

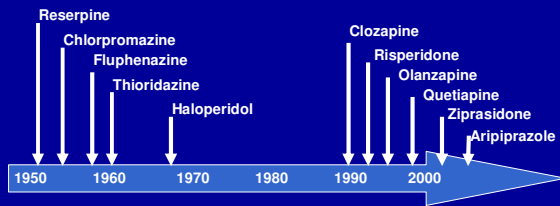
Clozapine (clozaril)

An under utilized evidence based treatment

Outline of the presentation

- Review evidence of the benefits and side effects of clozapine
- Examine current anti-psychotic prescribing practices
- Examine data from a survey conducted jointly by the Division of Mental Health and the N.C. Psychiatric Association examining barriers to clozapine use in N.C.
- Propose suggestions to facilitate increasing the use of clozapine

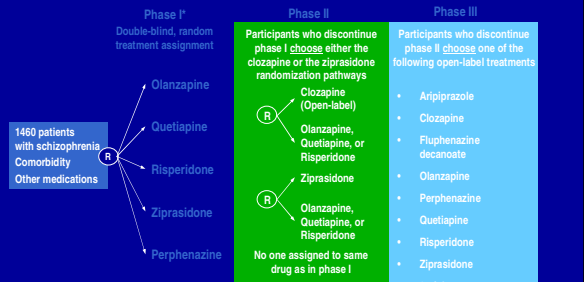
Antipsychotic Therapy: A Historical Perspective



Clozapine

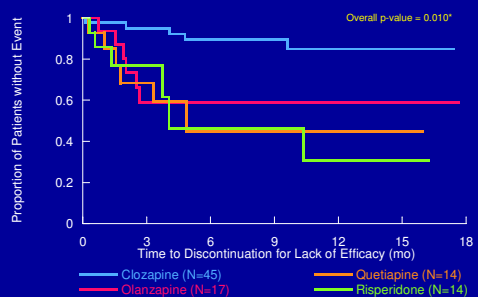
- Clozapine is the prototype atypical (no EPS)
- Introduced in 1990 in USA
- Kane et al published landmark study in the Archives of General Psychiatry(1990). Clozapine superior to chlorpromazine for treatment resistant schizophrenia patients (30% vs. 4%).
- Potential side effect of agranulocytosis (1%)
- Requires ongoing hematologic monitoring

CATIE Schizophrenia Trial: Practical Trial Design



¹Phase IA: participants with tardive dyskinesia (TD) (N=231) do not get randomized to perphenazine. Participants who fall perphenazine will be randomized to an atypical (olanzapine, quetiapine, or risperidone) before eligibility for phase II. Stroup TS, et al. Schizophr Bull. 2003;29(1):15-31.

Time to Discontinuation for Inefficacy (IIE)



Clozapine works!!

- The most well replicated finding is the ability to reduce the “positive” symptoms of schizophrenia (delusions, hallucinations, thought disorganization) in treatment resistant patients.
- It is estimated that 20-30% of patients with schizophrenia have persistent positive symptoms despite treatment with other antipsychotics

Other uses

- Treatment resistant Bipolar/Schizoaffective patients
- Schizophrenia patients with suicidal behavior
- Non-schizophrenic aggressive patients, i.e., Borderline Personality Disorder
- Tardive Dyskinesia

What about the side effects?

- Hematologic concerns (1% of users)
- Myocarditis/Cardiomyopathy (?? of users)
- Weight gain/metabolic concerns
- Sedation
- Seizures (risk increases at high doses)

Are these side effects associated with increased mortality?

- Tiihonen et al 2009 Lancet, published the results of an 11 year follow-up study of mortality in schizophrenia. Clozapine use was associated with a substantially LOWER mortality than any other anti-psychotic.

How frequently is clozapine used?

