Orphan Patients: A Case Series of Patients With Treatment-Resistant Psychosis Requiring Alternatives to Clozapine

American Psychiatric Association Institute on Psychiatric Services, Chicago, USA, Oct. 4-7, 2018

Simon Bow, MD, FRCPC; Ashley DeGraaf, MSc; William G Honer, MD, FRCPC; Jacky Tang, BSc; Randall F White, MD, FRCPC
British Columbia Psychosis Program and University of British Columbia, Vancouver, Canada

INTRODUCTION

Clozapine is the most effective antipsychotic medication therapy for treatment-resistant psychosis (TRP). An appropriate trial results in improvements in at least 30% of TRP patients. However, it can result in troublesome and sometimes life-threatening side effects that require close monitoring. Additional issues include its exclusively oral formulation which reduces adherence and real-world effectiveness. As such, many patients are unable to take clozapine and require alternative strategies.

The BC Psychosis Program (BCPP) is a 25-bed residential treatment centre at the University of British Columbia Hospital, that specializes in research and treatment of patients with psychosis that is refractory to treatment. Any appropriate patient in BC can be referred; mean duration of stay is about 6 months.

METHODS AND MATERIALS

We reviewed a chart appendix that includes a summary of details of a patient's psychiatric, social, and medical history recorded at a multidisciplinary case conference. "Orphan patients" were defined as patients

- with BCPP consensus diagnosis of schizoaffective disorder or schizophrenia
- admitted from Feb 2012 to Dec 2017
- admitted without clozapine and discharged without clozapine, or
- admitted on clozapine and discharged without clozapine (discontinued during admission for any reason)

Information in the descriptive analysis included

- demographic data
- length of stay at BCPP
- referral diagnosis and BCPP consensus diagnosis

Standardized ratings at admission and discharge

- Positive and Negative Syndrome Scale (PANSS)
- Social and Occupational Function Scale (SOFAS)
- Global Assessment of Psychopathology Scale (GAPS)
- Clinical Global Impression-Severity (CGI-S)

Treatment information recorded

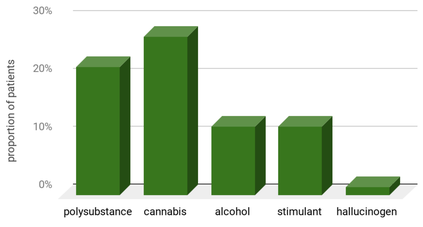
- comorbidities, psychiatric and medical
- details of previous clozapine trial
- details of alternative treatments, e.g. pharmacotherapy, ECT, psychotherapy
- Psychiatric medications at admission and discharge
- Calculated actual daily dose/defined daily dose (ADD/DDD)

PATIENT CHARACTERISTICS

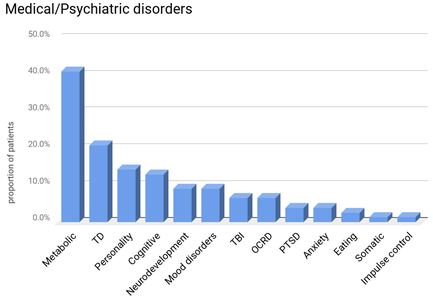
Of 274 patients treated at BCPP with available data, 77 patients met orphan criteria.

- 67.9% male
- Mean age, 43.2 years
- Mean duration of illness, 19.1 years

Concurrent disorders



Medical/Psychiatric disorders



By comparison, 163 patients were on clozapine at the time of discharge.

- 73% male
- Mean age 36.3 years
- Mean duration of illness, 12.7 years

ORPHAN PATIENT CLOZAPINE HISTORIES

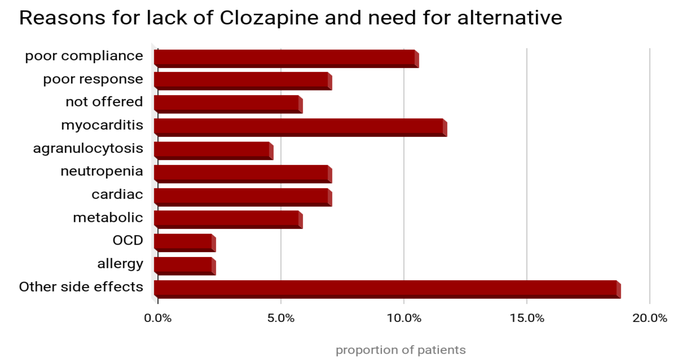
Of 77 patients

- 71% had a previous trial of clozapine
- 9% were on clozapine at admission but not discharge
- 7% had a trial during admission which was discontinued
- 14% never received clozapine in or out of hospital

