

Naturalistic Study: *Treating the Acutely Agitated Patient*

Andrew Francis, MD, PhD
Associate Professor
State University of New York at Stony Brook
Health Sciences Center
Medical Director
Inpatient Psychiatric and Day Treatment Services
University Hospital at Stony Brook
Stony Brook, New York

Disclosure

Type of Affiliation	Commercial Entity
Consultant	Eli Lilly and Company, Janssen Pharmaceutica, Pfizer, Inc.
Honorarium	AstraZeneca Pharmaceuticals LP, Pfizer, Inc.

Dr. Francis intends to discuss off-label/unapproved uses of products or devices.

Learning Objectives

Upon completion of this presentation, participants should be able to:

- Identify agitated patients who may respond to IM sedation with atypical neuroleptic agents
- Identify an expected course of clinical response after receiving atypical neuroleptic parenteral sedatives

Comprehensive Psychiatric Emergency Program (CPEP): *What Is it?*

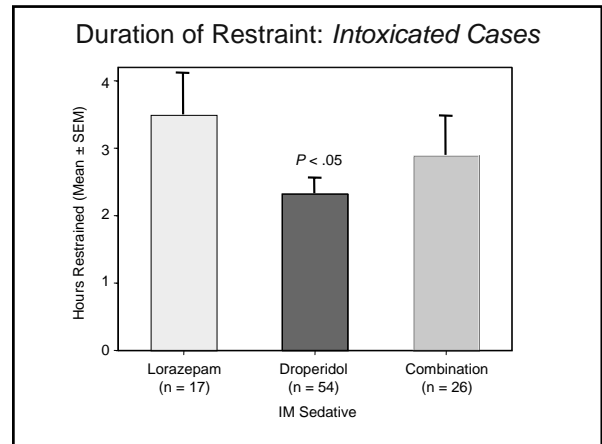
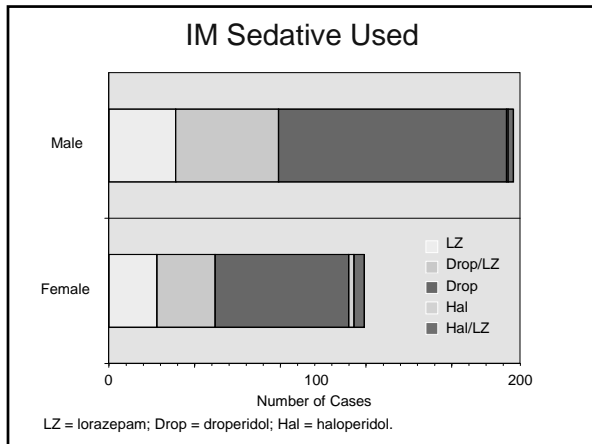
- ~ 15, New York State-sponsored/regulated
- 24-hour attending psychiatrist, psych RN, psychiatric social worker, resident, nursing aides
- Adjacent to ER
- Extended-observation bed (72 hours)
- SUNY Stony Brook: 6200-6700 cases/year

SUNY Stony Brook CPEP

- ~ 60% require police escort
- ~ 10% require extended-observation bed (up to 72 hours)
- ~ 40% involuntary admissions
- ~ 60%-80% major psychiatric illness and/or substance abuse, intoxication
- ~ 50% are medicated in CPEP

IM Sedative Study (1994-1997)

- SUNY Stony Brook CPEP site
- Restrained and IM-sedated cases
- Chart review using restraint log
- Era before droperidol abandoned, before atypical neuroleptics available as IM



- ### SUNY Stony Brook 2002 CPEP Study: *Rationale*
- Droperidol abandoned
 - Published ziprasidone studies (eg, Daniel et al) show promise, but excluded severe agitation, ETOH/substance intoxication
 - Published study (20 mg): 50% drop in agitation scores in 2 hours (rapid enough?)
 - Ziprasidone IM untested in routine CPEP cases
 - Ziprasidone more costly than conventional alternatives (haloperidol/lorazepam) but there is question whether advantages outweigh cost

- ### SUNY Stony Brook CPEP Study: *Background*
- Not industry-sponsored
 - Droperidol abandoned June 2002
 - Advent of IM ziprasidone
 - Initially, CQI (QA) project for internal use
 - Safe?
 - Effective?
 - Cost-benefit?
 - Pharmacy restricted use to CPEP, inpatient psych (not medical ED!)
 - CQI project
 - Not “research” (ie, not planned for publication)
 - IRB approval later obtained for retrospective reporting, publishing (converted QA data to research data)
- CQI = continuous quality improvement; QA = quality assurance.

