

Letters to the Editor

Cis-platinum ototoxicity and eye colour

Dear Sir,

We felt it essential to point out some basic errors in the analysis and presentation of this paper. The authors have taken multiple observations on some but not all subjects depending on the treatment regime, and this leads to an unbalanced repeated measures design. Such studies are extremely complex to analyse, but it is incorrect to use statistical tests which assume independent observations. The data in Fig. 2 are unsuitable for a linear regression as this would assume degrees of freedom based on 34 observations whereas there are only 16 patients and, therefore, can only be 16 independent observations. In addition the regression procedure (which we assume to be parametric in the absence of further information) requires at least interval scales for the variables, and there is no evidence that eye colour meets this requirement. Wilcoxon's test is designed for use with independent samples and, therefore, cannot be used on this data either.

Taking repeated measurements from the same individuals means that observations are dependent on each other. When such data is then analysed using statistical tests designed for independent samples, this greatly increases the chance of spuriously finding an apparently significant result. Analysis of this study would be complex as different numbers of observations were made on different patients, and the intervals and number of cycles of chemotherapy varied between observations. In addition to this, the number of patients in each eye colour group, though not quoted by the authors, is obviously very small. The title to Fig. 1 claims 22 observations between the start of treatment and the first test. This is impossible as there were only 16 patients.

This paper cannot support the conclusions drawn because of fundamental defects in the presentation and analysis of the results.

Yours faithfully,

Iain R. C. Swan, M.D., F.R.C.S.,
Consultant Otologist

Stuart Gatehouse, Ph.D.,
Scientist-in-Charge

MRC Institute of Hearing Research,
Glasgow Royal Infirmary,
Glasgow G31 2ER.

Reference

Barr-Hamilton, R. M., Matheson, L. M., Keay, D. G. 1991.
Journal of Laryngology and Otology, **105**: 7-11

Reply

Dear Sir,

The dangers of an unbalanced design with repeated measures are of course well known, and melanin content can certainly be regarded as a variable quantity, although its estimation by eye colour is undoubtedly crude. To satisfy Swan and Gatehouse, however, let us simply reduce the data to a single number for each subject to indicate degree of damage induced: the shift in threshold (average of 4 and 8 kHz of left and right) per dose administered. The difference between the brown-eyed and non-brown-eyed groups is significant at the 5% level on Mann & Whitney's modification of Wilcoxon's sum of ranks test.

The purpose of our paper was to present the hypothesis that susceptibility to damage from this oto-toxic drug might be predictable from eye colour. As stated in our discussion, we believe that the preliminary results do justify the performance of a larger study; the finding, if confirmed, stands to be of considerable interest and practicable benefit. To miss the wood for the trees is always regrettable, and I hope that quibbles about statistical significance do not obscure the potential clinical importance of this original study.

Yours faithfully,

R. M. Barr-Hamilton.