Original Research Paper

Sodium Valproate and Polycystic Ovary Syndrome in Women with Bipolar Disorder – A Cross Sectional Comparative Analysis with Other Mood Stabilizers

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Abstract

Background: In patients with epilepsy polycystic ovary (PCO) syndrome has been reported to be associated with the use of the anticonvulsant sodium valproate. Whether PCO syndrome is associated with valproate use in patients with bipolar disorder is not adequately explored.

Method: 76 female outpatients with a DSM-IV diagnosis of bipolar disorder between the ages of 18 and 45 years and who were taking monotherpy with valproate 38, lithium 18, oxcarbazepine 14 and lamotrigine 6 were evaluated. Patients completed questionnaires about their medical, psychiatric, and reproductive health histories and body mass indices were calculated. In the early follicular phase of their menstrual cycle, women were examined for hirsutism, given a transvaginal ultrasound, and assessed serum levels of testosterone, estradiol, luteinising hormone and follicle-stimulating hormone.

Results: 50% of females receiving valproate exhibited menstrual irregularities and polycystic ovaries. Only 7.9% receiving valproate had features of PCOS. Out of 4 cases of PCOS three were (75%) in the valproate group and one was in oxcarbazepine/lamotrigine group. Serum testosterone level was also high in vaproate group. Commonest menstrual problem in the valproate group was irregular menstrual cycle (34.2%) followed by amenorrhea (23.7%) and oligomenorrhea (21%). 45% patients receiving oxcarbazepine/ lamotrigine exhibited irregular menstrual cycle, 20% oligomenorrhea and 15% amenorrhea. Lithium group had lesser frequency of these symptoms. Comparison of individual menstrual problems showed menorhagia higher in the vaproate group. In the valproate group 3 patients had menstrual abnormalities before initiation of medication for bipolar disorder. Serum testosterone level was significantly higher and FSH was lower in the valproate group.

Conclusion: In this study of bipolar patients, PCO-like changes were common in women receiving valproate though there was no significant difference compared to other mood stabilizers. Independent of the therapeutic agent used, the bipolar women in this study reported high rates of menstrual disturbances, hormonal disturbances and PCOD suggesting that the hypothalamic-pituitary-gonadal axis may be compromised in some women with bipolar disorder.

Key words: valproate, lithium, oxcarbazepine, lamotrigine, bipolar, poly cystic ovary syndrome

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INTRODUCTION :

Bipolar disorder is an illness with a usual age of onset during the reproductive years. Lithium and anticonvulsant agents have demonstrated excellent antimanic efficacy and are prescribed for chronic use in patients with bipolar disorder. However, anticonvulsants have been reported to change the metabolism of reproductive hormones, including estrogen, progesterone, and testosterone, with resultant alterations in circulating blood levels of these hormones and secondary effects on the feedback loop of the hypothalamic-pituitary-gonadal (HPG) axis. This, in turn, may influence serum levels of reproductive hormones and consequently affect menstrual cyclicity and reproductive function.[1]

Polycystic ovary syndrome (PCOS) is one of the most common endocrine disorders among women of reproductive age, affecting about 4% to 7% of the population.[2] Recently, concerns have been raised about an association between the use of valproate and PCOS.[3] Disparate definitions for this syndrome have been proposed. Androgen Excess PCOS Society[4] narrowed the definition of PCO syndrome to the presence of excess androgen activity, oligoovulation/anovulation and/ or polycystic ovaries and the exclusion of other entities that would cause excess androgen activity. Clinically, hyperandrogenism is manifested as hirsutism, acne, alopecia, or anovulatlon. Women with anovulation may present with menstrual disturbances such as amenorrhea, oligomenorrhea or dysfunctional uterine bleeding. On ultrasound the ovaries appear to have multiple small cysts. Endocrine abnormalities associated with PCOS include elevated serum LH, testosterone, androstenedione, and LH/follicle-stimulating hormone (FSH) ratios.[5]

PCO syndrome is associated with many health risk factors including infertility, non insulin-dependent diabetes mellitus, ischemic heart disease, dyslipidemia, and endometrial carcinoma. [6] Furthermore, the symptoms associated with PCOS are recognized to cause psychological distress and decreased quality of life in women.[7]

