LETTER TO THE EDITOR

Commentary on: "Review of the Pharmacotherapy of Irritability of Autism": A Skeptic's View on Second Generation Antipsychotics in Autism

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Note: The following is an invited commentary of *Review of the Pharmacotherapy of Irritability of Autism*, by Elbe and Lalani, which appeared in the May 2012 issue of JACAP.

In "Review of the Pharmacotherapy of Irritability of Autism" (JCACAP, 21(2), 130-146), Elbe and Lalani provide a detailed review of available scientific literature on the psychopharmacologic treatment of Autism Spectrum Disorders (ASD). It is especially notable for its summary of the studies of second-generation antipsychotics (SGA). Given the current trends in SGA prescription in ASD, the authors' findings are particularly relevant to those of us who see and treat this population of children and adolescents. The paper highlights that there is *virtually no* scientific data to support the most common "real world" usage patterns of these agents.

The authors review ten randomized controlled trials (RCTs) specifically evaluating the efficacy of SGA's for individuals with ASD. On balance, they conclude that there is good data that SGA's are relatively safe and provide meaningful improvements in behavioural functioning for the immediate to short term. However, that's where the good news ends.

Studies on the effectiveness of SGA's in ASD suffer from a number of shortcomings, including the level of industry involvement in the research. The vast majority of the studies described were completed with some industry support or involvement. Although this alone does not disqualify the results, it does remind us that the authors would likely want to present the most favorable data—not necessarily all the data.

The prescription of SGA's to children and youth, including those with ASD, has increased rapidly in the last two decades. Between 1993 and 2002 by some estimates SGA prescriptions increased by 5-6 fold (Cooper et al., 2006). Elbe and Lalani cite the mounting literature on adverse metabolic effects of SGA's. As a society we have become alarmed by the growing public health crisis of childhood obesity, an even more salient health concern for individuals with ASD. Current estimates are that ASD individuals are up to three times as likely to suffer from obesity, and twice as likely to have hyperlipedimia (Tyler, Schramm, Karafa, Tang, & Jain, 2011). Elbe and Lalani advocate for active management of metabolic health—often requiring expensive tests and traumatic blood draws, and creating a new layer of medicalization for these children and families.

The greatest weakness of these studies is that nearly all of them were limited to *12 weeks or less*. Treatment courses with SGA's in the "real world" are more often measured in *years*, not weeks. That is, the pattern of use described in the studies does not resemble how most of us use these medications in our practices.

The generalizability of research results is dependent upon the degree to which a study population resembles the patients in your practice. Here as well, the study designs create challenges. In most of the studies, case definition is seriously flawed. Not a single study established ASD diagnosis in subjects utilizing gold-standard research methods. Most studies minimized the impact of IQ and age. As well, many studies either don't describe or simply exclude subjects with "psychiatric comorbidities" (like anxiety or attention deficit hyperactivity disorder). Such exclusion is problematic as the *RUPPAN* dataset found that "absence of co-morbid conditions" predicted *better* response to medications (Arnold et al., 2010). Current research suggests that psychiatric co-morbidities are present in upwards of two-thirds of individuals with ASD (Joshi et al., 2010). Does this therefore

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imply that the results apply to only the two-thirds without psychiatric comorbidity?

Judicious psychopharmacology can have great benefits for many individuals with ASD. An evidence-based approach necessitates a careful identification of psychiatric co-morbidities and utilizing diagnosis-specific treatment algorithms. Although it is *possible* that maintenance use of SGA's will prove to have sustained functional benefits, we currently lack robust research that long-term benefits outweigh the considerable *known* health risks. Should we risk the quality of life of an already vulnerable cohort of children by having them enter adulthood at even higher risk for chronic medical illness?

References

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Welcome – New Assistant Editor

Kristin Cleverley RN, PhD, CPMHN-C
Director, Practice Research and Innovation
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Kristin obtained a BSc (Nursing) and an MSc (Nursing) at McMaster University. She then completed a PhD (Health Research Methodology) in the Department of Psychiatry and the Offord Centre for Child Studies at McMaster University. During her PhD studies Kristin was the recipient of a 4-year CIHR/PHAC Clinician-Scientist Fellowship and obtained her certification in Psychiatric Mental Health Nursing (CPMHN) from the Canadian Nurses Association. Kristin is the recipient of several awards, including, the Graduate Programs Excellence Award, the Teaching Assistance Excellence Award and the Canadian Academy of Psychiatric Epidemiology Best Poster Award. Her clinical and research interests include developmental psychopathology (specifically aggressive behaviours and concurrent disorders), psychiatric/mental health nursing, poverty and homelessness, patient centered care, program evaluation, and analytical techniques for modeling longitudinal and multi-level data. Kristin has been an instructor in the graduate and undergraduate programs in Health Sciences at McMaster University since 2003 and is an Assistant Professor in the Faculty of Nursing and Associate Member of the Graduate Department of Nursing Science at the University of Toronto. Kristin is currently the Director of Practice Research and Innovation at the Centre for Addiction and Mental Health.