CORRESPONDENCE


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Required Sample Size for Randomized Clinical Trials

To the Editor—The recent article by Darmon et al.,1 concerning the evaluation of risk factors for laryngeal edema (LE) after tracheal intubation in adults and the proposed preventative role of dexmedetomidine, raises a number of interesting points.

The authors concluded that the overall incidence of LE was "not different between patients given dexmedetomidine and those given placebo." Furthermore, dexmedetomidine appeared to be no more effective than placebo in preventing reintubation due to LE. These conclusions were qualified, in part, by the following statement: "Assuming an incidence of LE in each group similar to that found in our study, more than 7,000 patients would need to be studied to evaluate adequately the presence of a type II error."

Unfortunately these statements raise more questions than answers: Are the authors suggesting that an inadequate number of patients (700) were included in the original study design? How was the sample size calculated at the planning stage and what assumptions were made for this calculation? It is inadequate to merely indicate that, in retrospect, the study should have included a far greater number of patients. Furthermore, it is inconceivable that a major, multicenter, clinical investigation chose to study 700 patients without good reason. A recent abstract by Villeneuve et al.2 and an earlier article by Freiman et al.3 both emphasize the importance of statistical power and sample size in the design and interpretation of studies where no statistically significant effect could be detected.

The probability of a type II error (beta) is likely to be large in the present study of 700 patients. The authors suggest a value for beta > 0.49, which is unacceptable and entirely predictable given the conceivable incidence of LE. A sample size with sufficient power to ensure a reasonable probability of achieving a statistically significant result could have been calculated at the planning stage, using methods described in standard statistical textbooks.4,5 Assumptions must be made concerning both the incidence of LE (derived either from a pilot study or previous comparable investigations) and the desired clinical effect (for example, a reduction in the incidence of LE between the two groups that was believed to be clinically significant by the investigators). A comparison of confidence intervals for the dexmedetomidine and placebo groups, although useful, does not answer the question concerning the initial calculation of sample size.

The relationships between sample size, statistical significance, and clinical significance are clearly important in the interpretation of data. Differences of no real clinical interest can be statistically significant with large samples, whereas clinically important effects may not be significant when the sample size is small.6 It is therefore equally important to estimate the required sample size. To quote B. R. Kirkwood: "An essential part of planning any investigation is to decide how many people need to be studied in order to answer the study objectives. Too often the number is just pulled out of a hat, or decided on purely logistic grounds. This is bad practice, and considered by many to be unethical."

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