Donovan et al and Mcntyre et al report high rates of menstrual disturbances and poly cystic ovary syndrome in women with bipolar disorder currently receiving valpoate.[8,9] However some studies have raised concerns about the association of divalproex and PCO syndrome.[10,11] Because of the common use of valproate in bipolar women of reproductive age, we sought to assess for PCO syndrome in women with bipolar disorder. We report the results of a cross-sectional study assessing the presence of PCO syndrome and evaluating reproductive function in women with bipolar illness taking valproate and other mood stabilizers.

METHOD

Subjects

Consecutive patients attending the bipolar clinic of IQRAA International Hospital and Research Center from the period January 2012 to January 2013 formed the study sample. Women of 17 to 45 years with DSM-IV diagnosis of bipolar disorder taking monotherapy with sodium valproate/ lithium/ oxcarbazepine/ lamotrigine for at least two months were recruited for the study.

Exclusion Criteria

Patients were excluded if they were receiving oral or injectable contraceptive medication or antipsychotics for at least 6 months before hand, had a current (or lifetime) diagnosis of type 1 or 2 diabetes mellitus, known dyslipidemia, primary reproductive endocrine disorder (e.g. prior history PCOS or infertility), assessed to be a suicide risk, have a diagnosis of substance dependence by DSM-IV criteria in the last 30 days, or had any known neurological D medical disorders.

Procedures

After signing the written informed consent patients completed a questionnaire assessing their medical, psychiatric, and reproductive health histories, including menstrual history, infertility problems, miscarriages, family history of menstrual and/or reproductive problems, and family psychiatric histories. Total 90 patients were recruited for the study and 76 gave consent to participate in investigative procedures.

Using the classifications as defined by Kiddy et al[12] the following were considered menstrual abnormalities: amenorrhea (no menstruation), oligomenorrhea (cycle length longer than 35 days), prolonged menstrual cycle (cycle length varying from less than 35 days to more than 35 days), and irregular menstrual cycle (cycle length varying more than 4 days from cycle to cycle, between 22 to 35 days). These abnormalities were considered to be "current" if they were present at the time the questionnaire was completed and had been present for at least 6 months.

All patients were examined for hirsutism using the Ferriman-Gallwey hirsutism scale.[13] Obesity was calculated using body mass index (BMI; the weight in kilograms divided by the square of the height in meters). Patients with a BMI exceeding 25 were considered obese.[14] PCOS was diagnosed according to the criteria suggested by Androgen Excess PCOS Society[4] 1. Excess androgen activity 2. Oligoovulation/anovulation and/or polycystic ovaries 3. Exclusion of other entities that would cause excess androgen activity.

Assays

Venous blood sample (30 ml) for hormone assay were obtained at 8 a.m. after an overnight fast during the early follicular phase of the menstrual cycle (days 3-7) in menstruating women and at random in women with amenorrhea. Assays completed on blood included FSH, LH, and testosterone (total). The automated chemiluminescence system (ACS: 180; Chiron Diagnostics, Bayer, Fernwald, Germany) was used for hormonal assay. Serum samples were kept frozen at) 20°C until analyzed.

A pelvic ultrasound using a vaginal transducer was performed on the same day using a Siemens Sonoline SL250 apparatus equipped with a transvaginal 5-MHz curvilinear probe (Siemens, Issaquach, Wash) by a female radiologist blinded to the medication status of the patient. The ovaries were considered polycystic if they contained a total of at least 10 cysts 2 to 8 mm in diameter arranged either peripherally around a dense core of stroma or scattered throughout an increased amount of stroma.[15]

Statistical analysis

The SPSS statistics package was used for data analysis. Descriptive statistics and analysis of data distribution were performed by the SPSS univariate process. An alpha-limit of 0.05 was considered significant for statistical differences. Categorical data were compared using the chi-square test, or where the expected values were <5, the Fisher exact test. Continuous variables were compared using one-way ANOVA.