Principal reasons for lack of clozapine treatment

- Dangerous adverse effects: myocarditis, neutropenia
- Patient factors: poor adherence, refusal
- Other adverse effects, often multiple
  - Cardiovascular
  - Sialorrhea
  - Sedation
  - Constipation
  - Metabolic
  - Obsessive-compulsive symptoms

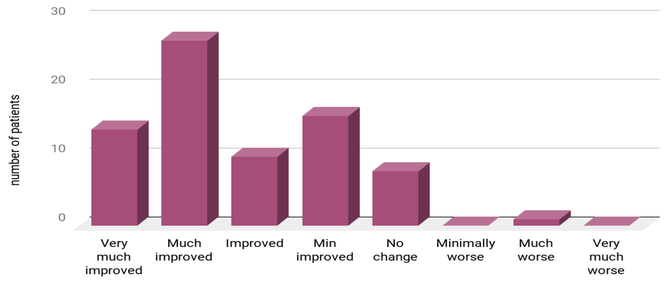
Reasons for lack of Clozapine and need for alternative



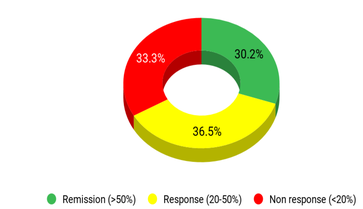
RESULTS OF TREATMENT AND INTERVENTIONS

Most patients showed improvement at the time of discharge as measured by CGI-I and reduction in total PANSS score.

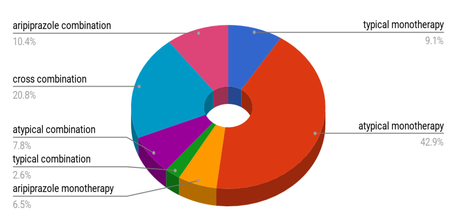
Clinical Global Impression - Improvement



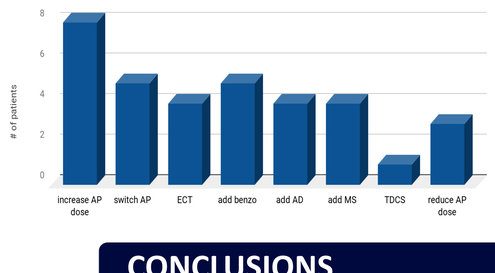
Reduction in PANSS score



Antipsychotic approaches at discharge



Main interventions in patients achieving remission (>50% PANSS reduction)



- ~50% of cases received a combination of antipsychotics
- patients that achieved remission typically had a ***decrease*** in ADD/DDD
- FGA monotherapy, most commonly loxapine or zuclopenthixol,had favorable outcomes on PANSS and CGI
- Combined FGA and SGA or combinations with aripiprazole had favorable outcomes

CONCLUSIONS

- BC Psychosis Program serves a heterogeneous population of patients with refractory psychosis
- Multidisciplinary team interventions also likely contributed to overall improvement
- CBT available although not all patients participate
- Considerations in treatment of orphan patients include
  - Trial of first generation antipsychotic, if not already done
  - Combination of a FGA + SGA, in particular aripiprazole
  - Augmentation with valproic acid, ECT, and CBT may prove useful in those with specific indications

LIMITATIONS

- The design is retrospective and nonrandomized
- Statistical analyses were not employed
- Sample size is limited as many patients at BCPP are successfully treated with clozapine with or without additional augmentation strategie
- The population presents clinical and research challenges in engagement and adherence
- Inter-rater reliability was not measured

REFERENCES

1. Mustafa F. Schizophrenia past clozapine. J Clin Psychopharmacol. 2013;33: 63-68.

2. Zheng W et al. Electroconvulsive therapy added to non-clozapine antipsychotic medication for treatment resistant schizophrenia: meta-analysis of randomized controlled trials. PLoS ONE. 2016;11(6):e0156510.