EDITORIAL

Return of the Troglodyte?

Every few years, I find myself writing an editorial in which I question reviewers' ongoing demands for randomized controlled clinical trials (RCTs) in implant dentistry. Usually this occurs after I attend a conference in which systematic reviews were performed in an effort to promote clinical recommendations based on those reviews. Currently, it seems that the only studies that are routinely accepted in these reviews are RCTs; other study designs are usually undervalued or are considered as fundamentally inferior to the RCT. As a journal editor, I am increasingly concerned that the RCT is often not the most appropriate design for some studies and may even lead to misrepresentation of the truth.

Readers may wonder why anyone would question the value of the RCT. Indeed, the RCT is often described as the best study design for clinical research primarily because it is one that may reduce research bias. Since many researchers consider bias to be the greatest threat to the identification of truth, the RCT has been elevated in the minds of many to the pinnacle of the research mountain.

If the aim is to reduce bias, then why would I question the use of the RCT? One reason is that it is possible to design studies using this method that are fundamentally biased. Said another way, if a research team wants to prove a point, there are ways to manipulate the materials and methods to ensure desired study results.

Perhaps an example is in order. Let's imagine that a new drug is introduced into the marketplace to address juvenile acne. The new product, Pimploff, poses a risk to the current market leader, Zitaway. To address this situation head on, the makers of Zitaway have decided to sponsor an RCT to demonstrate that Pimploff has no therapeutic advantage over Zitaway.

However, the study is designed to ensure that readers do not see it as nothing more than the marketing ploy that it clearly is.

The study will have inclusion criteria of healthy patients aged 13 to 60 years of either sex to be randomly assigned to either study arm based on a coin flip. In each study arm, 20 patients will apply the selected dermatologic cream to the right arm once daily at bedtime for 7 days; the performance of the drugs will be assessed over the 7 days of the study with no long-term follow-up.

The blinded results of the study indicate positive performance for each medication with the primary treatment outcome being the absence of juvenile acne lesions in the area of medication application. The two treatment groups identified in the scientific publication were statistically equivalent. In the control group, there were 12 female patients and 8 males with a mean age of 26.2 years with a standard deviation of 11.4 years. The test (Pimploff) group had 8 female patients and 12 males with a mean age of 29.6 years (SD 10.6 years). There were no statistically significant differences in age, sex, or primary treatment outcome. The results of this study were published in abstract form and were distributed to the sales representatives of Zitaway, who then provided brochures citing the study outcome, which hailed the equivalent performance of Zitaway to the far more expensive newcomer, Pimploff.

The errors in this imaginary study should be obvious. First, the study group is not representative of the population afflicted with juvenile acne since the age range extended well beyond the description of "juvenile." Second, the location of administration of the drug was inappropriate, since the right forearm is not a common site for juvenile acne. Third, the study duration is insufficient given the chronic nature of the disease. Fourth, the study population (study number) is inadequate given the incidence and risks associated with this dermatologic disorder.

Some readers will argue that this sort of study would never be conducted, yet careful perusal of the dental implant literature will reveal some equally egregious study designs. We have to understand that comparative studies that involve a surgical procedure with a device that may be dramatically different from another device in macro- and microstructure, and may have entirely different surgical demands, are subject to tremendous variability even if the study design is idealized. When treatment involves a specific intervention that may demand technical skills, it is critical to understand that skills are not equal for all clinicians or for all procedures (inter- or intraclinician reliability). The ability to differentiate skill-dependent outcomes from a physical response to the intervention may be difficult or impossible.

When I previously wrote an editorial questioning the value of the RCT design for dental implant studies, I questioned whether this made me a knuckle-dragging troglodyte. Today, I am pleased to say that others in the scientific community are raising similar questions. Sample size and appropriate study duration are obvious concerns, but the Agency for Healthcare Research and Quality (AHRQ) division of the US Department of Health and Human Services has also identified issues of consistency, precision, and directness of results (www.effectivehealthcare.ahrq.gov). Bias alone may not be sufficient justification for the use of one study design in preference to all others; other factors as identified by AHRQ also have an influence on the outcomes of research.

Indeed, clinical intervention studies are difficult to randomize. It is critical to understand that the skills of the clinicians administering both treatment arms may be dissimilar based on experience with one intervention or a lack of experience with the other.

If the two treatment arms are thought to be similar, establishing a meaningful sample size may also be difficult and costly. When outcomes are expected to be favorable but slightly different for control and test, sample sizes may need to be quite large if differences are to be identified. Likewise, if adverse results are not seen until many years have passed, the study design must extend beyond this time frame, making them prohibitively expensive.

For these reasons, the RCT cannot be considered the only study design for clinical research in implant dentistry. Although we should always call for the best research possible, the RCT may not be the design that is most appropriate in all clinical settings.

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