Results

Of 90 women screened, 85 met the inclusion criteria. Of these 9 patients refused to participate for personal reasons. Thus, 76 women who met the inclusion criteria participated in the study. All gave informed consent to be interviewed and to undergo venipuncture and vaginal ultrasound. Thirty eight patients were on valproate monotherapy, 18 were on lithium monotherapy, 12 were on oxcarbazepine monotherapy and 8 were on lamotrigine monotherapy. For the purpose of analysis oxcarbazepine and and lamotrigine receiving patients were clubbed into one group.

Patients' ages ranged from 17 to 46 years. Daily dose of lithium ranged from 800-1600mg/day (mean = 1029.9 mg), and the mean length of drug exposure was 11.1$\pm$26.0 (range, 3.0-16) years. The daily dose of valproate ranged from 600 to 1500 mg/day (mean = 471.1$\pm$510.9 mg), and the mean length of exposure was 8.8$\pm$16.1 (4.0-12.0) years. The mean daily dose of oxcarbazepine ranged from 600 to 800 mg/day (mean=482.9$\pm$211.3), and the length of exposure was 7.3$\pm$4.5 (4.0-8.0) years. The mean daily dose of lamotrigine ranged from 300 to 600 mg/day (mean=390.1$\pm$103.3), and the length of exposure was 1.1$\pm$4.7 (0.8-6.0) years. 2 patients were started on valproate before 20 years age.

Clinical information of the study sample is presented in Table 1. Mean age was comparable across groups. There were no significant differences between the groups in marital status, family history of psychiatric illnesses, medical illnesses, obesity, BMI, prevalence of hirsuitism, acne, PCOD and PCOS. 2 patients in the

valproate group had prior history of hirsutism and 1 had history of acne before starting treatment for bipolar disorder. Out of 4 cases of PCOS 3 were (75%) in the valproate group and 1 in oxcarbazepine/lamotrigine group.

Menstrual history of patients is shown in Table 2. Overall, 19 (50%) of valproate treated females reported menstrual irregularities compared with 5 (27%) receiving lithium and 10 (55.5%) receiving oxcarbazepine/lamotrigine group. Commonest menstrual problem in the valproate group was irregular menstrual cycle 13 (34.2%) followed by amenorrhea 9 (23.7%) and oligomenorrhea 8 (21%). 9(45%) patients receiving oxcarbazepine/lamotrigine group exhibited irregular menstrual cycle, 4 (20%) oligomenorrhea and 3 (15%) amenorrhea. Lithium group had lesser frequency of these symptoms. Comparison of individual menstrual problems showed menorrhagia significantly higher in the valproate group. In the valproate group 2 patents had menstrual abnormalities before the diagnosis of bipolar disorder and 3 had menstrual abnormalities before initiation of medication for bipolar disorder.

A comparison of hormonal values in the 3 groups appears in Table 3. Serum testosterone level was significantly higher in the valproate group. LH was highest in lithium group. FSH was lower in the valproate group.

Discussion

In this pilot study of patients with bipolar disorder, 50% of females receiving valproate exhibited menstrual irregularities and 50% exhibited ultrasonographic evidence of polycystic ovaries. Serum testosterone level was also high

Table 1 **Clinical Characteristics of Bipolar Women Receiving Valproate, Lithium and other Mood Stabilizers**

	Valproate (N=38)	Lithium (N=18)	Oxcarbazepine / lamotrigine (N= 20)	p
Mean Age (Yrs)	28.2±9.0	34.7±10.2	35.0±11.3	0.81
Married	20 (52%)	11 (61.1%)	6 (30%)	0.00
Family History of psychiatric Illnesses	21 (55%)	3 (16.6%)	12 (60%)	0.00
Medical illness	1(2.6%)	3 (16.6%)	0 (0%)	0.09
Obesity	14 (36.8%)	8 (44.4%)	5 (25%)	0.27
Mean BMI	25.2±3.8	25.4±3.6	23.1±2.8	0.68
Hirsutism	2 (5.2%)	0 (0%)	1 (5%)	0.67
Prior History of Hirsutism	2 (5.3%)	0 (0%)	0 (0)	0.56
Acne	4 (10.5%)	2 (11.1%)	2 (10%)	0.82
Prior History of Acne	1 (2.6%)	0 (0%)	0 (0%)	0.80
Presence of PCOD	19 (50%)	11 (61.1%)	6 (30%)	0.15
Presence of PCOS	3 (7.9%)	0 (0%)	1 (10%)	0.58

