Molecular Genetics and Metabolism Reports 10 (2017) 101

Contents lists available at ScienceDirect

Molecular Genetics and Metabolism Reports

journal homepage: www.elsevier.com/locate/ymgmr

Correspondence

Authors' reply — Clozapine for mitochondrial psychosis

We thank Drs J. Finsterer and S. Zarrouk-Mahjoub [1] for their comments regarding our report [2] on the beneficial effects of low dose clozapine for management of psychotic symptoms in a patient with neurogenic ataxia-retinitis pigmentosa (NARP mutation, m.8993T>C, maternally inherited from asymptomatic carrier mother). We agree that clozapine has many side effects, some of them being potentially lethal. Yet, 70% of patients on clozapine reportedly remained on the drug for a long period [3] and its mortality was reduced compared to that of other antipsychotics [4]. Indeed, because side effects usually occur at onset of treatment, careful monitoring allowed to prevent complications and its efficacy exempted from giving other antipsychotic medication and decreased suicide rate.

It is worth noting also that our patient neither experienced adverse haematological nor cardiac effects of clozapine. In France, monitoring blood count is mandatory in patients given clozapine (weekly for 18 weeks then monthly) [5]. The treatment is suspended if neutrophil count falls below 1500/mm^3. Similarly, side cardiac effects are below 1% and their early detection by systematic EEG and ultrasounds allows to prevent heart complications. Using low dose Clozapine also reduces the occurrence of complications [6]. While low doses were well tolerated in our patient (37.5 mg/25 mg per day alternatively), higher doses triggered myoclonus and falls. On the contrary, extrapyramidal symptoms notably improved upon introduction of clozapine but remained clinically significant. This is probably due to the long lasting effect of the previously administered antipsychotics (risperidone, cyamemazine and aripiprazole). Clozapine metabolites may also have a neuroprotective effect on dopaminergic neurons [7], as mentioned by our colleagues. While Clozapine had an overall beneficial effect, additional cases and long term follow-up are needed to consider clozapine as a first line treatment for psychotic symptoms in NARP syndrome.

References

[1] J. Finsterer, S. Zarrouk-Mahjoub, Clozapine for mitochondrial psychosis, Mol. Genet. Metab. Rep. 4 (10) (2017) 50.
[2] C. Demily, C. Duwime, A. Poisson, N. Boddaert, A. Munnich, Low dose clozapine controls adult-onset psychosis associated with the neurogenic ataxia-retinitis pigmentosa (NARP) mutation, Mol. Genet. Metab. Rep. 13 (10) (2016) 20–22.
[3] O. Ingimarsson, J.H. MacCabe, M. Haraldsson, H. Jónsdóttir, E. Sigurdsson, Clozapine treatment and discontinuation in Iceland: a national longitudinal study using electronic patient records, Nord. J. Psychiatry 70 (2016) 450–455.
[4] R.D. Hayes, J. Downs, C.K. Chang, R.G. Jackson, H. Shetty, M. Broadbent, M. Hotopf, R. Stewart, The effect of clozapine on premature mortality: an assessment of clinical monitoring and other potential confounders, Schizophr. Bull. 41 (2015) 644–655.
[5] N. Kar, S. Barreto, R. Chandavarkar, Clozapine monitoring in clinical practice: beyond the mandatory requirement, Clin. Psychopharmacol. Neurosci. 14 (2016) 323–329.
[6] M. Raja, S. Raja, Clozapine safety, 40 years later, Curr. Drug Saf. 9 (2014) 163–195.
[7] L. Jiang, X. Wu, S. Wang, S.H. Chen, H. Zhou, B. Wilson, C.Y. Jin, R.B. Lu, K. Xie, Q. Wang, J.S. Hong, Clozapine metabolites protect dopaminergic neurons through inhibition of microglial NADPH oxidase, J. Neuroinflammation 13 (2016) 110.

Caroline Demily
GénoPsy, Centre Hospitalier le Vinatier et Centre de Neuroscience Cognitive, UMR 5229 (CNRS et Université Claude Bernard Lyon 1), Bron, France
Corresponding author.
E-mail address: caroline.demily@ch-le-vinatier.fr.

Charlyne Duwime
Association l'Elan Retrouvé, Paris, France

Alice Poisson
GénoPsy, Centre Hospitalier le Vinatier et Centre de Neuroscience Cognitive, UMR 5229 (CNRS et Université Claude Bernard Lyon 1), Bron, France

Nathalie Boddaert
INSERM U1163, Université Paris-Descartes, Service de radiologie pédiatrique, Institut Imagine, hôpital Necker-Enfants malades, Paris, France

Arnold Munnich
INSERM UMR 1163, Université Paris Descartes-Sorbonne, Service de génétique clinique, Institut Imagine, Hôpital Necker-Enfants Malades, Paris, France

22 January 2017

http://dx.doi.org/10.1016/j.ymgmr.2017.01.012