- ### SUNY Stony Brook CPEP Study: *Design*
- Naturalistic outcome – not random assignment
 - Predominant sedative for October-December 2002
 - Typical CPEP cases: severe agitation, ETOH, substances
 - Data: Behavioral Activity Rating Scale (BARS) at baseline and up to 120 minutes (nonobtrusive, practical time limit)
 - Data: duration of restraints
 - Data: post hoc disposition time from CPEP
- (cont)

- ### SUNY Stony Brook CPEP Study: *Design*
- Compare to conventional sedatives – mostly haloperidol and/or lorazepam
 - Routine clinical monitoring, 17/69 ECG
 - Categorize cases as PSYCH agitation (toxicology negative), ETOH agitation (blood alcohol level range 50-460, median 285), SUBS agitation (miscellaneous substances including cocaine, marijuana, barbiturates, opiates, or combined with ETOH)

BARS Agitation Scale

- Simple, 1-item 7-point scale
- Used in published ziprasidone studies
- Validated against PANSS-agitation and CGI-S
- Entirely observational, not obtrusive
- High interrater reliability

The BARS 7-Point Observational Scale

- 7 Violent, requires restraint
- 6 Extremely or continuously active
- 5 Signs of overt activity; can be calmed
- 4 Quiet and awake
- 3 Drowsy, appears sedated
- 2 Asleep, but responds normally
- 1 Difficult or unable to rouse

- Validated as a reliable measure of activity levels in acute agitation, responsive to treatment differences
- When evaluated by 342 experienced raters, demonstrated inter- and intrarater reliability
- When correlated to scores in the CGI-S and PANSS negative scales, convergent and divergent validity were displayed

Swift RH et al. *J Psychiatr Res.* 2002;36:87-95.

SUNY CPEP Study (N = 69)

Males

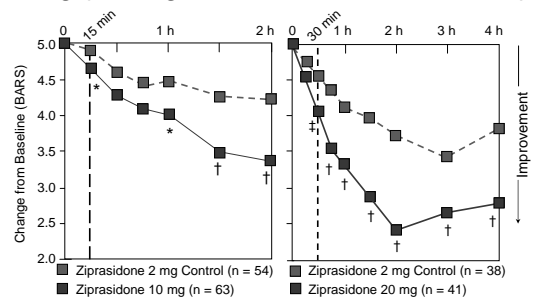
- n = 43
- Mean = 33.4
- SEM = 11.7
- Median = 34
- Range 18-67

Females

- n = 26
- Mean = 43.1
- SEM = 11.7
- Median = 43
- Range 19-68

SEM = standard error of the mean.

Published IM Ziprasidone Studies: 10 and 20 mg (Change in Baseline BARS Scale)

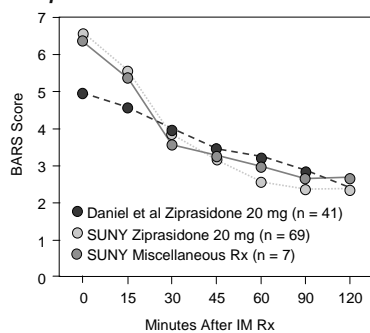


* $P < .05$. † $P < .001$. ‡ $P < .01$.

Brook S et al. *J Clin Psychiatry.* 2000;61:933-941.

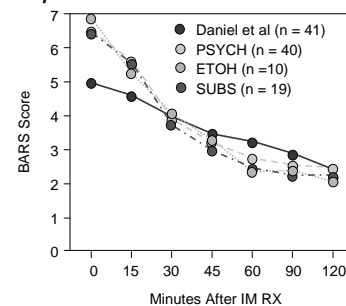
Daniel DG et al. *Psychopharmacology (Berl).* 2001;155:128-134.

SUNY Stony Brook CPEP Study: Comparison with Daniel et al Data



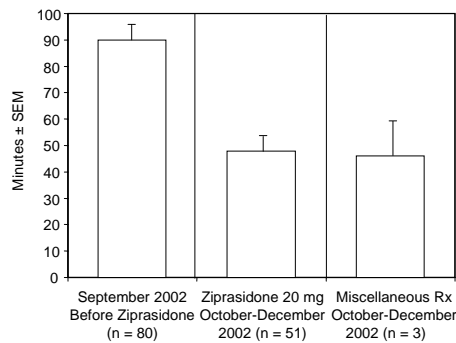
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SUNY Stony Brook CPEP Study: Comparison with Daniel et al Data



Ziprasidone 20 mg in all studies.

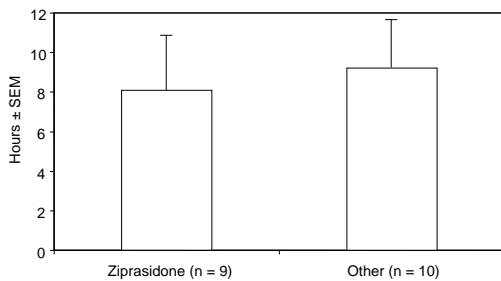
SUNY Stony Brook CPEP Study Restraint Times



QTc IM Ziprasidone

- N = 17/69, ~ 30 minutes post-Rx
- Mean = 0.418
- SEM = 0.026
- Median = 0.410
- Range = 0.370-0.462

Total Time in CPEP for Cases Restrained + IM Rx Day Shift



SUNY Stony Brook CPEP Study: *Results*

- Routine CPEP cases more agitated than cases in published study (BARS 6.6 vs 5.0)
- ~ 50% drop in BARS scores in 30-45 minutes with ziprasidone 20 mg, clinically significant
- Preliminary data for reduced restraint times
- Equally effective for intoxicated cases
- Safe, well tolerated
- One dystonic reaction: 17 ECGs, no QTc changes
- More prompt interview and disposition?

General Conclusions

- Ziprasidone is safe and effective for acute agitation
- Equally effective for agitation of all types
- Like droperidol, ziprasidone is effective for agitation with intoxication