in vaproate group. However only 7.9% had features PCOS. This could due to application of narrow definition to diagnose PCOS.[4] This finding is in agreement with the study by Rasgon et al[11] where PCO-like changes were not seen in bipolar women receiving divalproex or lithium. However, in our study independent of therapeutic agent used, the bipolar women reported high rates of menstrual disturbances, suggesting that the hypothalamic-pituitary-gonadal axis may be compromised in some women with bipolar disorder. In another study by the same group[16] only three of the 50 women (6%) taking valproate, and 0% of the 22 taking other antimanic medications, met criteria for PCOS**.** It has been reported that PCOS variably affects 2–7% of reproductive age women in the general population.[17] Polson et al[18] suggest that 23% of the general population has PCOS like features without obvious clinical significance. Some authors have failed to identify valproate associated reproductive endocrine disorders in bipolar disorder. [10,11] This may be due to a myriad of factors (i.e. the high reported prevalence of the syndrome in the general population, diverse patient populations studied and inconsistent descriptive boundaries of this syndrome). To date, most reproductive endocrine studies with valproate have enrolled individuals with a primary diagnosis of epilepsy.

We did not find significant difference in the radiological evidence of PCO-like changes in women treated with valproate compared to other mood stabilizers. However, the reported rate of 50% in the valproate group is higher than the rate in general population, 2%-22% using the widest range of definitions although of doubtful clinical significance.[18] Owing to the lack of a specific

Table 2 : Menstrual Characteristics of Bipolar Women Receiving Valproate, Lithium and other Mood Stabilizers

	Valproate (N=38)	Lithium (N=18)	Oxcarbazepine/ lamotrigine (N= 20)	p
Amenorrhea	9 (23.6%)	2 (11.1%)	3 (15%)	0.43
Oligomenorrhea	8 (21.0%)	0 (0%)	4 (20%)	0.07
Poly menorrhea	3 (7.9%)	0 (0%)	0 (0%)	0.37
Menorrhagia	3 (7.9%)	0 (0%)	4 (20%)	0.03
Irregular Menstrual Cycles	13 (34.2%)	5 (27.8%)	9 (45%)	0.71
Menstrual Abnormalities	19 (50%)	5 (27.8%)	10 (50%)	0.43
Menstrual Abnormalities Before Diagnosis of BPAD	2 (5.2%)	0 (0%)	0 (0%)	0.56
Menstrual Abnormalities Before Initiation of Medication for BPAD	3 (7.9%)	5 (27.9%)	3 (15%)	0.14

Table 3 - Comparison of Hormonal Values in Bipolar Women Receiving Valproate, Lithium and other Mood Stabilizers

	Valproate (N=38)	Lithium (N=18)	Oxcarbazepine/ lamotrigine (N= 20)	F*	p
Mean Serum Testosterone	26.1±1.1	19.2±1.1	23.8±2.1	159.7	**0.00**
Mean Serum LH	5.6±0.6	6.5±0.4	5.3±0.3	**37.1**	**0.00**
Mean Serum FSH	**4.9**± 0.4	**6.7**± 0.7	**4.0**± 0.4	**154.0**	**0.00**

