Arquivos Brasileiros de
Oftalmologia

EDITORIAL

Blinding or Masking: which is more suitable for eye research?

Cegamento ou Mascaramento: qual o mais adequado para pesquisa oftalmológica?

Rosália Antunes-Foschini[1], Monica Alves[2], Jayter Silva Paula[3]

1. Department of Ophthalmology, Otorrhinolaryngology and Head and Neck Surgery, Hospital das Clínicas, Universidade de São Paulo, Ribeirão Preto, SP, Brazil.

2. Department of Ophthalmology and Otorrhinolaryngology, Faculty of Medical Sciences, Universidade de Campinas, Campinas, SP, Brazil.

3. Department of Ophthalmology, Otorrhinolaryngology and Head and Neck Surgery, Ribeirão Preto Medical School, Universidade de São Paulo, Ribeirão Preto, SP, Brazil.

When planning and executing a clinical study, all sources of bias should be minimized, from the project's propositions to the written conclusions after the observations. In clinical researching scenarios, "blinding" involves approaches used to reduce bias after the randomization process. Not only the patients, but all subjects involved in the research may be kept unaware of the treatment group in which patients are allocated[1,2]. An investigation on "mesmerism" was one of the earliest experiments using "blinding". A commission that included Benjamin Franklin, appointed by Louis XVI in 1784, assessed the real healing effects of this method. Their placebo controlled blind trials proved that the Mesmer's universal fluid could not cure people and that imagination and imitation were the real causes of the observed effects [3].

Randomization minimizes differences between treatment groups, but it does not prevent differential group and outcome assessments, resulting in potential biased estimations of treatment effects; and, hence, biased results and conclusions. Thus, an optimal strategy to minimize bias is to blind as many individuals as possible who are working in a trial[4]. It is important to point that allocation concealment differs from "blinding"; the first eliminates selection bias during the process of recruitment and randomization, whereas "blinding" intends to reduce performance and ascertainment bias after randomization[5].

When a clinical study is not blinded, some threats may influence the internal validity of the trial, such as: changes in the patient's compliance, increased dropouts (especially when the patient knows his/her allocation in the control group), loss of the placebo effect (usually in the control group), co-intervention (patients from the control group seek adjunct treatments to minimize the lack of perceived treatment success), influence on the side effects and efficacy reports of the outcomes, partiality in the evaluation of the outcome of interest, favoring one of the groups (the observers' behaviors are influenced by their belief), unequal care provisions from the staff, and increasing the study's subjectivity[2].

"Blinding" can be applied to people involved in different research processes. The most important levels of "blinding" are: a) Simple - the participants (allocated to the treatment); b) Double – the participants and the investigators (the professionals who provide the intervention); c) Triple – participants, investigators and other people involved in data collection, data analysis, financing, and manuscript writing[2]

The process of "blinding" must consider that both interventions cannot be distinguishable by blinded individuals. For example, in the case of eye drops, the bottle's format and color, appearance of the solution, frequency of instillation, and ocular sensation should ideally be the same. In the case of tablets, weight, odor, and touch should also be considered. Concerning the side effects, some of them should also be present on the placebo group (in this cases the placebo group is known

Submitted for publication: January 22, 2019
Accepted for publication: February 6, 2019

Funding: No specific financial support was available for this study.

Disclosure of potential conflicts of interest: None of the authors have any potential conflicts of interest to disclose.

Corresponding author: Rosalia Antunes-Foschini.

Departamento de Oftalmologia, Otorrinolaringologia e Cirurgia de Cabeça e Pescoço - Universidade de São Paulo. Av. Bandeirantes, 3.900 - Ribeirão Preto - SP 14049-900 - Brazil E-mail: antunesfoschini@gmail.com

as active placebo). The route of administration must also be considered. If the interventions being compared have different routes of administration, or if a new drug will be compared with a standard treatment already in use, a double dummy design[6], in which one drug and one placebo for each group exist, should be applied. Although all described precautions should be taken to promote "blinding", they need to be uncovered in some trials with robust inadvertent results or new highly advantageous treatment options[7]. In rehabilitation trials, in which the outcomes are measured using subjectivity, such as quality of life or pain level, the blinding process is particularly ineffective. That is why objective outcomes are always preferred. Indeed, randomized controlled trials of surgical interventions are frequently more difficult to blind than trials using medications. It may be possible for researchers to blind other members of the treatment team; and, thus, limit the potential for differential treatment. As no analytical techniques can correct a drawback due to treatment selection or assessment of outcomes and results from unblinded trials, they need to be interpreted with caution[5]. Besides, researches should be aware of some disadvantages of the blinding process, including increased costs, the need for more researchers involved, ethical and logistic issues, and the fact that the study may not reflect a real health care approach in specific trials.

The use of the "masked" approach as an alternative to "blinded" one in ophthalmology may be considered "far too precious" to non-ophthalmologists, as pointed out Morris and Fraser[8]. However, those authors justify its use with a scenario in which an elderly woman with age-related macular degeneration, invited to a double-blinded macular study, may be terrified and withdraw the trial due to the "chance of becoming blind" related to the experiment. Thus, in eye studies, some researchers prefer the term "masked" to "blinded," to avoid a term that denotes one of the potential, unfortunate outcomes in an ophthalmic trial. Schulz et al.[4] argued that the inappropriate use of the "blinding" terminology in ophthalmological settings should not dictate the use of the term "masking" for all other randomized trials.

Finally, "blinding" must be considered one of the hallmarks of methodological quality and is largely encouraged in clinical trials. Researchers are encouraged to inform the "blinding" status of the whole team involved in the trial, complying with the CONSORT recommendations[1], when practically and ethically possible.

REFERENCES

1. Moher D, Hopewell S, Schulz KF, Montori V, Gøtzsche PC, Devereaux PJ, Elbourne D, Egger M, Altman DG; Consolidated Standards of Reporting Trials Group. CONSORT 2010 Explanation and Elaboration: Updated guidelines for reporting parallel group randomised trials. J Clin Epidemiol. 2010;63(8):e1-37. Erratum in: J Clin Epidemiol. 2012;65(3):351.
2. Fregni F, Illigens BM, editors. Critical thinking in clinical research: applied theory and practice using case studies. New York: Oxford University Press; 2018.
3. Best M, Neuhauser D, Slavin L. Evaluating mesmerism, Paris, 1784: the controversy over the blinded placebo controlled trials has not stopped. Qual Saf Health Care. 2003;12(3):232-3.
4. Schulz KF, Altman DG, Moher D. Blinding is better than masking. BMJ. 2007;334(7600):918.
5. Schulz KF, Grimes DA. Blinding in randomised trials: hiding who got what. Lancet. 2002;359(9307):696-700. Comment in: Lancet. 2002;360(9328):259.
6. Forder PM, Gebski VJ, Keech AC. Allocation concealment and blinding: when ignorance is bliss. Med J Aust. 2005;182(2):87-9. Comment in: Med J Aust. 2005;183(3):165; author reply 166.
7. Park J, Bang H, Canette I. Blinding in clinical trials, time to do it better. Complement Ther Med. 2008;16(3):121-3.
8. Morris D, Fraser S. Masking is better than blinding. BMJ. 2007; 334:799. doi: https://doi.org/10.1136/bmj.39175.503299.94