Treatment with the direct oral anticoagulants (DOACs) Apixaban and Rivaroxaban associated with significant worsening of behavioural and psychological symptoms of dementia (BPSD)

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Objective. To demonstrate the increasing evidence for an aetiological role of cerebral mitochondrial dysfunction in neuropsychiatric disorders.

To raise awareness of the importance of frontline staff partaking in post marketing surveillance of medications.

Case report. We report the cases of two patients who developed worsening BPSD, coinciding with starting the factor Xa inhibitor DOAC medications Apixaban and Rivaroxaban respectively. Both patients required detaining under the Mental Health Act (MHA). Their symptoms improved significantly, within two weeks, on switching to alternative anticoagulant therapies and they were both discharged from the acute psychiatric ward.

Discussion. Frontline healthcare staff in acute settings and the community manage a heavy workload. It is all too easy to overlook potential neuropsychiatric drug side effects, especially if they are not clearly listed. They may be easily missed amongst older patients and wrongly attributed to dementia.

Rivaroxaban is structurally related to the antibiotic Linezolid which has been reported to cause mitochondrial toxicity. Pre marketing In vitro studies concluded the risk of mitochondrial toxicity associated with this anticoagulant to be low. However a more recent in vitro study, using rat kidney mitochondria, reported evidence of mitochondrial swelling and a collapse of the membrane potential following exposure to low doses of Rivaroxaban. The effect of Apixaban, which is structurally related to Rivaroxaban, has yet to be investigated on mitochondrial function.

Recent research supports not only an association between reduced cerebral mitochondrial function and neuropsychiatric symptoms and disorders, but also the aetiological role it may play.

There is a need for a far greater awareness and understanding of the potential cerebral mitochondrial toxicity of drugs commonly prescribed to our older populations.

Conclusion. Cerebral mitochondrial toxicity can have a significant impact on the health and well-being of patients.

Older patients are particularly prone to experiencing neuropsychiatric side effects that may not have been apparent during preclinical trials.

Development of a rating scale of drugs that are potentially less toxic to cerebral mitochondria could inform national prescribing guidelines and enable safer treatments to be offered to older people, reducing the likelihood of them experiencing apparent behavioural and psychological symptoms of dementia.

Dyeing to live – a case of clozapine in disguise, and physicians' courage

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Objective. … in which clozapine tablets were dyed pink, to work around a delusion preventing treatment, and physicians tolerated and monitored an alarming early response to the drug.

Patient. 56-year-old female with severe enduring Bipolar I Disorder, current episode manic with psychosis, already an inpatient for six months. When first seen by us, polypharmacy was evident including haloperidol 25 mg daily. Thorough trials of mood stablisers and second generation antipsychotics in various combinations had all failed. She had never had a clozapine trial.

MSE. Dishevelled middle-aged woman of European descent. Restless; shuffling gait; speech pressured, rapid and whispering, often to the point of unintelligibility. Affect labile: anxious and distressed, suspicious, angry, elevated and demanding. Thought form tangential+++ content paranoid persecutory themes, preoccupied with sexual trauma and delusional belief that yellow medication whether solid or liquid was poisonous. Risks of vulnerability, falls, aggression, neuroleptic malignant syndrome (NMS) and protracted psychotic mania requiring long term hospitalisation.

Plan. Change to clozapine.

Problem. All formulations are yellow.

Solution. Team discussion, ethical analysis, clozapine tablets dyed with red vegetable dye.

Ethical analysis. Potential benefit to patient great; current medications not effective and NMS possibly developing; she was fully informed about clozapine with no attempt made to hide the identity of the now crimson tablets.

Outcome. Patient accepted the clozapine. Temperature, C reactive protein (CRP) and troponin were all normal at baseline but all rose above normal in week 1 of initiation. They peaked in week 3 and by week 4 were dropping, normalising completely within a few weeks. She was transferred to a medical ward for monitoring during weeks 2 and 3 of titration. There were no electrocardiogram changes, no chest pain, no signs of bowel obstruction and no evidence of agranulocytosis. Clinically, she remained well throughout except for the rise in temperature. Once the yellow medicine delusion receded she accepted undyed yellow tablets; the result was discharge home with her best mental state and level of functioning in 15 years.

Significance of this case. There are no cases in the literature that we could find where tablets had been dyed, or where clozapine had been persisted with when such rises in temperature, CRP and troponin occurred. This case illustrates both. The risks in our view were outweighed by the simple fact that clozapine was her only hope of a life worth living.

Lockdown and visual hallucinations in older people: a community perspective

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Objective. After COVID-19 was declared as a pandemic, different countries have enforced lockdowns, and shielding to mitigate the spread of the virus as preventing loss of lives was the priority.

Our aim is to look for possible explanations for increased rates of visual hallucinations presented to Community Mental Health Teams for Older People during the period of lockdown.

Case report. A review of clinical cases presenting with new onset visual hallucinations to the Community Mental Health Teams for