08	38	.939
No. Of Past depressive episodes	0.50±0.88	0.25±0.64	1.02	38	.313
No. Of Past total episodes	3.6±2.41	3.30±2.05	.42	38	.675

Table-3: Comparison of serum prolactin level at baseline, after first and last ECT in patients with BPAD currently received ECT for manic episode.

Variables	(Mean±SD) N=20	Pillai's Trace F	P	Post hoc Analysis
Baseline Prolactin	54.024±19.91	16.880	.000	Prolactin 1<2, 1<3, 2>3
Pralactin After 1st ECT	78.655±23.29			
Prolactin After Last ECT	67.22±21.71			

Table-4: Comparison Between Baseline and Post treatment prolactin changes in group not receiving ECT

VARIABLES	(Mean±SD) N=20	T	Df	P
BASELINE PROLACTIN	**49.74**±25.56	**8.70**	**19**	**.000**
PROLACTIN AFTER 3 WEEKS	**59.13**±26.16	**10.11**	**19**	**.000**

Table-5: Correlation of post ECT prolactin surge with number of ECTs and change in Psychopathology

VARIABLES	PROLACTIN2-PROLACTIN1		
	(Mean±SD) N=20	SPEARMAN P	P
Number of ECT	8.75±1.74	.08	.79
YMRS 1	44.75±6.37	.08	.78
YMRS3	7.3±3.54	-.19	.49
YMRS3-YMRS1	38.73±7.32	.16	.55

Table-6: Correlation of prolactin change over a coarse of ECT with number of ECT received and improvement in psychopathology

VARIABLES	PROLACTIN2-PROLACTIN3		
	(Mean±SD) N=20	SPEARMAN P	P
Number of ECT	8.75±1.74	-.14	.60
YMRS 1	44.75±6.37	.42	.12
YMRS3	7.3±3.54	-.12	.94
YMRS3-YMRS1	38.73±7.32	.36	.18

DISCUSSION OF RESULTS

Sample Characteristics

Socio Demographic Characteristics

Our sample contained 16 male (40%) and 4 female (10%) in cases. Females were less in number as women may be more likely to present with an initial depressive episode before onset of mania (Viguera, Baldessarini, & Tondo, 2001) some small; more recent cross-sectional studies suggested that women may have a later age at onset of mania and bipolar disorder (RAYMONT, BETTANY, & FRANGOU, 2003). The mean age at onset for mania was 32.9 years; age at onset was later for women than for men. The mean age at first contact with a health professional for bipolar disorder was 31.2 years; first contact was later for women than for men (KENNEDY et al., 2005). Our study had less number of females as the mean age of the group was small and as less number of people sought in patient management. The mean age of the patients in experimental active group is 27.45 ± 6.91 years. Most of the patients were in early and late adulthood. This represented the usual age of presentation of bipolar patients. Most of the bipolar patients in ECT group was unemployed and belonging to the lower socio-economic status representing the significant vocational disturbances in BPAD patients. It has been suggested that between 30% and 50% of patients with bipolar disorder experience significant social disability that may be linked to persistent cognitive impairment (Goodwin, Martinez-Aran, Glahn, & Vieta, 2008; Zarate, Tohen, & Baraibar, 1997). As few as 1/3 of BPD patients achieve full social and occupational functional recovery to their own premorbid levels (HUXLEY & BALDESSARINI, 2007).

Clinical Characteristics

The mean age of onset of illness in present study was 19.6±4.03years representing the usual age of onset of illness. In a study of 100 patients, two third were hospitalized before the age of 25, and at least 20% had already shown evidence of illness as adolescents. The early 20s was the peak period of onset (Kessler et al., 2005). Another study quoted ages 21 and 28 were derived from the analysis to define age-at-onset in bipolar patients (KENNEDY et al., 2005).Study conducted on bipolar patients in 2002 relating panic disorder also showed the mean age of onset as 19.4±4.51years(MACKINNON et al., 2002).Among BPAD patients there was increased prevalence of family history of affective illness. Previous studies indicated Familial aggregation of major affective disorders in bipolar probands (STROBER, 1992). This was reflected in our study. Around 40% of patients in the intervention group had family history of BPAD. Studies suggest more number of depressive episodes occur in life time of a BPAD patient. The majority were in depressive episodes. Depressive symptoms were more common and more predictive of functioning than manic symptoms (Meeks, 1999).Our findings were contrast to it. Average numbers of past manic episodes being was higher (3.1±2.24) than the average number of past depressive episodes (0.50±0.88). This can be explained by the fact that the guardian recollected manic episode more actively than the depressive episodes in the patients, as manic episodes disturbed the social life more severely than did depressive episodes. The estimated overall prevalence of personality disorders in general population was 9%(Samuels et al., 2002). In our study 3 patients out of 20 patients had dissocial personality traits, giving rise to the prevalence of 15 % which is more than indicated in the general population. This can be explained on the basis of past studies which suggested increased co-occurrence of personality disorder in BPAD patients (PERRY, LAVORI, & HOKE, 1987).

