Pharmacovigilance during the COVID-19 pandemic and beyond

Pharmacovigilance and adverse drug reactions

Pharmacovigilance is the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem. Although all medicines are required to undergo rigorous testing for safety and efficacy through clinical trials before they receive a marketing authorisation (licence), the full extent of their potential adverse effects cannot be known at that point. The clinical trials process generally involves a relatively small number of selected participants, studied over a relatively short period of time. Some rarer adverse drug reactions (ADRs, sometimes referred to as 'side-effects') may only emerge after medicines are used more widely among tens of thousands of people, who are less carefully selected and monitored, have other diseases, take potentially interacting drugs, and are exposed to the new medicine over a longer period.

The COVID-19 pandemic and vaccine development

The COVID-19 pandemic has forced us all to confront these issues head on. The impact of infection has put significant pressures on healthcare services by causing illness, hospitalisation and deaths. Over 150,000 people across the UK have died within 28 days of a positive test for COVID-19. Part of the response has been a major effort to develop and deploy effective COVID-19 vaccines around the world.

In the UK, a national immunisation campaign has been underway since early December 2020. Three COVID-19 vaccines (Pfizer/BioNTech, Oxford/AstraZeneca and Moderna) are currently used in the UK. All have been approved by the Medicines and Healthcare products Regulatory Agency (MHRA) following a thorough review of safety, quality and efficacy information from clinical trials. However, this was done under emergency or temporary authorisation (Regulation 174), after a much shorter than usual development and clinical programme.

In those pre-authorisation clinical trials, the vaccines showed high levels of protection against symptomatic infections with COVID-19. Subsequent 'real world' data confirmed the efficacy of the vaccines in preventing serious illness and hospitalisation during 2021. But what of safety?

Reviewing suspected adverse effects

Following emergency approval, it was recognised that an intensive pharmacovigilance process would be necessary. The pre-authorisation clinical trials in around 44,000, 23,000 and 30,000 volunteers respectively had demonstrated that some predictable vaccine side-effects were very common (injection site pain, fatigue, headache, muscle pains, chills,

joint pains, and fever). The key question was, would anything else emerge? Healthcare professionals and the public were urged to report adverse events suspected to be related to vaccination through a dedicated reporting portal. To date, around 48 million Pfizer/BioNTech, 46 million AstraZeneca and 3 million Moderna first or second vaccine doses have been administered. In addition around 36 million booster vaccinations have been administered. As of 12 January 2022, 158,933 Yellow Card reports have been reported for the Pfizer/BioNTech vaccine, 242,148 for the AstraZeneca vaccine and 33,630 for the Moderna vaccine (around 3.5 Yellow Cards per 1,000 doses administered). These data, including the nature of the adverse event, number of reports made and number of deaths have been continuously available and regularly updated on a dedicated MHRA website, openly available to scrutiny by all.

The data have been widely cited, debated and also misused. However, these discussions have provided us with the opportunity to disseminate some very important messages relevant to pharmacovigilance:

The safety profile of any new medicine (not just those approved under emergency authorisations) is never fully known at the point it is launched onto the market

Although the scientists and manufacturers have primary responsibility for the safety of medicinal products, everyone (including members of the public) has a role to play in that process by reporting suspected ADRs

It can be hard to distinguish adverse events occurring in association with medical treatment from spontaneous events that happen frequently in the population; a causal association only becomes clearer as more Yellow Cards reports are made ('signal generation').

The future

The profile of the MHRA as a body has been greatly increased during the pandemic, even if the comments have not always been supportive. Although the administration of nearly 136 million vaccine doses is impressive, it is important to remember that there are around a billion prescriptions issued every year in the UK for thousands of other medicines. These collectively result in around 30,000 reports annually.

The pandemic now offers a golden opportunity for those of us involved in the process of pharmacovigilance to harness the awareness of and enthusiasm for reporting suspected ADRs in the coming years. The value of the Yellow Card scheme reporting has been demonstrated on many occasions and has led to regulatory changes that enhance safety for patients.

If you read this and are inspired to contribute to the pharmacovigilance process, please consider reporting any suspected adverse drug reactions at

yellowcard.mhra.gov.uk or contact us at yccscotland.scot.nhs.uk.

Key messages

• Pharmacovigilance is the science relating to the detection and prevention of adverse drug reactions

• The safety profile of any new medicine is never fully known at the point it is launched onto the market • We all have an important role as healthcare professionals to participate in the pharmacovigilance process and encourage others to do so

• The Centre for Adverse Reactions to Drugs (CARDS)/YCCScotland is based in Edinburgh and is always happy to be contacted on questions about adverse reactions.

Professor Simon Maxwell, Medical Director, YCC Scotland and Consultant Physician