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Vigilant doctors ensure better vaccine safety

LEDER

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Newly developed COVID-19 vaccines are being widely administered. Spontaneous reports from doctors on suspected adverse reactions have rarely been more important.

Only a few days after the first international news reports of serious blood clots following vaccination with the AstraZeneca vaccine, several similar cases were reported in Norway (1, 2). Observant doctors reacted to unexpected and serious clinical pictures in recently vaccinated health workers who were otherwise in good health. The doctors reported these as possible adverse drug reactions (ADRs) via the melde.no webpage, and also contacted the Norwegian Medicines Agency directly.

Following a fatal case in Denmark involving blood clots, the Norwegian Institute of Public Health quickly decided to put use of the AstraZeneca vaccine in Norway on hold. This happened at the same time as news of the first fatality in Norway was announced (1). The pause in vaccination gave the authorities time to investigate the cases in Norway more thoroughly as well as an opportunity to gain a better overview of what had been reported in other countries. They also took part in the Pharmacovigilance Risk Assessment Committee's (PRAC) joint review of this new safety issue.

Spontaneous reports, i.e. reports of suspected ADRs observed in clinical practice, are crucial in monitoring patient safety when using medicines and vaccines. In Norway, we benefit from having healthcare professionals who take this task seriously and have a robust reporting culture. All spontaneously reported ADRs from EU/EEA countries are compiled in a common European database – EudraVigilance. Similarly, ADR reports from all over the world are entered into VigiBase, the WHO global database. In the weeks following the first reports of suspected adverse reactions in the form of blood clots combined with low blood platelets, several hundred such cases were reported to these databases (3). The spontaneous reports, together with the speedy contributions of clinicians and researchers (2, 4), constituted an adequate decision-making basis for taking regulatory action, i.e. the introduction of new precautions as well as descriptions of adverse reactions to the AstraZeneca vaccine, and later also to the Janssen vaccine. These steps were taken even though the underlying mechanisms are not yet fully understood.

In the course of a few weeks, we have acquired new knowledge of the condition now termed

vaccine-induced immune thrombotic thrombocytopenia (VITT) (2, 4, 5) or thrombosis with thrombocytopenia syndrome (TTS) (6). The condition is thought to be triggered by vaccination with two different viral vector-based vaccines, but the clinical picture is complex. It will take a long time to uncover the details. So far, the typical clinical picture seems to show thrombosis at unusual locations combined with thrombocytopenia. The condition has occurred in young, mainly healthy individuals with no obvious risk factors. So far, more women than men appear to be affected, and the majority are under 60 years of age. This observation must be interpreted with caution, since the AstraZeneca vaccine in the EU/EEA has mainly been administered to individuals under the age of 65, and to health personnel and teachers – professions in which there is a majority of women.

As yet, thrombosis with thrombocytopenia syndrome has only received a preliminary definition and it is still unclear whether there are different degrees of the condition – or if it forms a continuum. Unfortunately, some patients presented with a very severe, and even fatal clinical course. Since the syndrome has not been fully mapped, reports of adverse reactions with elements of the clinical picture, such as haemorrhaging and blood clots with or without low blood platelets, are of great value (7).

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Spontaneous reports from doctors in Norway have been largely instrumental in the speedy discovery of the association between the vaccine and the serious clinical picture. Adverse drug reactions should preferably be reported via the melde.no website. The more detailed the description of the event and related factors, the more valuable the report.

The drug regulatory authorities are responsible for monitoring the vaccines but are almost powerless when it comes to taking swift action if healthcare professionals are not observant and fail to report suspected ADRs. All spontaneous reports of ADRs end up in the Norwegian Adverse Drug Reaction Registry, which was recently established as a national health registry in line with others. As well as having a good reporting system, the health system in Norway is organised such that we can detect any accumulation of special cases such as thrombosis with thrombocytopenia syndrome more easily because these patients are mainly treated at a few, specialised units.

Think adverse reactions – report adverse reactions

The monitoring system is currently in a state of full alert during the COVID-19 vaccination programme, but the spontaneous reporting system is used for all medicines at all times. This ensures that the benefits of medicines in general use outweigh the risk, also in the long-term. Consequently, the challenge is to: Think adverse reactions – report adverse reactions! This applies especially when introducing new medicines, when dosage is increased or in relation to other changes in the medicines. The aim of the system is to detect new and unknown ADRs. This means that you cannot wait until you are sure of the causal association before reporting – you must report your suspicions immediately.

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