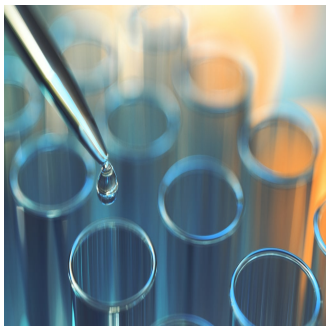
ICU
MANAGEMENT & PRACTICE

Life-Saving Effect of Dexamethasone in COVID-19



Dexamethasone is a life-saving treatment for severe COVID-19, though patients exhibit varied responses to the therapy. Researchers at the German Center for Neurodegenerative Diseases (DZNE) and Charité – Universitätsmedizin Berlin have uncovered how this cortisone compound influences the impaired inflammatory response and which patients benefit from it. Their method, utilising single-cell analyses, also shows promise for creating a precise prediction tool for other therapies and diseases. The findings are published in Cell.

Scientists have long wondered why certain drugs work well for some people but not for others. Researchers at DZNE and Charité — Universitätsmedizin Berlin have tested a method to uncover these underlying molecular mechanisms more precisely. They investigated the molecular effects of dexamethasone in patients with severe COVID-19, who responded differently to the treatment.

At the onset of the coronavirus pandemic, it became clear that the immune system of severely ill patients often overreacted to the virus. Dexamethasone, a cortisone derivative used to treat numerous diseases, was administered to influence the immune response. While many patients saw rapid improvement, others did not and sometimes worsened, leading to death. The current study reveals how dexamethasone works in effective cases.

Using single-cell analyses, the researchers discovered that a specific type of immune cell is responsible for the differing reactions. They also identified a way to predict early in the treatment whether it will be effective for a given patient. This approach could be useful for treating other diseases as well.

Study data show that the life-saving effect of dexamethasone is linked to the reaction of monocytes, a type of white blood cell and a central component of the immune system. Some monocytes responded to the treatment, but only in patients who improved and survived. Researchers studied blood samples from patients treated with dexamethasone at Charité early in the pandemic, revealing that the monocytes' reaction indicated the future course of therapy.

Why this reaction occurs in some patients and not others remains a mystery, though it's known that dexamethasone doesn't work equally well in all individuals.

In a 2020 study on the immune response in severe COVID-19 patients, the researchers identified a pathological monocyte "signature," a molecular fingerprint reflecting the characteristics of these immune cells. When effective, dexamethasone treatment reversed these changes. The monocytes' response precedes health improvement by several days. Treatment can be deemed effective if the immune cells respond early to dexamethasone. If not, additional medications may be required to help the patients.

The researchers elucidated these processes using single-cell sequencing, which allows individual characterisation of every single cell. Analysing cell signatures in such detail provides insights into the organism that was not possible just a few years ago.

According to the study authors, the significance of these results extends beyond COVID-19. Combining well-designed clinical trials with high-resolution molecular analysis can provide crucial insights into how medicines work. This approach could identify factors predicting response to therapy early in drug testing. In the future, this could speed up drug development and enable personalised therapies.

This research approach can also be used in infectious diseases where immune cells, easily accessible via blood samples, play a key role. It also has the potential for non-infectious diseases with systemic effects, such as cancer or Alzheimer's, which can be reflected in blood immune cells.

Source: DZNE - German Center for Neurodegenerative Diseases

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