Serum prolactin and psychopathology in Bipolar disorder

Prolactin being secreted from the pituitary gland and being regulated by dopamine (De, Macconi, & Spada, 1979), a key neurotransmitter involved in the affective disorder, is assumed to play a role in the disease process (OREN, LEVENDOSKY, KASPER, DUNCAN, & ROSENTHAL, 1996). Hence its levels are assessed by various studies and correlated with the psychopathology (Abrams & Swartz, 1985b; C. M. Swartz, 1985a). Some studies viewed affective disorder as a disturbance of hypothalamic downregulation of hormones (Daban, Vieta, Mackin, & Young, 2005). The tuberoinfundibular pathway is constrained to the hypothalamus and regulates some functions of the anterior pituitary and thus prolactin through the release of dopamine into the portal vessels (Fink, 2000). Studies of prolactin in depression have found mixed results; Studies of basal prolactin in seasonal affective disorder have also yielded inconsistent results. Two studies have shown that prolactin was reduced in patients with seasonal affective disorder compared to normal subjects (DEPUE et al., 1990; Stojek, Kasprzak, & Słabikowski, 1991). Another study found that basal prolactin did not differ between patients and normals. An earlier study indicated that prolactin levels were raised in patients with affective disorder (JACOBSEN, SACK, WEHR, & ROSENTHAL, 1987), but the unusually low prolactin levels seen in the controls in that study limit the meaning of that finding. Our study did not compare the prolactin level in BPAD patients with healthy controls, but we found no

correlation between the serum baseline prolactin and baseline psychopathology.

Serum prolactin levels in Bipolar disorder undergoing ECT treatment

The serum prolactin levels assessed after 15 minutes of ECT showed significant rise in the prolactin amount, this was consistent with the previous studies that prolactin acutely increased following seizures, whether natural or induced (Kronfol, Hamdan-Allen, Goel, & Hill, 1991; Markianos, Hatzimanolis, & Lykouras, 2002; A. P. Zis et al., 1996). It is a well-replicated finding that shortly after ECT serum prolactin levels are elevated (Lerer & Sitaram, 1983).This was attributed to the temporary withdrawal of the tonic inhibition of dopamine, which leads to the prolactin surge, which normalises within one hour. This release likely depends on the location, intensities and duration of the synaptic neurotransmission in the brain that are part of grand mal seizures (C. M. Swartz, 1985b). Thus post-ictal prolactin elevation might reflect the amount of hypothalamus stimulation during ECT(Abrams & Swartz, 1985b).Over subsequent course of ECTs like in previous studies(C. M. Swartz, 1985b) in our study also it was observed that the post ictal ECT levels gradually decreases. Previous studies stated compared to pre-ECT concentrations, there were significant increases in post-ECT, prolactin these hormonal changes induced by ECT may reflect changes at the neurotransmitter level (Kronfol et al., 1991). The prolactin (PRL) increases in plasma, induced by the electrical stimulus during electroconvulsivetherapy (ECT), is a consistent finding that can be studied in order to obtain information about its actions on the brain neurotransmitter systems, the most probable candidates being the serotonergic and the dopaminergic system. Central serotonergic and dopaminergic responsivity may also be assessed using neuroendocrine challenge tests. One study assessed the central serotonergic and dopaminergic responsivities, by measuring the prolactin responses to the administration of the serotonin uptake inhibitor clomipramine (CMI) intravenously and the prolactin responses to dopamine receptor blocker haloperidol (HAL), administered intramuscularly. Correlations among the prolactin responses to the three ECT stimuli in the patient's group showed that the prolactin responses to ECT were significantly correlated to the prolactin responses to haloperidol and not to the prolactin responses to clomipramine. It is suggested that the rises in prolactin during ECT reflect the responsivity of the hypothalamus-pituitary dopaminergic system, and seem to be the result of a transient decrease in the inhibitory dopaminergic input of the hypothalamus to the pituitary lactotrophs, caused by the electrical stimulus and the subsequent seizure (Markianos et al., 2002). When the dopamine receptor antagonist metoclopramide was given intravenously 30 min before ECT it reported a blockade of the prolactin increases by ECT The drug causes a substantial elevation of plasma prolactin to a mean of 196 ng/ml, and the application of the electrical stimulus did not cause any further increases. The authors concluded that seizure-induced prolactin increases occur only when some degree of dopaminergic inhibitory tone on the pituitary lactotrophis operative (A. ZIS et al., 1992). Another study found that Increases in the concentrations of the dopaminemain metabolite homovanillic acid (HVA) but not of the serotonin or noradrenaline metabolites, have been found in CSF after ECT ((RUDORFER, RISBY, OSMAN, GOLD, & POTTER, 1991). These results increase the evidence that our finding PRL release by ECT is a dopaminergic rather than a serotonergic effect.

