Homeopathic Drug Provings

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Homeopathic drug provings (HDPs) are a clinical research tool unique to homeopathy. They are used to gather qualitative information on the use of homeopathic medication in healthy subjects. This in turn guides prescribing with patients. HDPs offer a scientific method for new drug discovery, form part of the evidence base for homeopathy, and are sometimes compared with Phase I trials in conventional medicine. During the last 30 years, there has been a steady evolution in the scientific methodology used to conduct HDPs. It has been formalized by a number of organizations, including the Homoeopathic Pharmacopoeia Convention of the United States (HPCUS), the European Committee for Homeopathy (ECH), and the Liga Medicorum Homoeopathica Internationalis (LMHI). These organizations, independently and in joint meetings with experts, have created formal guidelines for HDPs aligned with the scientific recommendation for good clinical practice (GCP) and health research reporting guidelines. Contemporary HDP guidelines cover a variety of protocol-driven research parameters, including clinical trial design, investigator qualifications and training, the handling of the investigational proving substance, data collection and analysis, safety assurances and adverse events, legal concerns and ethics.

Protocol approval by an Ethics Commission (EC) or Institutional Review Board (IRB) is encouraged using protocols aligned with the principles outlined in the *Guideline for Good Clinical Practice (E6)* issued by The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) (2016). The ICH "*is unique in bringing together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of drug registration*." Further, ICH strives *"to respond to the increasingly global face of drug development"* and "*to ensure that safe, effective, and high quality medicines are developed and registered in the most resource-efficient manner*." IRB-/EC-approved HDP protocols address the distinction between mild and transient proving symptoms that are specific to homeopathy and adverse event reporting in clinical trials.

Homeopathic drug provings provide information on the symptoms associated with the use of homeopathic medications in healthy people that guide their prescribing to patients. In turn, the use of homeopathic medications is further clarified through clinical research (Mathie et al. 2013) and clinical practice.

The HDP results presented in this Materia Medica were conducted with IRB-/EC-approved protocols, explicitly followed GCP guidelines, and predetermined homeopathic symptom selection criteria. Subjects participating in an HDP ex-

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1

perience a range of mild, temporary symptoms that are a key component in establishing a symptom picture for that homeopathic medication. The quality and range of symptoms are often not known prior to the HDP. The symptoms experienced in an HDP are organized into a pattern to facilitate evaluation by regulatory authorities and use by clinicians.

In the *Organon of Medicine* (1983), Hahnemann emphasized that an HDP was essential in determining the effects of a substance on the human being to "*correctly ascertaining the characteristic action of medicines on human health […] [through] administering individual medicines experimentally to healthy people in moderate doses in order to ascertaining what changes, symptoms, and effects each in particular brings about in the body and the psyche*" [§108]. The *Organon* provides additional scientific directions on the methodology of an HDP [§§105–145].

The Similarity (Similia) Principle in homeopathy hypothesizes that homeopathic substances capable of causing symptoms in healthy subjects, can be used as medicines to treat similar patterns of symptoms experienced by patients when they are ill—there are examples of this in conventional medicine as well such as allergy desensitization therapy. Recognizing the symptoms of an individual when they are sick and matching those symptoms with the symptom pattern from an HDP, forms part of the foundation of homeopathy.

Proving symptoms are defined as those changes of the mental, emotional, or physical state of the subject that are associated with the administration of the homeopathic medication and are patterns of reaction not noted for the subject during the pre-proving observational period. Proving symptoms are generally temporary symptoms, lasting for several hours or days. In an HDP, symptoms recorded by the subjects may become components of the homeopathic symptom picture for that homeopathic medicinal product and are selected according to symptom selection criteria outlined in the protocol.

The HDPs reported in this Materia Medica lasted on average six weeks per subject. The medications were prepared in either a 12C, a 24X, a 30X , or—in one case (Ubichinonum)—a 30C potency and administered three times daily until the subjects developed symptoms, up to a maximum of seven days. No homeopathic proving medications were taken after a subject began to experience symptoms. During the post-administration, or observation phase, the provers continued with their self-observations and journaling, with the support of their assigned supervisor, for a duration of approximately four weeks. After an additional six-week follow-up period, the prover and supervisor had a so-called exit meeting to discuss the prover's proving experience. In a case where a prover was still experiencing ongoing symptoms, the supervisor continued to follow up the prover until he or she was back to their normal state of health. Scientific research methods were incorporated into the protocols to reduce bias and increase transparency. The medications used in these provings were either verum or placebo, given to subjects according to a computer-generated randomized code, unknown to the investigators until the blind was broken at the HDP's conclusion. Placebo controls ensured that neither the subjects nor the investigator knew which subject was receiving verum or placebo while the HDP was ongoing. All subjects who participated in these

HDPs were recruited via advertisements, selected using inclusion and exclusion criteria, and signed an informed consent approved by an IRB or EC.

The central investigational tool of these HDPs was a journal kept by each subject throughout the proving, beginning with the pre-proving observation period through to the end of the study. The subjects described the baseline rhythm of their life during the pre-proving observation phase and then went on to record the symptoms associated with the administration of the homeopathic preparation. The subjects met regularly with their supervisor during the HDP to review their journals and their reported symptoms.

Other groups have developed scientific recommendations for HDPs recommendations, particularly in the areas of blinding and controls, adverse events, and risk of bias (Higgins et al. 2019; Sterne et al. 2019; Teut et al. 2010; HPCUS 2015). Homeopathic recommendations for HDPs incorporated most of these recommendations. We believe that the HDPs in this Materia Medica address some of the methodological concerns regarding historical HDPs and form the basis for a more accurate and transparent role for homeopathy in healthcare.

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