CRITIQUE II

Are Selective Serotonin Reuptake Inhibitors Effective in Treating Symptoms of Autism?

Case of Citalopram

Class

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In their study on use of citalopram in pervasive developmental disorders (PDDs), Namerow and others (2003) hypothesized that this particular selective serotonin reuptake inhibitor (SSRI) is an effective, safe, and well-tolerated treatment for some autistic symptomology of children and adolescents. This hypothesis arises from previous work on autistic symptoms being responsive to other SSRIs, and the benefits of citalopram over other SSRIs, such as less drug interactions and less side effects. Also, citalopram has been previously reported to improve symptoms of depression, obsessive-compulsive disorder, and anxiety in other young populations, with symptoms comparable to symptoms of PDDs. The medical charts of 15 patients, ages 6 to 16-years-old, with PDD-Not-Otherwise-Specified (7), Autism (2), and Asperger syndrome (6) are retrospectively and systematically reviewed for the duration of approximately one year. The ratings of the Clinical Global Impression Severity and Improvement scale range from not ill (1) to extremely ill (7), and from very much improved (1) to very much worse (7). The researchers hoped to conclude that with its high selectivity, fewer side effects, and less potential for drug interactions, citalopram may be a more effective, safer, and well-tolerated treatment for alleviating some symptoms of pervasive developmental disorders in the youngest population. Furthermore, they expected to see better results with citalopram than other medications already in use for this group's PDDs.

The study has a number of important limitations; first, it considered only 15 young patients diagnosed with pervasive developmental disorders, making it difficult to generalize the results with such a small sample size (Price, 2012). Also, the study is a retrospective review of previously reported PDD cases in which citalopram was used, without controls being used. In addition to citalopram, other medications were being used concurrently by some of the 15 patients. Based on the results of this study, it cannot be deduced whether apparent effectiveness was the result of the combination of medications, or either one alone (see Breedlove for review of neurotransmitter

systems and myriad interactions). Also, compliance to using citalopram is questionable. Similarly, alternative psychoeducational and social interventions were not addressed in the present study, such as socialization skills and behavioral management all of which have undergone rigorous scrutiny and show efficacy (Schreibman, 2000).

Based on their conclusions regarding citalopram's effectiveness and safety in children and adolescents with PDDs, the authors suggest a venue for future research, which involves a larger, controlled study. According to Namerow and colleagues (2003), such experimental study with implemented controls "will help to determine [citalopram's] efficacy in the treatment of specific PDD symptoms and to establish guidelines for optimal dosing, safety, and tolerability," As opposed to the present naturalistic study, a controlled experimental design will allow patients to be seen at identical time points. This will be especially helpful in a more precise determining of time needed to achieve response to citalopram. Also, blood samples could be obtained in the future study, assuring compliance to taking citalopram, and controlling for concurrent medications. Finally, in addition to using the Clinical Global Impression Severity and Improvement scales, other scales could be used for more precise rating of autistic symptoms.

However, some findings of the present study require closer examination and reinterpretation. In their discussion of the study's limitations, the authors fail to consider other potential weaknesses of their results and conclusions. In addition to a very small sample size, only two young patients met the DSM-IV criteria for autism. Only one of these two patients (50%) responded to citalopram, making such results inconclusive for children and adolescents diagnosed with autism, and requiring further examination. Similarly, only four out of seven patients (57%) diagnosed with PDD-NOS were responders to citalopram. The only group with a promising response rate (100%) was comprised of six children and adolescents with Asperger's. Thus, the very optimistic claims should

have been made only for those youngsters who meet the DSM-IV criteria for Asperger syndrome. Also, 87% of the patients were male, making the sample even more unrepresentative.

Furthermore, other aspects of this study require careful reconsideration. The ages of patients in the sample size range from 6 to 16 years old. With great inter-personal variability of any PDD, and its spectrum character, comes additional variability of possible responsiveness to the same medication. Surprisingly, the median dose of citalopram (17mg/day) in the current study was similar to that recommended for adults (20 mg/day) (Namerow et al., 2003). Other cause for concern was that if patients took citalopram even for 1 day, they were included in this analysis, which seems to disregard drug use patterns (SSRIs take 2 weeks to have effects) (Breedlove, Watson & Rosenzweig, 2010). Also, this study fails to carefully consider the possible behavioral side effects of citalopram, some of which closely resemble the autistic symptomology, such as agitation and aggression. Despite its limitations and weaknesses, the present study can be a valuable model for another naturalistic and retrospective study, in which some of those limitations and weaknesses are addressed. For the proposed study, more than 15 medical charts are to be reviewed for a more representative sample. Finally, the study would have benefited by a one-time visit with the patient and his/her caretaker is to be arranged, in order to assess the present rating on CGI scale, as well as other treatment methods which may have affected symptom changes. A redesigned version of the present study will be valuable for making more informed claims about effectiveness of SSRIs in treating autism, leading the way to experimentally-controlled drug trials.

References

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