On further ECT sessions we also observed that the prolactin surge seen after the ECT gradually declined over course of ECT. The mean prolactin after first ECT was 78.65ng/ml which dropped to 67.22ng/ml overcourse of ECTs. This finding correlated with previous studies (Abrams & Swartz, 1985b; CHAUDHRY et al., 2000; Deakin et al., 1983). When the amount of surge was taken into consideration by noting the difference between baseline prolactin and prolactin after ECT, the difference gradually attenuated. Previous study reported around 30% drop in the prolactin levels over a course of ECT(Deakin et al., 1983). Previous studies measuring post ECT prolactin levels in depressed patients attributed this to the increased sensitization of post synaptic dopamine receptors as ECT progresses(Abrams & Swartz, 1985b). Repeated electrically induced seizures in animals or humans increased the responsiveness of post synaptic dopamine receptor (Modigh, Balldin, Eriksson, Granerus, & Walinder, 1984). A study done in 2010 consisting of depressed patients, assessed changes in the D2 receptor sensitivity using PET scan, before and after ECT treatment. Study showed ECT induced decrease in d2 receptor binding, suggesting reduced density of dopamine receptor. The decreased density of the receptor was attributed to the increased dopamine concentration in synaptic cleft, and increased sensitivity of dopamine receptor after a course of ECT (RUDORFER et al., 1991).

Serum prolactin and prognosis of Bipolar disorder.

Prolactin levels at each step were correlated with psychopathology in respective stage, but unlike the studies in depressive patients we did not get any correlation between prolactin levels and psychopathology. To clarify this, study was taken one step further and the amount of prolactin surge after ECT and the amount of prolactin drop over subsequent ECT were correlated with the improvement in psychopathology which also failed to relate these. Our study was consistent with the study conducted in mania patients who also showed no correlation between prolactin level and the psychopathology (CHAUDHRY et al., 2000). Studies conducted in depressive patients showed inconsistent results. Deakin et al. could not find any correlation between the changing prolactin level and improvement in psychopathology. Whereas another study conducted in depressed patients showed that psychopathology improved as the postictal prolactin levels dropped (Abrams & Swartz, 1985b). Authors explained this correlation on the bases of increase post synaptic dopamine receptor sensitivity after ECT. This fall of prolactin over series of treatment were inversely related with outcome and interpreted in terms of dopamine receptor sensitivity. Authors presumed the patient with larger prolactin were more resistant to prolactin inhibiting effect of dopamine because of relatively unresponsive dopamine receptors, and such people required more number of ECT. But we found there is no correlation between the prolactin level and improvement in psychopathology after ECT in BPAD mania patients, and the rise in prolactin after ECT purely seems to be epiphenomenal to ECT.

CONCLUSION

- Baseline prolactin levels are significantly high in female population.
- Prolactin levels 15 minutes after ECT significantly increased compared to baseline prolactin levels.
- Amount of post-ictal rise of prolactin gradually decreased over course of ECTs.
- There is no significant difference either in prolactin level or in final psychopathology scores between patients who received ECT and patients who did not receive ECT at the end of 3 weeks.
- There is no significant correlation between the prolactin changes and improvement in psychopathology suggesting the prolactin rise may be an epiphenomenon to ECT rather than reflecting any therapeutic process.

Limitations and Future Directions:

Limitations of our study were Confounding factors like TSH, cortisol, smoking or tobacco intake, ghrelin that could alter the level of prolactin were not evaluated.

Both the group of patients were put on antipsychotic (T. Haloperidol 10mg) that could have altered the prolactin responses. Effects of anaesthetic agent on prolactin were neglected. In the future studies which involve the assessment confounding factors like TSH, cortisol, smoking or tobacco intake, ghrelin should be evaluated simultaneously. Patients who are drug free should be taken for better results. And use of Benzodiazepine aided ECT to avoid the effect of anaesthetic agent on prolactin.

