Research Article

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How Can Pharmacogenomics Be Used in UK Primary Care?

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Introduction

Pharmacogenomics is a part of precision medicine, a rapidly advancing field which enables healthcare to be tailored to the individual patient. Precision medicine has the potential to be a paradigm shift in the way healthcare is delivered, moving from a reactive model to a proactive and preventative one. Recent advances in genomics, big data analysis and artificial intelligence have enabled this to occur, but there are public concerns over data security and ethical and social implications too. Additionally, can pharmacogenomics be translated into routine UK primary care?

Definition

Precision medicine is a move away from a "one size fits all" approach in healthcare to one that is finely tuned to the individual. In simplest terms, it could be described as giving the right treatment to the right patient at the right time. Every individual is different and if their treatment could be tailored to their own individual characteristics, then the hope is that they would have more responsive preventative and therapeutic interventions, thus relieving the patients of unnecessary side effects and sparing healthcare systems from unintended costs. Precision medicine is more than "personalised medicine", which considers individuals' genetic make-up, but encompasses models of healthcare delivery relying on big data an analytics. It is certainly patient-centred looking at a genomic and molecular level but also vast as it integrates huge amounts of data into algorithms to enable predictive and preventative models to be developed. Thus precision medicine works on both micro and a macro level. NHS England have identified four "p"s of precision medicine [1]:

- Prediction (and prevention) of disease (thus moving from a reactive to a proactive model of care)
- More precise diagnoses,
- Personalised (targeted) interventions,
- Increased patient participation.

In the UK, the Royal College of Physicians and British Pharmacological Society produced a report [2] on "Personalised prescribing" and how pharmacogenomics can be used to improve patient outcomes. It defined pharmacogenomics quite simply as "…the study of how genes affect a person's response to drugs" and the speciality marries pharmacology (the science of drugs) to genomics (the science of genes and their functions). As the individual's genes rarely change throughout their lifetimes, pharmacogenomic testing, undertaken once, could be used throughout that person's lifetime to decide on the most effective drug for a particular condition, at the earliest opportunity. This would cause fewer side effects and would enable the clinician to also use the most effective dose. This could save the NHS £530 million annually in hospital admissions from adverse drug reactions. Pharmacogenomic testing is already a reality in UK secondary care for certain conditions and treatments, for example it is used in breast and colon cancer to ascertain if the drug 5-fluorouracil can be safely prescribed. It is however rarely used in primary care. This paper seeks to partly rectify this.

Method

In August 2019, Alconbury and Brampton Surgeries in Cambridgeshire commenced pharmacogenomic testing for patients already on antidepressants, to ascertain which ones would be most effective for them. Recruitment was completed by November 2019. The testing was undertaken by a GP, after appropriate consent was granted, using a cheek swab which was sent to an external laboratory for analysis. Results were received and conveyed to the patients within a week. Major alerts were placed on their electronic health records and results coded as active problems, using SNOMED codes. The wider healthcare team was also made aware of this quality improvement project through an educational meeting held at the practice.

The laboratory looked at two pathways in the cytochrome P450 system: CYP2C19 and CYP2D6. A report was produced which informed the GP if the patient was an extensive (normal) metaboliser of various common antidepressants, an intermediate metaboliser, a poor metaboliser or an ultra-rapid metaboliser. This was presented in an easy to understand green/amber/red traffic light system to guide the GP on which drugs were suitable or otherwise for the patient. The GP could then make the decision on whether to continue or discontinue the antidepressant that the patient was currently taking. The results were also re-evaluated at 4 years (in May 2023) to see if any changes were sustainable. The swabs and testing was paid for by a grant from the Eastern Academic Health Sciences Network.

Results

23 patients were recruited: 11 male and 12 female, all with a pre-existing diagnosis of depression and on anti-depressants prescribed in primary care. They were all of white European ancestry and the age range was 23 to 74 years. All results were received within a week from the laboratory and conveyed to the patient in the following week by the GP. All the patient records were then reviewed at 4 years. Of the 23 patients on the CYP2C19 pathway, 10 were extensive (normal) metabolisers, 8 intermediate metabolisers, 0 poor metabolisers and 5 ultra-rapid metabolisers. At one week review, all 5 ultra-rapid metabolisers had had their treatment changed by the GP and the rest were reassured they were on the right treatment. At four year review, 20 of the 23 original patients were still on the appropriate antidepressant treatment (2 patients had had their treatment discontinued as they were clinically better but 1 patient had been commenced on an inappropriate antidepressant treatment by a locum GP.) On the CYP2D6 pathway, 19 of the 23 patients were extensive (normal) metabolisers, 1 intermediate metaboliser, 2 poor metabolisers and 0 ultra-rapid. The remaining patient had an inconclusive result. At the one week review, the two patients who were poor metabolisers had had their treatment changed.

At the four year review, 19 out of the original 23 patients were still on appropriate treatment for their depression, but 2 had anti-depressant treatment that was inappropriate for their genetic make-up. The other two had had their treatment discontinued as they were clinically better.

Conclusion

As can be seen from the original results and the four year review, pharmacogenomic testing in primary care can work and can be integrated into routine patient care. Patients were readily recruited and the wider healthcare team was engaged. Results were easily transferred to the patient record and there were no concerns over data breaches. Results were sustainable at 4 years (95% of patients on the CYP2C19 were still on appropriate drugs and 90% of patients on the CYP2D6 pathway). However a small number of patients had their treatment inappropriately changed, which was done by locum GPs at the practice who were perhaps not aware of the research project. This point was mentioned at a whole practice meeting in June 2023 and those patients had their treatments then changed.

Future Work

The sample size was small at 23, so in future a much larger size would be beneficial, to make the study more powerful. Additionally, recruiting patients from more diverse ethnic backgrounds would also be beneficial and it would raise awareness of this important subject amongst other communities. The project benefited from a grant and as costs of testing can be prohibitive, to fully realise the potential of pharmacogenomic testing in primary care, costs need to come down.

References

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