***One Way ANOVA**

definition for PCOD in those studies, it is difficult to compare this rate with the studies of women with epilepsy or of women with bipolar disorder treated with valproate. Some of this variation in results may also be due to the use of suprapubic transabdominal ultrasound (rather than the transvaginal ultrasound used in our study), which is less likely to detect cysts. However, differences in ultrasound technique cannot explain the differences in our results and those of Rasgon et al.[11] The mean length of valproate exposure and daily dose did not appear to differ between these studies. The similarity in figures with the epilepsy sample makes it less likely that prior use of antipsychotics can explain this syndrome. Thus, it is possible that bipolar disorder itself is a risk factor for menstrual abnormalities and/or PCOS with a similar temporal lobe-hypothalamic gonadal abnormality as suggested in the epilepsy literature.[19] Moreover, it is noted that reproductive morbidity (including PCOS) and endocrine disorders are reportedly more common among epileptic females compared with the general population.[20]. In the study by Isojarvi et al[3] in epileptic patients, 29 women (40%) receiving divalproex monotherapy had hyperandrogenism, polycystic ovaries, or both. In that study, length of exposure to divalproex was shorter, although the mean dose for bipolar patients was somewhat higher.

The long term impact of valproate on female reproductive function is an important area for future research since there is an increasing recognition that bipolar disorder can begin in both prepubertal and adolescent time and that vaproate is effective in the treatment of mania in adolescents.[21] In humans, the only published report[22] described a case of reversible, delayed puberty onset associated with valproate treatment. In rodents, chronic administration of valproate delayed reproductive and skeletal maturation in genetically epilepsy prone mice.[23] In our study, 2 patients were started on valproate therapy prior to age 20 years thereby exposed to the risk of developing PCOS.

The impact of both length and timing of exposure to divalproex on reproductive functioning merits further study with larger sample sizes, longitudinal designs, and longer lengths of exposure. It is possible that the PCO-like changes reported in the epileptic patients may be due to epilepsy per se or a therapy-epilepsy interaction.[24] Future studies should therefore also examine whether patients' diagnoses (epilepsy vs. bipolar disorder) influence the likelihood of an association between valproate use and PCO-like changes.

In this study, 50% of females receiving valproate exhibited menstrual irregularities, higher serum testosterone level and lower FSH. The occurrence of menstrual disturbances and hormonal changes in bipolar women may represent a trait marker of HPG dysregulation in women with bipolar illness. Our preliminary findings might suggest that women with bipolar disorder have a high prevalence of menstrual disturbances independent of therapeutic agent used and, in some cases, preceding the onset of bipolar disorder. In our study also few patients had

menstrual disturbances and clinical features of hyperandrogenism even before the imitation of treatment for bipolar disorder.

One case report and one case series have described reproductive hormone changes in bipolar women.[25,26] Matsunaga and Sarai[25] reported reproductive endocrine changes in 12 women with manic-depressive psychosis exacerbated by menstrual cyclicity. They described both radiological and biochemical evidence of PCO syndrome in 8 of 12 women with affective disorder. Three of the 8 women were diagnosed with PCO syndrome several years before the onset of a psychiatric disorder. Their findings, however, may be confounded by the use of antipsychotic medication at the time of the investigation, which is known to alter HPG function (via hyperprolactinemia), and use of oral contraceptives in one case. Further, hormonal sampling was done during both phases of the menstrual cycle, and the ultrasonography was performed in the luteal phase of the menstrual cycle, which does not allow for comparison with our data**.**

Whether PCO-like changes can be induced in bipolar women with exposure to valproate over many years remains to be determined and might be able to be evaluated in a large, longitudinal multicenter study. The Study by Isojarvi[3] however, suggests that if such changes occur, they are reversible. The authors found that the number of ovarian follicles was decreased within 1 year in epileptic women who were switched from divalproex to lamotrigine. Our findings, as did those of Isojarvi et al indicate a need for a longitudinal controlled evaluation of reproductive function in women taking mood stabilizers, whether they have epilepsy or bipolar disorder. Our data also suggest that some women with bipolar disorder may have compromise in reproductive endocrine function even prior to treatment, as do women with epilepsy.[27] The clinical manifestation of a menstrual disturbance may represent a marker for an underlying HPG axis dysregulation. Certainly the hypothalamic-pituitary-adrenal and hypothalamic-pituitary-thyroid axes have been studied in bipolar women and have been found, in many cases, to be dysregulated. Valproate may influence hormonal homeostasis through both peripheral (liver metabolism) as well as central (increasing LH pulses) mechanisms. [27]