REFERENCE

1. Abrams, R., & Swartz, C. M. (1985a). Electroconvulsive Therapy and Prolactin Release: Effects of Stimulus Parameters. The journal of ECT, 1(2), 115-120.
2. Abrams, R., & Swartz, C. M. (1985b). Electroconvulsive Therapy and Prolactin Release:

Relation to Treatment Response in Melancholia. The journal of ECT, 1(1), 38-42.
3. Arey, B., Kanyicska, B., & Freeman, M. (1991). The endogenous stimulatory rhythm regulating prolactin secretion is present in the lactating rat. Neuroendocrinology, 53(1), 35-40.
4. Bhadoria, R., Watson, D., Danson, P., Ferrier, I. N., Mcallister, V. I., & Moore, P. B. (2003). Enlargement of the third ventricle in affective disorders. Indian journal of psychiatry, 45(3), 147.
5. CHAUDHRY, H. R., HOFMANN, P., LOIMER, N., KOTTER, M., QUEHENBERGER, F., & FUEGER, G. (2000). Prolactin and beta-endorphin serum elevations after ECT in manic patients. Acta Psychiatrica Scandinavica, 102(5), 386-389.
6. Coppola, J., Leonardi, R., Lippmann, W., Perrine, J., & Ringler, I. (1965). Induction of pseudopregnancy in rats by depletors of endogenous catecholamines. Endocrinology, 77(3), 485-490.
7. Daban, C., Vieta, E., Mackin, P., & Young, A. (2005). Hypothalamic-pituitary-adrenal Axis and Bipolar Disorder. Psychiatric Clinics of North America, 28(2), 469-480.
8. De, P. C., Macconi, D., & Spada, A. (1979). Dopamine inhibits adenylate cyclase in human prolactin-secreting pituitary adenomas. Nature, 278(5701), 252-254.
9. Deakin, J., Ferrier, I., Crow, T., Johnstone, E., & Lawler, P. (1983). Effects of ECT on pituitary hormone release: relationship to seizure, clinical variables and outcome. The British Journal of Psychiatry, 143(6), 618-624.
10. DEPUE, R., ARBISI, P., KRAUSS, S., IACONO, W., LEON, A., MUIR, R., & ALLEN, J. (1990). Seasonal independence of low prolactin concentration and high spontaneous eye blink rates in unipolar and biopolar II seasonal affective disorder. Archives of general psychiatry, 47(4), 356-364.
11. Fink, M. (2000). Electroshock revisited. American Scientist, 88(2), 162-179.
12. Goodwin, G. M., Martinez-Aran, A., Glahn, D. C., & Vieta, E. (2008). Cognitive impairment in bipolar disorder: neurodevelopment or neurodegeneration? An ECNP expert meeting report. European Neuropsychopharmacology, 18(11), 787-793.
13. HUXLEY, N., & BALDESSARINI, R. J. (2007). Disability and its treatment in bipolar disorder patients. Bipolar disorders, 9(1-2), 183-196.
14. JACOBSEN, F., SACK, D., WEHR, T., & ROSENTHAL, N. (1987). Neuroendocrine response to 5-hydroxytryptophan in seasonal affective disorder. Archives of general psychiatry, 44(12), 1086-1091.
15. KEMPTON, M. J., GEDDES, J. R., ETTINGER, U., WILLIAMS, S. C., & GRASBY, P. M. (2008). Meta-analysis, Database, and Meta-regression of 98 Structural Imaging Studies in Bipolar Disorder. Archives of general psychiatry, 65(9), 1017-1032.
16. KENNEDY, N., BOYDELL, J., KALIDINDI, S., FEARON, P., JONES, P. B., VAN OS, J., & MURRAY, R. M. (2005). Gender differences in incidence and age at onset of mania and bipolar disorder over a 35-year period in Camberwell, England. The American journal of psychiatry, 162(2), 257-262.
17. Kronfol, Z., Hamdan-Allen, G., Goel, K., & Hill, E. M. (1991). Effects of single and repeated electroconvulsive therapy sessions on plasma ACTH, prolactin, growth hormone and cortisol concentrations. Psychoneuroendocrinology, 16(4), 345-352.
18. Lerer, B., & Sitaram, N. (1983). Clinical strategies for evaluating ECT mechanisms—Pharmacological, biochemical and psychophysiological approaches. Progress in Neuro-Psychopharmacology and Biological Psychiatry, 7(2-3), 309-333.
19. MACKINNON, D. F., ZANDI, P. P., COOPER, J., POTASH, J. B., SIMPSON, S. G., GERSHON, E., . . . DEPAULO, J. R. (2002). Comorbid bipolar disorder and panic disorder in families with a high prevalence of bipolar disorder. The American journal of psychiatry, 159(1), 30-35.
