Carbon dioxide (CO2) challenge test

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Challenge models that demonstrate relevant pharmacological effects of novel compounds can be valuable in the early clinical development of CNS drugs. Acute inhalation of carbon dioxide represents a validated, translational challenge for inducing panic symptoms in healthy volunteers and patients. The CO2 challenge test is used at CHDR to demonstrate panicolytic effects of novel anxiolytic drugs.

A safe, reliable and customisable instrument

We administer the CO2 challenge using the CO2 Tolerance Tester (CTT) from Maastricht Instruments, the engineering arm of Maastricht University Medical Center+, one of our academic partners. Coupled with fully integrated, tailor-made software, the CTT system enables safe and reliable intrapulmonary administration of a controlled gas mixture, combined with real-time monitoring of the physiological parameters associated with CO2-induced autonomic nervous system activation (such as heart rate and blood pressure). The gas mixture consists of 35% CO2 and 65% O2 and is administered through a protected inhalation system. Standard operating procedures (SOPs) guide the performance of the CO2 inhalation challenge. Our dedicated clinical and technical staff are highly trained in the application of this technique.

Proven value in clinical research

CHDR researchers have recently applied the CO2 inhalation challenge in a study[1] with a novel, CNS-penetrant, selective and high-affinity/potent orexin-1 receptor (OX1R) antagonist. In this study, CO2-sensitive healthy volunteers underwent a 35% CO2 inhalation challenge at steady-state plasma concentrations with two doses of the investigational compound, alprazolam as active comparator, or placebo. The investigational compound induced a statistically significant reduction of panic symptoms compared to placebo-treated subjects, as measured using the Panic Symptom List (PSL-IV). Panic symptoms were also reduced in alprazolam-treated subjects, demonstrating assay sensitivity. These findings show the value of the CO2 challenge for future early-phase studies with novel anxiolytics, as well as promoting further exploration of the efficacy of OX1R antagonists in relevant patient populations.

[1] https://chdr.nl/library/the-selective-orexin-1-receptor-inhibitor-jnj-61393215-decreases-subjective-anxiety-evoked-by-co2-inhalation-in-healthy-subjects/download

Why choose CHDR?

The Centre for Human Drug Research specialises in early-phase clinical drug research. CHDR's overall mission is to improve the drug development process by collecting as much information as possible regarding the candidate drug in the early phases of development. This information helps sponsors make informed decisions regarding the course of clinical development for their product.

Why choose CHDR?

Research at CHDR covers a wide range of fields, including the central nervous system (CNS) and pain, the cardiovascular system, haemostasis, immunology, and dermatology. In addition, CHDR is at the forefront in developing novel biomarkers and methods for measuring drug-related effects in all of these research areas.

Pharmacology matters

Whether studying a new cognitive-enhancing drug, a next-generation painkiller, or a new monoclonal antibody designed to treat rheumatoid arthritis, the goal is to determine how the compound's effects correlate with both the dose and blood concentration at any given moment. In addition, understanding which biological systems are activated is an essential first step towards quantifying this relationship. At CHDR, our focus on pharmacology is reflected clearly in what we call question-based drug development.

Question-based drug development

CHDR actively uses question-based drug development - or QBD - as a more rational approach to drug development compared to conventional approaches. QBD can be best described as a series of questions that are addressed throughout the process. These questions often seem simple enough, but failing to answer even one question - or even addressing the questions in the wrong order - can have dire consequences. Thus, using this approach can potentially save companies millions of dollars by helping predict a catastrophic issue early in the development process, before the more expensive latter stages (for example, large-scale clinical trials or the marketing phase).

From a general perspective, the most important questions are:

1. Does the biologically active compound and/or active metabolite(s) reach the intended site of action?
2. Does the compound cause its intended pharmacological and/or functional effect(s)?
3. Does the compound cause any unintended pharmacological and/or functional effect(s)?
4. Does the compound have a beneficial effect on the disease and/or clinical pathophysiology?
5. What is the compound's therapeutic window?
6. How does any variability with respect to the drug response in the target population affect the product's development?

Contact

To learn about CHDR's full range of services, contact us today.

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