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The Importance of Early Identification and Treatment of Childhood Onset Bipolar Disorder: Creating Specialty Care

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Introduction

We highlight the severity and high incidence of childhood onset bipolar disorder in the United States (US) in order to help generate changes in clinical and public health approaches to this problem. We outline the scope of the problem of early onset bipolar disorder in the US and suggest ways of intervening earlier and more effectively.

Background

Childhood onsets are common in the United States

Childhood onset bipolar disorder as it is currently treated in the United Stated carries a poor prognosis in the short term based on prospective follow-up studies of clinical samples [1-4] and into adulthood based on retrospective studies in adults [5,6]. This is a problem of enormous proportions given the several percent incidence of the illness in adolescents in the US [7,8] and the findings that two-thirds of all adult bipolar illness had it onset in childhood and adolescence (before age 19) and more than a quarter of the illness began in childhood (prior to age 13) [5,9]. Those with childhood onset do much more poorly than those with adult onsets.

Treatment is often delayed and inadequate

Some 20 years ago, the delay from the onset of first episode of mania or depression to first treatment averaged more that 15 years for childhood onset and more than 10 years for adolescent onset [6]. The duration of delay to first treatment is an independent predictor of poor outcome in adulthood and associated more time and severity of clinician-rated depression [10]. While the delays to first treatment may be shorter currently, they are still often substantial, and treatment over an 8 year period of follow up in 37% of youngsters was inappropriate as it never involved any of those that are concensus recommended, such as atypicals, anticonvulsant mood stabilizers, and lithium [11].

Bipolar disorder is more severe in the US compared to Europe

The consequences of early onset bipolar disorder and treatment delay appear to last a life time as the illness is more severe and complex in the US than in the Netherlands and Germany (abbreviated here for convenience as Europe) [12]. In addition to early onset, adult outpatients with bipolar disorder in the US have significantly more anxiety, alcohol, and substance abuse comorbidity, more episodes and rapid cycling, more medical comorbidities, and more treatment nonresponsiveness than those in Europe [13].

More genetic and psychosocial risk factors in the US

The question immediately arises as to why there should be more childhood onsets in the US than in Europe [9,14,15]. There appears to be a greater amount of both genetic and psychosocial vulnerability. Compared to those from Europe, patients from the US have greater genetic loading from their parents for bipolar disorder as well as many other psychiatric conditions. They also have more psychosocial vulnerability, both in childhood with more verbal, physical, and sexual abuse and in the year prior to the onset of their illness with multiple stressors and loss of social support [13]. Perhaps because of these two factors, studies of high risk offspring of a parent with bipolar illness in the US is associated with an earlier onset and higher incidence of bipolar spectrum disorders than similar studies conducted in Europe or Canada [9].

Greater sensitization effects in the US than in Europe

Thus, children, adolescents, and adults with bipolar illness from the US carry a greater burden of stressors, manic and depressive episodes, and substance abuse than their European colleagues. The recurrence of stressors, episodes, and substance abuse is each associated with sensitization effects (increased responsivity upon repetition) as well as cross sensitization to the others, each of which further drives illness progression in an adverse direction. Sensitization to stressors, episodes, and substance abuse likely involves epigenetic mechanisms leaving the DNA of patients from the US carrying more permanent genetic sequence alterations inherited from their parents, as well as accumulating epigenetic marks based on environmental experience of stressors, episodes, and substance use [16-18]. It is likely that both mechanisms will carry vulnerablitity to psychiatric illness into the next generation, not only via conventional genetic transmission, but possibly via transgenerational epigenetic transmission which is now increasingly recognized for parental exposure to stressors and substance abuse [19-22].

