SÃO PAULO MEDICAL JOURNAL

EDITORIAL

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Methodologies to assess moderate therapeutic effects

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How to assess moderate effects of medical treatment? Suppose that a preventive type of treatment for cardiovascular death would be able to reduce 20% of such an outcome. Let us assume that the expected incidence of death due to cardiovascular disease is 10% per year.

If 1,000 cases were properly randomized and 100% of them were followed up, the expected deaths in the control group would be 50 (10% of 500) and the incidence in the treated group would be around 40 deaths (20% risk reduction). In this situation, results may be attributed to chance ($P > 0.05$). In order to detect an actual difference, or in other words, to have the statistical power to detect such a difference, it would be necessary to study thousands of patients. Conducting a clinical trial like this requires collaborative multicenter research, trained personnel and extensive funding. However such a task is possible, and we do have good examples like the ISIS-2 studies — The Second International Study of Infarct Survival. The ISIS-2 study has included 17,187 cases of suspected acute myocardial infarction showing odds reduction of 25% in mortality by using low doses of aspirin.

There is still another method of assessing the moderate effects of treatment assuming that some clinical trials have already been carried out, published or not, that can be studied through a systematic review. With this method, all the randomized clinical trials performed on a subject will be searched out worldwide, and the results will be put together (after excluding the ones not considered properly designed or conducted).

I would refer the interested reader to three publications of the Antiplatelets Trialists' Collaboration (1) — the "Aspirin Papers" in the British Medical Journal.

The first publication is a masterpiece of systematic review and has a very clear explanation of the methodology and the statistical treatment applied to the development of these systematic reviews. Again it was a collaborative enterprise (ATC) and the results show an important reduction of cardiovascular events, cardiovascular death and deaths in general when antiplatelet therapy is preventively administered to high-risk patients. The authors considered high-risk the patients with a history of myocardial infarction, stroke or transient ischemic attack, or a mixed category of increased risks of vascular events that included diabetes and renal diseases. The benefit of this treatment was not observed in the low-risk group.

Through this review, which took many years of effort and required more goodwill than funding, an important question was eventually answered and medical practice improved.

Simple and large clinical trials — provided that they are well designed and conducted — and systematic reviews, are two types of collaborative studies that are appropriate to assess the moderate effects of treatment which may have a high clinical significance.

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