20. Markianos, M., Hatzimanolis, J., & Lykouras, L. (2002). Relationship between prolactin responses to ECT and dopaminergic and serotonergic responsivity in depressed patients. European archives of psychiatry and clinical neuroscience, 252(4), 166-171.
21. Modigh, K., Balldin, J., Eriksson, E., Granerus, A., & Walinder, J. (1984). Increased responsiveness of dopamine receptors after ECT: a review of experimental and clinical evidence ECT: Basic Mechanisms (pp. 18-27): Libbey London.
22. Ohman, R., Balldin, J., Walinder, J., Wallin, L., & Abrahamsson, L. (1976). Prolactin response to electroconvulsive therapy. The Lancet, 308(7992), 936-937.
23. OREN, D., LEVENDOSKY, A., KASPER, S., DUNCAN, C., & ROSENTHAL, N. (1996). Circadian profiles of cortisol, prolactin, and thyrotropin in seasonal affective disorder. Biological psychiatry, 39(3), 157-170.
24. PERRY, J., LAVORI, P., & HOKE, L. (1987). A Markov model for predicting levels of psychiatric service use in borderline and antisocial personality disorders and bipolar type II affective disorder. Journal of psychiatric research, 21(3), 215-232.
25. RAYMONT, V., BETTANY, D., & FRANGOU, S. (2003). The Maudsley bipolar disorder project: Clinical characteristics of bipolar disorder I in a Catchment area treatment sample. European psychiatry, 18(1), 13-17.
26. RUDORFER, M., RISBY, E., OSMAN, O., GOLD, P., & POTTER, W. (1991). Hypothalamic-pituitary-adrenal axid and monoamine transmitter activity in depression: a pilot study of central and peripheral effects of electroconvulsive therapy. Biological psychiatry, 29(3), 253-264.
27. SACKEIM, H., DECINA, P., PORTNOY, S., NEELEY, P., & MALITZ, S. (1987). Studies of dosage, seizure threshold, and seizure duration in ECT. Biological psychiatry, 22(3), 249-268.
28. Samuels, J., Eaton, W. W., Bienvenu, O. J., Brown, C. H., Costa, P. T., & Nestadt, G. (2002). Prevalence and correlates of personality disorders in a community sample. The British Journal of Psychiatry, 180(6), 536-542.
29. Stojek, A., Kasprzak, B., & Słabikowski, A. (1991). Intraocular pressure and prolactin measures in seasonal affective disorder. Psychiatria polska.
30. STROBER, M. (1992). Relevance of early age-of-onset in genetic studies of bipolar affective disorder. Journal of the American Academy of Child and Adolescent Psychiatry, 31(4), 606-610.
31. SWARTZ, C., & ABRAMS, R. (1984). Prolactin levels after bilateral and unilateral ECT. British journal of psychiatry, 144, 643-645.
32. Swartz, C. M. (1985a). Characterization of the Total Amount of Prolactin Released by Electroconvulsive Therapy. The Journal of ECT, 1(4), 252-257.
33. Swartz, C. M. (1985b). Time Course of Post-Electroconvulsive Therapy Prolactin Levels. The Journal of ECT, 1(2), 81-88.
34. Tucker, H. (1981). Physiological control of mammary growth, lactogenesis, and lactation. Journal of Dairy Science, 64(6), 1403.
35. Viguera, A. C., Baldessarini, R. J., & Tondo, L. (2001). Response to lithium maintenance treatment in bipolar disorders: comparison of women and men. Bipolar disorders, 3(5), 245-252.
36. Zarate, C. A., Tohen, M., & Baraibar, G. (1997). Combined valproate or carbamazepine and electroconvulsive therapy. Annals of clinical psychiatry, 9(1), 19-25.
37. ZIS, A., MCGARVEY, K., CLARK, C., LAM, R., & ADAMS, S. (1992). The role of dopamine in seizure-induced prolactin release in humans. Convulsive therapy, 8(2), 126-130.
38. Zis, A. P., Yatham, L. N., Lam, R. W., Clark, C. M., Srisurapanont, M., & McGarvey, K. (1996). Effect of stimulus intensity on prolactin and cortisol release induced by unilateral electroconvulsive therapy. Neuropsychopharmacology, 15(3), 263.