Correspondence

The future of ECG monitoring – can psychiatry take the 'lead'?

Electrocardiogram (ECG) monitoring is an essential part of safe prescribing in psychiatry, especially when a patient is admitted to an acute in-patient ward in England. Any psychiatrist who has worked on such a ward will appreciate the challenges that come with completing this 'simple' investigation.

Despite it being almost 100 years since Willem Einthoven was awarded the Nobel prize 'for the discovery of the mechanism of the electrocardiogram' and almost 70 years since the American Heart Association published their recommendation for standardisation of 12-lead electrocardiogram, there have been few recent practical changes in the way ECGs are obtained in UK clinical practice.

Although 12-lead ECG machines have become smaller and more advanced, patients are still required to expose their chests; allow for all ten physical leads to be attached, often using uncomfortable or irritating stickers and clips; and lie still for several seconds while a reading is taken.

We recently completed a regional service evaluation across Yorkshire and the Humber examining ECG compliance on adult, older adult and forensic wards. Our data, gathered from 529 patients across 25 wards, demonstrated that only 82% ($n = 432$) of patients had an ECG at any point during admission, of which only 63% ($n = 272$) were completed in 24 h. Concerningly, among the patients taking antipsychotics ($n = 378$), these numbers were lower–80% ($n = 303$) and 50% ($n = 188$), respectively.

Qualitative analysis of results demonstrated that the most common reasons for not having an ECG completed were 'patient-related factors'. Where a specific reason was given, the most common were 'aggressive, agitated, anxious, paranoid' (159 of 257; 62%). ECGs can appear threatening and intrusive; clothes on the upper body need to be removed, body hair may need to be shaved and the chest leads can look frightening. When someone is already distressed, this fear is likely to be exaggerated. Anxiety, past physical and sexual abuse, or gender identity concerns may further exacerbate this.

ECG monitoring in psychiatry is safety driven and exists because antipsychotics (particularly at high doses),[1] some antidepressants and methadone can predispose to life-threatening heart arrhythmias.[2,3] Examples include QTc prolongation, PR interval prolongation and, in extremis, torsade de pointes.[1] ECGs should be conducted as soon after admission as possible, preferably within the first 24 h.[4] Our results show that patients are therefore at risk of potentially fatal side-effects, and prescribers fall short of evidence-based and guideline-directed practice.[1–4]

Improving compliance with ECG monitoring, particularly in those prescribed pro-arrhythmic drugs, is a patient safety priority. Educating patients and mental health professionals about the need for ECGs is important, but reducing the intrusiveness and increasing the accessibility of ECG monitoring is called for. Technological advancements are being embraced in other areas of psychiatric practice; why not extend this to ECG monitoring? The advent of handheld ECG machines could be a solution to ensure all patients receive high-quality safe healthcare. These devices are yet to be approved in the UK for measuring QTc, but early validation work seems positive.[5]

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Declaration of interest

None

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RE: Routine clozapine assay monitoring to improve the management of treatment-resistant schizophrenia

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Routine clozapine assay monitoring should start during initial titration of clozapine dosages

Kitchen and colleagues have published a very clinically relevant paper highlighting the importance of routine clozapine assays.[1] We would support their conclusion of increased use of routine monitoring using clozapine assays.

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However, it is difficult to fathom why routine therapeutic drug monitoring (TDM) is still not considered justifiable in clinical practice. Clozapine fulfils the criteria for TDM as it has a narrow therapeutic index, substantial inter-individual variations in daily dose and plasma concentration relationship, and complex metabolism. We suggest that TDM should start during the initial titration to determine the target dose, rather than being restricted to annual monitoring.

The *British National Formulary* mentions that the usual dose of clozapine is between 200 and 450 mg, and the maximum is 900 mg per day. The Summary of Product Characteristics of clozapine further suggests that once patients have achieved maximum therapeutic benefit, many can be maintained effectively on lower doses. Owing to the significant inter-individual variations in bioavailability (up to 50 times), complex metabolism and wide range of recommended oral dosages, in clinical practice the dosage of clozapine is usually guided by nomograms. These nomograms were developed many years ago to predict plasma levels of clozapine taking into account only two covariates, gender and smoking status. These nomograms' predictive values are associated with wide confidence intervals.[2] Hence, it is not surprising that the authors found significant variations in plasma clozapine levels (<0.1 to >1 mg/L). We are assuming that most patients were receiving the recommended dosages of clozapine.

Clozapine is associated with many significant adverse effects, and these are the most commonly cited reasons for discontinuation during the initial phase of treatment.[3] The most important adverse effects from the patients' perspectives are sedation, hypersalivation and constipation, and these are probably dose-related adverse effects.[3,4] Moreover, clozapine is the only evidence-based treatment for patients with treatment-resistant schizophrenia, and most patients will stay on it on a long-term basis; hence it is important that patients should be treated with the minimum effective dose.

The recommended plasma clozapine levels of 0.35–0.60 mg/L are for the management of active psychotic symptoms. The recommended plasma levels for maintenance treatment might be lower than the above range.[4]

The authors have highlighted concerns about high clozapine levels and their potential association with high mortality. Lower clozapine levels are also of concern, especially if a patient has partially responded to clozapine. Hence, there is now increasing support for the view that TDM should be used during the initial phase of clozapine treatment to achieve minimum therapeutic levels.[4] Subsequently, dosages can be optimised, based on the response and side-effects burden. At present, this is difficult as clozapine assays are done by selected centres in the UK, and it can take a few days to weeks to get the results. Even then, it will be prudent to obtain plasma clozapine levels soon after the titration. In the future, point-of-care testing for clozapine might make it easier to titrate the dose to achieve the minimum therapeutic level.[5]

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Declaration of interest

S.G. has received honorariums for lectures from Viatris, one of the marketing authorisation holders of clozapine.

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Author's Reply. RE: Routine clozapine assay monitoring to improve the management of treatment-resistant schizophrenia

I would very much like to thank Sumeet Gupta and Liyana Nur Mohamad for their supporting comments. Hopefully, there are many more like-minded clinicians who would also wish to see further developments in this area. The potential benefits to all involved are truly enormous.

Clozapine is a unique and usually efficacious treatment for a significant group of the mental health population with treatment-resistant schizophrenia (TRS). However, in my experience, it would seem that only a fraction of the people who fulfil the criteria for a diagnosis of TRS are actually considered for clozapine treatment. The reasoning for this under-treatment is multifactored, but the general theme of various safety concerns with regard to the longer-term management of clozapine is invariably foremost in clinicians minds.

The robust moves we have made to ensure that clozapine therapeutic drug monitoring is a significant facet of every patients care plan have allowed us to: (a) identify previously unknown clinical risk and manage it carefully; (b) build a data-set of results for each patient, which is a helpful tool for overall clinical assessment; (c) improve clinical outcomes and reduce mortality; (d) improve the confidence of clinicians, which has allowed them to be more agile with their prescribing of clozapine; and (e) support clinicians to feel encouraged to consider more patients for clozapine, which is reflected in our above-average recruitment of patients for treatment.