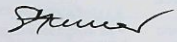
The Challenge and Future of Clinical Research in Orofacial Pain

After holding the position of Associate Editor for 1 year, it seemed to me that offering some perspectives on the future of clinical research in orofacial pain would be a good idea. Enormous achievements in the treatment of acute illness have been witnessed in the past decades. However, it has become increasingly clear that many breakthrough interventions for acute illness have either no value or only limited value in the treatment of chronic diseases. This unmet healthcare need of subjects with chronic disabling diseases forms the basis for much needed research. Chronic orofacial pain conditions are no exception in this regard.

Careful observation and systematic evaluation of human material is essential to the understanding of disease phenomena or treatment effects. Clinical research, as defined by the United States National Institutes of Health, consists of all biomedical and behavioral research that involves human subjects in which an investigator obtains data through intervention or interaction with the individuals or uses identifiable, private information. This includes all research that involves the use of human organs, tissues, and body fluids from living individuals, as well as graphic, written, or recorded information that is derived from living individuals. Essential to any meritorious clinical project are a logical study design, an appropriate case definition and study sample, and the employment of valid, reliable clinical measurements. Diagnostic tests should be reproducible, with limited variability attributable to the assessor or data handling process. The number of potential confounding factors should be restricted, or controlled in the study design by the randomization of subjects. Known obstacles to quality clinical research include rigid belief systems, which tend to limit the scope of an investigation, and insufficient validity of diagnostic criteria and great observer variation, which invite the erroneous interpretation of findings. While the shortcomings and pitfalls of clinical research are increasingly understood, methodologic questions often arise in the planning of trials for which a scientifically correct answer is simply not available. Only after essential pilot work on matters of study design will it be possible to launch the full-scale clinical trials that are expected to produce definitive knowledge of disease etiology and intervention.

While understanding of the common physical, psychologic, social, and economic aspects of patients with orofacial pain defines the personal and societal significance of the problem at hand, the underlying disease mechanisms will likely not be discovered by this kind of descriptive research. For persistent orofacial pain conditions, the etiology remains unknown and attempts to identify a single cause or group of causes have been unsuccessful. Rather than emphasizing common features, there is a great need to define the dissimilarity of cases that have been assigned a particular diagnostic label. Only through better understanding of phenotypic case heterogeneity will it be possible to assemble more homogenous study samples that are likely to have similar underlying disease mechanisms. As exemplified by the recent success stories of research into the genetic basis of disease, homogenous populations exhibit stronger associations with factors of interest than a phenotypically polymorphic study sample.

Once these mostly methodologic challenges have been overcome, clinical research is expected to enter its brightest period ever. Influenced by advances in cellular and molecular biology and biotechnology, novel models of disease are expected to impact both trial design and the manner in which research will be performed. The inclusion of relevant basic science expertise will be critical to the successful execution of future clinical trials. By adopting an ecogenetic concept of disease with the formulation of multifactorial models of genetic-environmental interaction, broadly defined conditions will be viewed as consisting of subtypes that have different genetic or environmental causes. Questions of genetic susceptibility and causative agents will be explored even in diseases that do not constitute uncommon chromosomal and single gene disorders. The subset of patients that exhibit catastrophic failure of alloplastic temporomandibular joint implants comes to mind as an example of a promising study target. The next generation of clinical research is likely to impact clinical matters in ways that will revolutionize both understanding and care in the field of orofacial pain.



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