Letter to Editor

Piracetam induced psychotic symptoms in a preadolescent girl with intellectual disability

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Piracetam, a nootropic agent, is believed to improve higher brain functions, like learning & memory justifying use in individuals with intellectual disability. It has a GABA-mimetic action, activating AMPA type glutamate receptors and its uses extend beyond the nootropic effects. It's commonly used as an off-label drug, usually prescribed for learning difficulties, poor memory and speech disorders [1]. Due to its purported effects as intelligence enhancers/memory boosters, nootropics are also referred to as 'smart drugs' and are construed as wonder drugs with 'only beneficial effects' and no side effects [2]. Literature reports that this is a serious public health concern similar to that associated with anabolic steroid use [2]. Since, piracetam crosses blood brain barrier, its central nervous system stimulatory effects- psycho- motor agitation, aggression, irritability, dysphoria, sleep disturbances, headache, decreased appetite are reported in literature [3,4]. In this background, we discuss the case of a girl with intellectual disability who developed auditory and visual hallucinations in addition to CNS adverse effects on prescription of piracetam. Till date, to the best of our knowledge no such case with piracetam induced psychotic symptoms has been reported.

An 11 years old girl was admitted to the psychiatry emergency room for recent onset change in behaviour i.e., irritability, agitation and hallucinatory behaviour. History exploration and assessments revealed that she had a preterm birth, delayed cry, delayed development in all domains. She had learning difficulties since early childhood but no help was sought. In May 2021, for persisting academic difficulties and poor academic performance, parents consulted a private pediatrician who prescribed her Syrup Piracetam (syrup Noofit 500 mg/ 5 ml) 500 mg BD. Within 5-6 days of its initiation, she was observed to remain fearful, complained of hearing and seeing things which others could neither see nor hear, was agitated and confused, with sleep and appetite disturbances. Attributing these behaviors due to the new drug started, parents discontinued it. Within next 45 days, improvement was observed in agitation, confusion, hallucinatory behaviour and sleep.

Parents restarted syrup piracetam but this was associated withreemergence of earlier symptoms. They again discontinued piracetam following continued worsening for 5-6 days and brought her to psychiatry emergency services. No history of seizures, other neurodevelopmental disorders, substance use, skin rash (porphyria), drug use (steroids) was obtained. Mental status examination revealed, confused state, increased psychomotor activity, perseveration, echolalia, palilalia and impaired attention-concentration. Naranjo algorithm score was 5 indicative of probable drug indued adverse effect.

A provisional diagnosis of Piracetam induced psychotic symptoms with moderate intellectual disability was kept. She was admitted and kept drug naïve. Investigations (serum lactate, urine for ketones/ porphyrins, EEG, MRI) did not reveal any abnormalities. She improved within 4-5 days of ward stay and within a week was her premorbid self. The family members were educated about intellectual disability, and that medicines/supplements would not improve her memory, rather constant practice in doing things will bring about some change. She was discharged in a satisfactory condition with attainment of premorbid level of functioning. The index case highlights indiscriminate use of piracetam for intelligence enhancer/ memory booster effect in a girl with intellectual disability despite literature reporting thatpiracetam therapy does not improve cognitive function rather is associated with adverse effects.[4] It is approved for use in Europe for treatment of seizure disorder; however, it is not US FDA approved for any indication and its sale as a dietary supplement is also prohibited [5]. Despite having insufficient evidence to establish its safety, piracetam is available in markets and being used as off label/over the counter drug [6].

Its use in dose of 500 mg twice/day (higher range of usual dose 40 mg/kg/d; body weight 27 kg) in a girl with already compromised brain functions exposed her to the unwarranted CNS adverse effects, to the extent that she experienced visual and auditory hallucinations in addition to irritability,

psychomotor agitation, confusion, sleep and appetite disturbances which are reported in literature. It was further supported by a score of 5 in Naranjo algorithm scale for adverse drug reactions. CNS adverse effects are explained on the basis of its neuroexcitatory effect on AMPA receptor induced calcium influx, thus increasing maximal density of AMPA glutamate and acetylcholine receptors and potassium induced glutamate release in the brain. It has also been postulated to have a role in increasing the availability of oxygen, permeability and fluidity of the mitochondrial cell membrane in the intermediate stages of the Krebs cycle, increasing activity of adenylate kinase, thus increasing ATP production in the brain. [7]. Adverse effects like anxiety, insomnia, agitation, irritability is identical to symptoms of excess acetylcholine/glutamate neuroactivity as seen in one of the previous case reports[8] and are in sync with the index case.

Clinical research on clinical use of nootropics is yet inconclusive. However, the use of nootropics to treat cognitive problems among healthy as well as in children with learning difficulties/ memory disturbances/ poor academic performance cannot be prevented. Casual, unsupervised, nonmedical use of nootropic drugs to improve academic performance could have unanticipated negative mental health effects. Health professionals need to be cognizant of the fact that nootropics may be to the human mind what steroids are to the body (misuse/abuse for muscle building, improving performance/physical shape despite dverse physical & psychological effects) and thus promote judicious use.

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