





CLOZAPINE DEATHS

Antibody deficiency in patients taking clozapine

Mark J Ponsford ST5 clinical immunology and Welsh clinical academic trainee, Stephen Jolles consultant clinical immunologist, honorary professor, and clinical lead

Immunodeficiency Centre for Wales, Cardiff CF14 4XW, UK

Although clozapine reduces overall mortality in schizophrenia,¹ a growing body of evidence links its use with higher rates of admission to hospital for pneumonia²⁻⁴ and mortality.⁵⁻⁸ Various mechanisms have been proposed for the rise in pneumonia, including sedation, sialorrhoea and aspiration, agranulocytosis, and smoking. 9 10 Following the introduction of calculated globulin screening in Wales,11 we found a novel and striking association between use of the antipsychotic clozapine and antibody deficiency.¹² Patients taking clozapine follow an intensive regimen of blood testing for the rare risk of agranulocytosis (with cumulative incidence of <1% cases), but antibody testing is not included in existing clozapine monitoring programmes. We urge consideration of this potential mechanistic explanation as a modifiable risk factor for the higher rates of pneumonia and sepsis related mortality reported in this vulnerable cohort.

Competing interests: SJ has received support from CSL Behring, Shire, LFB, Biotest, Binding Site, Sanofi, GSK, UCB Pharma, Grifols, BPL SOBI, Weatherden, Zarodex and Octapharma for projects, advisory boards, meetings, studies, speaker, and clinical trials.

Tiihonen J, Lönnqvist J, Wahlbeck K, etal. 11-year follow-up of mortality in patients with schizophrenia: a population-based cohort study (FIN11 study). *Lancet* 2009;374:620-7. 10.1016/S0140-6736(09)60742-X 19595447

- Leung JG, Hasassri ME, Barreto JN, Nelson S, Morgan RJ3rd. Characterization of admission types in medically hospitalized patients prescribed clozapine. *Psychosomatics* 2017;58:164-72. 10.1016/j.psym.2016.11.013 28153339
- 3 Stoecker ZR, George WT, O'Brien JB, Jancik J, Colon E, Rasimas JJ. Clozapine usage increases the incidence of pneumonia compared with risperidone and the general population: a retrospective comparison of clozapine, risperidone, and the general population in a single hospital over 25 months. Int Clin Psychopharmacol 2017;32:155-60. 10.1097/VIC.00000000000000162 28059928
- 4 Kuo CJYS, Yang SY, Liao YT, etal . Second-generation antipsychotic medications and risk of pneumonia in schizophrenia. Schizophr Bull 2013;39:648-57. 10.1093/schbul/sbr202 22282455
- 5 Rohde C, Polcwiartek C, Kragholm K, Ebdrup BH, Siskind D, Nielsen J. Adverse cardiac events in out-patients initiating clozapine treatment: a nationwide register-based study. *Acta Psychiatr Scand* 2018;137:47-53. 10.1111/acps.12827 29064084
- 6 Taylor DMD-HP, Douglas-Hall P, Olofinjana B, Whiskey E, Thomas A. Reasons for discontinuing clozapine: matched, case-control comparison with risperidone long-acting injection. Br J Psychiatry 2009;194:165-7. 10.1192/bjp.bp.108.051979 19182180
- Mustafa FA, Burke JG, Abukmeil SS, Scanlon JJ, Cox M. "Schizophrenia past clozapine" reasons for clozapine discontinuation, mortality, and alternative antipsychotic prescribing *Pharmacopsychiatry* 2015;48:11-4.25376977
- 8 Dyer C. Coroners warn health secretary of clozapine deaths. *BMJ* 2018;363:k5421.
- 9 Abdelmawla N, Ahmed MI. Clozapine and risk of pneumonia. Br J Psychiatry 2009;194:468-9. 10.1192/bjp.194.5.468a 19407284
- Bello S, Menéndez R, Antoni T, etal . Tobacco smoking increases the risk for death from pneumococcal pneumonia. Chest 2014;146:1029-37. 10.1378/chest.13-2853 24811098
- Jolles S, Borrell R, Zouwail S, etal. Calculated globulin (CG) as a screening test for antibody deficiency. Clin Exp Immunol 2014;177:671-8. 10.1111/cei.12369 24784320
- 12 Ponsford M, Castle D, Tahir T, etal . Clozapine is associated with secondary antibody

deficiency. Br J Psychiatry 2018;214:83-9. 10.1192/bjp.2018.152 30259827

Published by the BMJ Publishing Group Limited. For permission to use (where not already granted under a licence) please go to http://group.bmj.com/group/rights-licensing/

•

Subscribe: http://www.bmj.com/subscribe