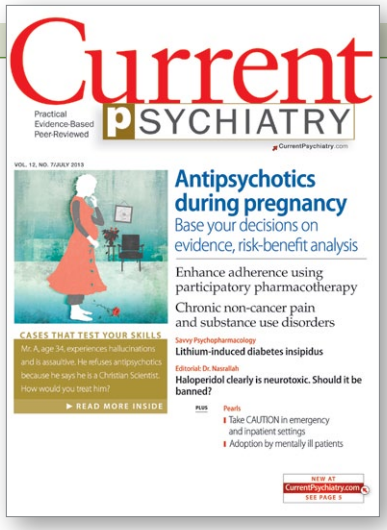

July 2013

'Farewell' to haloperidol?

In response to "Haloperidol clearly is neurotoxic. Should it be banned?" (Current Psychiatry, From the Editor, July 2013, p. 7-8; http://bit.ly/1eMegnr), let me clarify several issues before a consensus is established on whether to discontinue the use of haloperidol.

Remember that since the first use of haloperidol—one of the butyrophenones—more than a half a century ago, practitioners and researchers were aware of its neurotoxicity. Nevertheless, butyrophenones are unique chemicals capable of controlling psychotic symptoms and severe brain dysfunctions, such as extrapyramidal reactions, neuroleptic malignant syndrome, akathisia, tardive dyskinesia, and galactorrhea, among others. Dr. Paul Janssen—founder of the laboratory that first released haloperidol—made a fortune that subsequently prevented him from being awarded the Nobel Prize in Physiology or Medicine.[1]

A product that was the cornerstone of psychiatric treatment for half a century deserves a better farewell than the one Dr. Nasrallah is offering. Atypical antipsychotics present a number of drawbacks and have dangerous toxicity levels that still need study. I am concerned about metabolic syndrome (diabetes mellitus, hypercholesterolemia, gynecomastia, severe obesity, etc.), which may cost even more to treat than the cost of psychiatric care. In addition to the burden of their high and often unreasonable cost, quetiapine, olanzapine, clozapine, aripiprazole, risperidone, and other atypical antipsychotics have clinical limitations that often restrict their use.

If psychiatry needs a good, immediate fix, it would be in the development and approval of new chemicals that are both better tolerated than the butyrophenones and more affordable than atypical antipsychotics.[2]

Enrique S. Garza-Trevino, MD
Medical Director
San Antonio Mood Disorders Clinic
San Antonio, Texas

References

1. Healy D. The psychopharmacologist II: interviews by David Healy. Philadelphia, PA: Lippincott-Raven Publishers; 1998.
2. Garza-Trevino ES, Hollister LE, Overall JE. Combination of intramuscular hypnotics and neuroleptics for control of psychotic agitated patients. Am J Psychiatry. 1989;146:1598-1602.

Superior efficacy of atypical antipsychotics

Regarding Dr. Nasrallah's editorial (July 2013) on the research delineating some of the neurotoxic aspects of first-generation antipsychotics, including haloperidol, he seems to shoot clinical psychiatry in the foot when he describes second-generation agents as having been "much safer for the brain than their older-generation counterparts (although they are *not* more efficacious)." This closing assertion is not followed by a reference. Indeed, one would anticipate that the newer agents would display greater efficacy given the neurotropic properties of the atypicals described by Dr. Nasrallah in his previous editorial, "Beyond dopamine: The 'other' effects of antipsychotics" (Current Psychiatry, June 2013, p. 8-9; http://bit.ly/1aA7MZw).

The only real study attempting to clarify this issue has been the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study; patients in that study were chronic and refractory to any intervention. In my practice, I have seen clear and compelling evidence supporting the superiority of atypical antipsychotics—as well as chronicity with multiple relapses and rehospitalizations.

More research into this matter is necessary. In the meantime, we need to be mindful of assertions that might be premature and damaging.

Robert Barris, MD
Nassau University Medical Center
East Meadow, New York

Dr. Nasrallah responds

I appreciate the comments of Drs. Garza-Trevino and Barris in response to my editorial. Here is my reply to the points they addressed:

The efficacy and neurotoxicity of haloperidol are independent mechanisms. Blocking dopamine receptors controls psychotic symptoms, but neurotoxicity involves triggering apoptosis, increasing free

Keep in touch!

The Editors welcome your letters on what you've read in Current Psychiatry

Write to:

letters@currentpsychiatry.com

Comments & Controversies
Current Psychiatry
7 Century Dr., Suite 302
Parsippany, NJ 07054

radicals, binding to sigma receptors, increasing intracellular calcium, decreasing neurotropic factors, increasing P53, T-box, Jun kinase, etc. Neurotoxicity is separate from extrapyramidal side effects. Similarly, the neuroprotective effects of atypical antipsychotics, such as enhancement, neuroplasticity, increasing neurogenesis, and growth factors, are separate from their antipsychotic efficacy.