The results of our study, although not very postive, are based on a small number of patients, and larger studies are needed to make definitive conclusions. At present, clinicians treating bipolar women should assess for obesity, menstrual abnormalities (e.g.,oligomenorrhea, amenorrhea), and iatrogenic hair growth. If a psychiatrist has a female patient who is being or will be treated with valproate, he or she should consider a diagnostic workup if the patient presents with at least 2 of the following symptoms: hirsutism, menstrual disturbances (oligomenorrhea, amenorrhea), obesity, alopecia, or infertility. The workup should be limited to a blood test for bioavailable testosterone and DHEA, with a subsequent referral to a specialist. Pelvic ultrasounds are not necessary, nor are they diagnostic of PCO syndrome.

Our study is greatly limited by its cross-sectional descriptive design, lack of diagnostic interviews, and small sample size. Furthermore, pre-treatment clinical and laboratory data were unavailable. Furthermore, we did not know the time interval from treatment initiation to the onset of menstrual abnormalities. We do see these results as hypothesis generating in need of replication and controlled examination. We are continuing to assess the reproductive function in young women with bipolar disorder in our current studies.

References

1. Mattson RH, Cramer JA. Epilepsy, sex hormones and antiepilepiic drugs. Epilepsia 1985; 26(suppl I): 40- 51.
2. Lobo RA, Carmina E. The importance of diagnosing the polycystic ovary syndrome. Ann Int Med 2000; 132:989-993.
3. Isojarvi Jl, Laatikainen TJ, Pakarinen AJ, et al. Polycystic ovaries and hyperandrogenism in women taking valproate for epilepsy. N Engl J Med 1993; 329:1383-1388.

4. Azziz R, Carmina E, Dewailly D, et al. Criteria for defining polycystic ovary syndrome as a predominantly hyperandrogenic syndrome: An Androgen Excess Society guideline. J Clin Endocrinol Metab.2006; 91:4237-4245.
5. Rosenfield RL. Current concepts of polycystic ovary syndrome. Baillieres Clin Obstet Gynecol 1997; 11:307-333, Robinson S, Rodin DA, Deacon A, et al. Which hormone tests for the diagnosis of polycystic ovary syndrome? Br J Obstet Gynaecol 1992; 99: 232-238.
6. Solomon CG. The epidemiology of polycystic ovary syndrome: prevalence and associated disease risks. Endocrinol Metab Clin North Am 1999; 28:247-263.
7. Cronin L, Guyatt G, Griffith L,et al. Development of a health related quality of life questionnaire (PCOSQ) for women with polycystic ovary syndrome (PCOS). J Clin Endocrinol Metab 1998; 83:1976-1987.
8. O'Donovan C, Kusumaker V, Graves GR, Bird DC. Menstrual abnormalities and polycystic ovary syndrome in women taking valproate for bipolar dosrder. J Cli Psychiatry 2002; 63:322-330
9. McIntyre RS, Mancini DA, McCannan S, Srinivasan J, Kennedy SH. Valproate, bipolar disorder and polycystic ovary syndrome. Bipolar Disorders 2003; 5:28-35.
10. Popovic V, Spremovic S. The effect of sodium valproate on luteinizing hormone secretion in women with polycystic ovary disease. J Endocrinol Invest 1995; 18: 104–108.
11. Rasgon NL, Altshuler LL, Gudeman D, Burt VK, Tanavoli S, Hendrick V, Korenman S. Medication status and polycystic ovary syndrome in women with bipolar disorder: A Preliminary Report. J Clin Psychiatry 2000; 61:173-78.
12. Kiddy DS, Sharp PS, White DM, et al. Differences in clinical and endocrine features between obese and non-obese subjects with polycystic ovary syndrome: an analysis of 263 consecutive cases. Clin Endocrinol (Oxf) 1990; 32:213-220.
13. Ferriman D, Gaflwey JD. Clinical assessment of hair body growth in women.J Clin Endocrinol Metab 1961; 21:1440-1447.
14. Kiddy DS, Sharfl PS, White DM, et al. Differences in clinical and cndocrine features between obese and non obese subjects with polycystic ovary syndrome: an analysis of 263 consecutive cases. Clin Endocrinol (Oxf) 1990; 32:213-220.
15. Swanson M, Sauerbrei EE CooperberflPL Medical implications of ultra-sonically detected polycysde ovaries. J Clin Ultrasound 1981; 9:219-222.
16. Rasgon LR, Altshuler LL, Fairbanks L, Elman S et al. Reproductive function and risk for PCOS in women treated for bipolar disorder.Bipolar Disorder 2005; 7(3):246–259.
17. Chappell KA, Markowitz JS, Jackson CW. Is valproate pharmacotherapy associated with polycystic ovaries? Ann Pharmacother 1999; 33: 1211–1216.
18. Polson DW, Adams J, Wadsworth J, et al. Polycystic ovaries: a common finding in normal women. Lancet 1988; 1:870-872.
19. Morrell MJ. Effects of epilepsy on women's reproductive health. Epilepsia 1998; 39:32-37.
20. Gross A, Devinsky O, Westbrook LE, Wharton AH, Alper K. Psychotropic medication use in patients with epilepsy: effect on seizure frequency. J Neuro-psychiatry Clin Neurosci 2000; 12: 458–464.
21. Price AL ,Marzani-Nissen GM. Bipolar Disorders: A Review. Am Family Physician 2012; 85(2): 483-493.
22. Cook JS, Bale JP Jr, Hoffman RP. Pubertal arrest associated with valproic acid therapy. Pediatr Neurol 1992; 8:229-231.
23. Snyder PJ, Badura LL Chronic administration of sodium valproic acid slows pubertal maturation in inbred DBA/2J mice: skeletal, histological, and endocrinological evidence. Epilepsy Res 1995; 20:203-211.
24. Herzog AG. A relationship between partial reproductive endocrine disorders and the laterality of epileptiform discharges in women with epilepsy. Neurology 1993; 43; 1907-1910.
25. Matsunaga H, Sarai M. Elevated serum LH and androgens in affective disorder related to the menstrual cycle: with reference to polycystic ovary syndrome. Jpn J Psychiatry Neurol 1993; 47:825-842.
26. Ghaziuddin M. Polycystic ovary disease, manic depressive illness and mental retardation. J Ment Defic Res 1989; 39:559-560.
27. Herzog AG. Polycystic ovarian syndrome in women with epilepsy: epileptic or iatrogenic? Ann Neurol 1996; 39:559-560.