Clinical Implications

Potential treatment approaches

Given this extremely adverse set of circumstances for great numbers of children in the US with bipolar disorder which will likely extend throughout their life and even into their offspring in the next generation, what kinds of interventions might be considered to help ameliorate this situation? Miklowitz et al [23] have found that family focused therapy (FFT) is effective in reducing symptoms in children at high risk because of a first degree relative with bipolar and the presence of an anxiety, depressive, or BP NOS disorder. Improving family communication and problem solving skills and reducing family

discord may be a critical first step in providing a supportive environment for the child with prodromal or full-blown illness. This might even be considered in children at very high risk by virtue of mood disorders in both the parental and grandparental generations [24,25]. A focus on healthy habits such as diet and exercise may also be helpful in preventing obesity and inflammation which often accompany childhood onset mood disorders. Omega 3 fatty acids and vitamin D3 supplementation might also be considered.

In those with a full syndrome of BP-NOS, BP II, or BP I disorder, pharmacotherapy as well as psychotherapy should be considered as BP I and II can take some 9 months on average to stabilize and BP-NOS often twice as long [1]. Treating BP-NOS is of major import as Birmaher et al. [1] has found that some 40% of children with BP-NOS convert to a BP I or II diagnosis after several years of follow up. Based on the data of Geller et al [26] on the superiority of risperidone over lithium and valproate, use of a well-tolerated atypical as an adjunct to a mood stabilizer may be a necessary combination in a large number of children. In those with residual anxiety and depression, and particularly if there is comorbid substance abuse (including marijuana, alcohol, cocaine or heroin), augmentation with N-acetylcysteine (NAC) may also be useful [18].

Better outcomes with specialty care and education

In those with a first manic episode, the best course of treatment is now very clear. Kessing et al. [27] randomized those with a first hospitalization for mania to two years of either a specialty clinic or to treatment as usual (TAU) in the community. The specialty clinic was vastly superior to TAU not only for reducing rehospitalization for a new episode, but also for enhancing compliance and patient satisfaction. Remarkably, when all patients returned to TAU after the end of the 2 years, the group previously given the specialty clinic treatment continued to do exceedingly well over the next 4 years, while the TAU continued to show increasing relapses such that the differences between the two original groups not only persisted but increased in magnitude. The specialty clinic offered an array of services including: an initial adaptation period post hospitalization, psychoeducation about the illness and medication management, cognitive behavior therapy, development of a good monitoring system to catch early evidence of symptom breakthrough and rehearsal of procedures to follow should symptoms emerge.

These data cap off an already robust literature that psychoeducation has lasting benefits [28,29] and cognitive behavioral therapy is especially helpful early in the course of illness, but not after dozens of episodes have occurred. Thus, it is clear that special combined treatment efforts, including education, therapy, and medications are required to help achieve a good long term treatment outcome. Otherwise, prospective follow up studies of children and retrospective studies of adults indicate that extremely adverse outcomes await a large proportion of children as they are currently being treated in the US.

A critical role for improved care and education in the US

Since the equivalent of specialty clinics for adolescents and young adults employed in the study of Kessing et al. [27] does not currently exist in the US, it behooves the treating clinicians to cobble together and jerry-rig such an entity out of available resources. The model would be like that used in childhood onset diabetes where a host of clinicians including doctors, nurses, social workers, dieticians, family members, and the patients themselves are all part of an integrated team to deliver optimum care to a person with a life-threatening illness that requires precise monitoring and management in a youngster who is ill prepared for such a role which is absolutely foreign to his self-concept and world view. However, the evidence is in that such careful comprehensive team management now results in decades of enhanced quality of life, with a great delay in the onset of complications that used to be all-too-frequent such as blindness, kidney and heart failure, and loss of limbs to amputation because of peripheral vascular disease.

While we do not have the unequivocal and long term evidence that equivalent results would be achieved in the treatment of child and adolescent onset bipolar disorder, the initial data of Kessing et al. [27] are highly suggestive that this would be the case, and it is hard to imagine that such a multimodal approach to one of the most complex and pleiomorphic illnesses in all of medicine would not also yield positive results. Patients, family members, advocacy groups, clinicians, and investigators must all insist that such an integrated multimodal approach become the standard of care and reimbursed by insurance companies in the same fashion as if it were childhood onset diabetes or cancer. Until such a day arrives, clinicians must strive to create enhanced specialty treatment program for each individual patient in hope of moderating an otherwise potentially devastating and lethal disorder.

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