



# THE PRIMARY CARE COMPANION FOR CNS DISORDERS

## **Supplementary Material**

**Article Title:** Mask Off? Lithium Augmentation for Clozapine Rechallenge After Neutropenia or Agranulocytosis: Discontinuation Might be Risky

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Supplementary Table 1. Reports of Lithium Augmentation in Clozapine Rechallenge With Enumerated Succeeded and Failed Cases

Report	Summary	Number of Succeeded Cases	Number of Failed Cases
(1)	Literature review of 30 rechallenged cases after neutropenia/agranulocytosis who were additionally treated with g-csf either prophylactically, or as needed. Five cases were also co-administered lithium (prophylactically for blood dyscrasia). Of these two failed rechallenge.	3	2
(2)	Retrospective analysis of 51 rechallenged patients, 19 of whom had previously developed neutropenia. Of the 19 with previous neutropenia 16 were co-administered lithium during challenge. Four of the 16 failed rechallenge. Of those who failed rechallenge clinical characteristics are shared.	12	4
(3)	Case series of three successful rechallenge cases after neutropenia. All were stable after rechallenge for at least a 24 month period.	3	0
(4)	Case of clozapine rechallenge after lithium addition in setting of previous drop in ANC with clozapine use.	1	0
(5)	Case of clozapine challenge with prophylactic lithium after previous quetiapine induced neutropenia.	1	0
(6)	Case series of 10 patients successfully rechallenged on clozapine with prophylactic lithium after prior episode of neutropenia. One of these was of a patient who failed	10	0

	rechallenge twice and when finally augmented with lithium was successful. Two of these were patients who had ANC's >1.5 on previous failure. One was a patient with prior neutropenia not associated with clozapine.		
(7)	Case of patient of Ashkenazi Jewish origin failing clozapine rechallenge with prophylactic lithium with consequent protracted (27 day) blood dyscrasia.	0	1
(8)	Case of patient successfully rechallenged on clozapine and prophylactic lithium after having previously developed neutropenia (in setting of combined clozapine and valproic acid).	1	0
(9)	Case of patient who failed clozapine challenge, but eventually succeeded with combination clozapine and lithium.	1	0
(10)	Successful rechallenge in benign ethnic neutropenia patient with three previous failures due to neutropenia, successful finally on combination clozapine and lithium.	1	0
(11)	Patient rechallenged after previous neutrophil decline in setting of clozapine treatment. Patient challenged on combination clozapine, lithium, and single dose of g-csf.	1	0
(12)	Retrospective analysis of 25 clozapine rechallenged patients (with prophylactic lithium) who had previously developed CIN. One of these was unsuccessful, going on to develop an atypical infection raising suspicion for lithium having masked blood dyscrasia. In the one patient dyscrasia was more rapid, though not more severe.	24	1
(13)	Two cases who had previously developed neutropenia, with ANC <1.5, and went on to successfully tolerate clozapine rechallenge in setting lithium augmentation.	2	0
(14)	Case series of two cases, both previously developing neutropenia in setting of clozapine treatment, one of the	2	0

	two cases had developed neutropenia after lithium was discontinued. Both patients were subsequently successfully rechallenged on clozapine with prophylactic lithium.		
(15)	Case of a patient who successfully was rechallenged on clozapine and lithium after a previous clozapine failure due to neutropenia.	1	0
(16)	Case series of two patients. First patient developed neutropenia in setting of clozapine treatment, was subsequently successfully rechallenged on clozapine with aid of lithium. Second patient failed first challenge of clozapine, having developed agranulocytosis. Second patient was started on lithium after first clozapine discontinuation for purpose of increasing blood counts, with successful response to lithium.	1	0
(17)	Case of patient who failed clozapine challenge due to neutropenia, was subsequently successfully rechallenged with prophylactic lithium.	1	0
(18)	Case of patient who developed neutropenia with clozapine treatment, was discontinued, later restarted on clozapine and lithium with successful rechallenge.	1	0
(19)	Case of patient who developed agranulocytosis shortly after first clozapine challenge, was later successfully rechallenged with clozapine and lithium co-administration.	1	0
(20)	Case of patient who developed neutropenia with initial clozapine challenge, when rechallenged with combination vitamin c, lithium, and clozapine was unsuccessful, developing agranulocytosis shortly after rechallenge.	0	1

(21)	Case of patient who developed agranulocytosis on previous clozapine challenge. Patient was successful in clozapine rechallenge with combination lithium.	1	0
(22)	Retrospective analysis of 172 children challenged with clozapine. Of these 24 patients developed neutropenia requiring clozapine discontinuation, 20 of the 24 were subsequent rechallenged once more. Seven of the rechallenged patients were rechallenged with co-administered lithium. One of the patients rechallenged with co-administered lithium failed rechallenge.	6	1
(23)	Case of patient who failed previous clozapine challenge due to neutropenia was successfully rechallenged on combination lithium and clozapine.	1	0
(24)	Case of a patient who was successfully rechallenged on clozapine with prophylactic lithium after previous CIN. At first rechallenge with lithium augmentation patient had done well, however, when lithium was discontinued patient developed neutropenia requiring clozapine discontinuation with subsequent improvement in neutrophil count. Patient was eventually again rechallenged with prophylactic lithium and has been stable on the combination.	1	0
(25)	Case series of 7 patients with previous neutropenia who were successfully rechallenged with prophylactic lithium. Only two of the seven cases had developed previous neutropenia in the setting of clozapine use. All, but 1 were continued on lithium and clozapine. Subject 3, who was discontinued off lithium re-developed neutropenia, but successfully tolerated clozapine with lithium rechallenge.	6	1

(26)	Case of a patient successfully rechallenged on clozapine with prophylactic lithium after previous neutropenia. Patient was on clozapine for 14 months, but eventually required lithium discontinuation due to an intolerable tremor. The patient subsequently developed repeat neutropenia within two weeks requiring clozapine discontinuation.	0	1
(27)	Review of patients rechallenged on clozapine subsequent to previous adverse events. Discussed cases reporting on 35 patients rechallenged with co-administered lithium after prior neutropenia or agranulocytosis. Their reviewed articles have been reviewed above and we did not include Manu et al's numbers to avoid redundancy.	As above	As above
Total		N=82	N=13

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