Original Research Paper

Profile Of Risk Factors Related To Attempted Suicide In Sikkim, India

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Abstract

Background: The rates of suicide attempts are found to be higher than the completed suicides. Attempted suicide is a common clinical problem in a general hospital setting, encompassing a wide variety of medical and social disciplines, some important psychosocial variables such as life events and social factors have not been explored in depth in Sikkim.

Aims: To study the socio-demographic factors, methods and to identify the risk factors leading to suicidal attempts.

Setting and Design: Hospital based study.

Material and Methods: All the consecutive cases of suicide attempts (n =100) treated in a general hospital were evaluated for psychosocial, clinical risk factors, suicide characteristics, psychiatric morbidity co morbidity and psychiatric diagnosis by using ICD–10. Presumptive stressful life event scale was utilized to calculate life events score. A self designed proforma was administered to the subjects relating the factors responsible for the attempts. The data thus obtained was compiled and analyzed.

Result : Peak occurrence of suicidal attempts was found in the second and third decades (21-30 years). In this study, 49% were males and 51% were females. Nuclear family, rural background, self employed, matriculation educated were more represented. Hindus constituted 59% of the total suicide attempters and 56% were from middle (class II) socio-economic groups. More than 75% of attempters had psychiatric diagnosis and precipitating life events prior to attempts. The most common method of attempt was by hanging. Depressive disorder (44%) constituted a major category of psychiatric disorders.

Conclusion: Majority of attempters were young adults, had lower educational achievement with a high prevalence of psychiatric morbidity and co-morbidity. Early identification and treatment of these disorders would have prevented the mortality associated with this. A proper psychiatric referral system should be built up to reduce the incidence of suicidal death.

Key words : Attempted suicide, Risk factors.

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