- Sernyak and Rosenheck 2008, Psychiatric Services found that only 2-3% of schizophrenia patients were prescribed clozapine. No change from 1999-2006
- 2007 Medicaid data from 5 states:
Florida 2%, Georgia 3%, N.C. 2%,
Texas 2%, West Virginia 2%

If clozapine isn't used then what is used for treatment resistant patients?

- Antipsychotic polypharmacy is very prevalent despite no evidence that supports it working

Why isn't clozapine used more often????

- The N.C. Division of Mental Health, Developmental Disabilities, and Substance Abuse Services, and the N.C. Psychiatric Association (NCPA) developed a survey that addressed that question. It was distributed via survey monkey to all psychiatrists affiliated with the NCPA in November 2009.

Characteristics of the survey

The survey addressed the following:

- 1) Where in NC do they practice?
- 2) What type of practice?
- 3) How many people did they treat/start on clozapine in the past year?
- 4) What were the barriers to its use?
- 5) What were the psychiatrists opinions on ways to increase clozapine use.

Who responded?

- 60 psychiatrists from 22 different counties
- Academic 11 (18%)
- Private Outpatient 21 (35%)
- Private Inpatient 2 (3%)
- Public Agency 22 (36%)
- Hospital, Community 6 (10%)
- Hospital, Gov. 9 (15%)
- Hospital, Private 2 (3%)
- HMO/Managed Care 1 (2%)
- Administrative 5 (8%)

How many psychiatrists treated a patient with clozapine in the last 12 months?

- Zero patients 15 (25%)
- One 11 (19%)
- Two 6 (10%)
- Three 4 (7%)
- More than 3 23 (39%)

75% of the sample treated at least 1 patient with clozapine over the past 12 months

How many psychiatrists started a patient with clozapine in the last 12 months?

- Zero patients 37 (64%)
- One 4 (7%)
- Two 6 (10%)
- Three 3 (5%)
- More than 3 8 (14%)

Almost 2/3rds of the sample did not prescribe clozapine for even one patient in the past year

What about private outpatient psychiatrists (n=21)?

- 62% treated at least 1 patient with clozapine (29% treated more than 3 patients)
- 75% did not start any patients on clozapine. Only 5%(n=1) started more than 3 patients on clozapine.

What about Public Agency Psychiatrists (most likely to prescribe clozapine)?

- 64% treated 3 or more patients with clozapine (87% at least one person)
- 64% did not start any patients on clozapine.

Barriers to clozapine use

Patient refusal of blood draws	64%
Logistical problems	59%
Patient not reliable enough for weekly blood draws	59%
Confusing registration process	38%
Too difficult on an outpatient basis even if blood draws are not an issue	36%

Would offering an inpatient admission help with starting clozapine?

- Of all responders 52% thought that it would help
- 76% of Public Agency psychiatrists thought that it would help

Summary of Survey Results

- Initiating clozapine treatment was far less frequent than maintaining someone on clozapine.
- A sizable majority of respondents did not start anyone on clozapine in the past year.
- There are considerable logistical barriers to initiating clozapine treatment.
- The majority of respondents thought a hospital admission would help the process.

What is the best strategy for increasing the use of clozapine?

These data would suggest, based on practice patterns, that the initial initiation process may be the critical step. Facilitating an inpatient hospitalization whereby clozapine could be started and then appropriate aftercare plans could then be set up is likely a useful strategy.

What about keeping up with blood draws after discharge??

- Once a week for the first 6 months
- One every two weeks for the next 6 months
- Once a month thereafter

Grant from the Health and Wellness Trust Fund

- Collaboration of the Departments of Psychiatry of UNC-Chapel Hill and Duke Universities with OPC and possibly other LME's (Durham and Wake)
- Set up a clozapine data base
- Clozapine Case Manager
- Two year project

Our goals

- Increase the use of clozapine
- Reduce polypharmacy and high doses of medication
- Improve the quality of life for people with treatment resistant illnesses
- Demonstrate cost effectiveness
- Use this data to apply for a larger federal grant