Only some of the CATIE study patients who responded to clozapine in phase II after not responding to any of the antipsychotics in phase I were refractory.

The assertion about the neurotoxicity of haloperidol is based on 28 published studies in neuroscience journals (which are rarely accessed or read by clinicians). Thus, the terms "premature and damaging" do not apply. I served as a messenger summarizing all these destructive properties of haloperidol[1] and I certainly was prepared to parry and deflect some arrows.

Meta-analysis of the efficacy of first- and second-generation antipsychotics (SGAs) showed that most SGAs are similar to first-generation antipsychotics (FGAs).[2] What the SGAs do that gives the appearance of additional efficacy is avoid the secondary negative and cognitive deficits associated with extrapyramidal side effects, which are much lower with SGAs.

The treatment of primary negative symptoms and cognitive impairment of schizophrenia remains a huge, unmet need—but there is some emerging data on glutamate modulation as a path to improving negative symptoms.

Finally, just as the FGAs vary in their extrapyramidal side effect profile, so do SGAs in their metabolic adverse effects. There are several SGAs that are metabolically benign, and there are also some FGAs that can cause serious weight gain and hyperglycemia.

Henry A. Nasrallah, MD
Editor-In-Chief

References

1. Nasrallah HA, Rush S. First generation antipsychotics are neurotoxic and impair neuroplasticity via multiple mechanisms. Biol Psychiatry. 2013;73:61S.
2. Davis JM, Chen N, Glick ID. A meta-analysis of second-generation antipsychotics. Arch Gen Psychiatry. 2003;60:553-564.

Did the authors slip on SOAPP?

I found "Chronic non-cancer pain and substance use disorders: Challenges and strategies." (Current Psychiatry, July 2013, p. 35-41; http://bit.ly/162NTCO) interesting. However, as an author of one of the references cited, I feel I should speak up when there is a factual error. The authors cite our Moore et al 2009[1] study as finding that "the SOAPP-R is 90% sensitive in detecting CNCP/SUD."

First, what was identified was those patients misusing opioid medications in some way that might or might not represent a substance use disorder. Second, the sensitivity was 73%, not 90%. Most important, the instrument to which the authors are referring is the SOAPP, not the SOAPP-R. Our later studies have shown that the SOAPP-R has much less sensitivity than the SOAPP and, therefore, the two tools are not comparable.

Ted W. Jones, PhD
Psychologist
Behavioral Medicine Institute, P.C.
Pain Consultants of East Tennessee
Knoxville, Tennessee

Reference

1. Moore TM, Jones T, Browder JH, et al. A comparison of common screening methods for predicting aberrant drug-related behavior among patients receiving opioids for chronic pain management. Pain Med. 2009;10(8):1426-1433.

Malingering
continued from page 38

8. Small IJ, Small JG, Andersen JM. Clinical characteristics of hallucinations of schizophrenia. Dis Nerv Syst. 1966;27(5):349-353.
9. Rosenhan DL. On being sane in insane places. Science. 1973;179(70):250-258.
10. Miller HA. M-FAST interview booklet. Lutz, FL: Psychological Assessment Resources; 2001.
11. Hom J, Denney RL. Detection of response bias in forensic neuropsychology. Binghamton, NY: Haworth Medical Press; 2002.
12. Whitney KA, Hook JN, Steiner AR, et al. Is the Rey 15-Item Memory Test II (Rey II) a valid symptom validity test?: comparison with the TOMM. Appl Neuropsychol. 2008;15(4):287-292.
13. Kelly PJ, Baker GA, van den Broek MD, et al. The detection of malingering in memory performance: the sensitivity and specificity of four measures in a UK population. Br J Clin Psychol. 2005;44(3):333-341.
14. Hanley JR, Backer G, Ledson S. Detecting the faking of amnesia: a comparison of the effectiveness of three different techniques for distinguishing simulators from patients with amnesia. J Clin Exp Neuropsychol. 1999;21(1):59-69.
15. Rogers R. Clinical assessment of malingering and deception, 3rd ed. New York, NY: The Gilford Press; 2008:54.
16. Myers W, Hall R, Tolou-Shams M. Prevalence and assessment of malingering in homicide defendants using the mini-mental state examination and the Rey 15-Item Memory Test. Homicide Stud. 2013;17(3):314-328.
17. Resnick PJ. In session with Phillip J. Resnick, MD: malingering of psychiatric symptoms. Prim Psychiatry. 2006;13(6):35-38.