Reviewer's report

Title: A Randomized, Placebo Controlled, Trial of Preoperative Sustained Release Betamethasone Plus Non-Controlled Intraoperative Ketorolac or Fentanyl on Pain After Diagnostic Laparoscopy or Laparoscopic Tubal Ligation

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Reviewer: John M Hughes
Level of interest: not specified
Advice on publication: Other (see below)

Compulsory Revisions:

The many analyses that the authors perform must be greatly simplified. Within group analyses are not relevant because the stated aim of this study is a comparison between groups randomised to betamethasone or placebo. Thus the analyses presented in Tables 2 and 3 should not be performed and the model proposed below will perform a simplified analysis of the data presented in Figures 1 to 3.

What is needed but conspicuous by its absence is a statement of what is the clinically important difference in pain score. Without this any analysis is meaningless because recruiting more patients can make the p-values significant as the standard error becomes smaller.

The main difficulty with the authors? method arises because they attempt to analyse all the serial measurements that were taken on their patients. Several reasons are given in reference (1) why this approach is wrong. The most important of these is that the measurements at each time point are from the same individual. The problem with their independent t-tests is that they cannot take account of the other pain affecting factors so it is impossible to attribute any differences in pain score only to the factor analysed with each of these tests.

The authors need to develop a general linear model (2) of the form:

\[ y = a + b1.x1 + b2.x2 + b3.x3 \ldots + e \]

where \( y \) is a summary of the pain measurements and the \( x \)s are explanatory variables and the \( b \)s their coefficients. A number of measures could be used to summarise the pain score, including the AUC, but the mean of the measurements may be the most appropriate because this preserves the
original measurement scale. The measurement at discharge was taken at varying times and it is possible that patients may have self medicated with their own analgesic in addition to prescribed analgesics at 24 hours so it may be better if these two time points are not used.

The explanatory variables that the authors have analysed include pre-operative pain score, type of operation, intra-operative and post-operative pain relieving drugs. It is for them to decide which variables are relevant to pain score and how they are to be entered into the model. Post operative pain relief could for example be entered Yes/No or preferably by the number of units taken during the assessment period. However it seems unlikely that the number of doses was normally distributed as they claim since the distribution must be positively skewed with a mean of 5 but a range of 0 to 17. A transformation may be required though the analysis suggested is reasonably robust to departures from normality.

The most important feature of the model given above is that it allows calculation of the difference in pain score between groups, adjusted for the other variables, and their confidence limits which will be far more informative than p-values. The regression coefficient will show the significance of continuous variables in the model. Both differences, coefficients and their confidence intervals should be presented in one table which will succinctly summarise the results of the analysis reducing the bewildering number of tests performed by the authors who made no adjustment in p-value for multiple testing.

The use of correlations of either type will not now be needed, if they ever were, except that the square of r, the product-moment correlation coefficient gives the percentage of variability explained by their model. This is produced routinely by most statistical software.

The patient disposition presented in Table 1 must include the number randomised to each treatment group, N, and the number, n, used to calculate the statistic. At present the number randomised only appears in the text. The same paragraph also incorrectly states that patients were randomly assigned to "betamethasone treatment (BM) and placebo (P)" instead of "betamethasone treatment (BM) or placebo (P)". It is also usual to present the minimum, maximum, median and standard deviation. The standard error can be derived from the standard deviation when the number in each group is given. This is not necessarily the same for all groups as illustrated by Tables 2 and 3 both of which have inexplicably small N bearing in mind that 66 patients were randomised, 31 to betamethasone and 35 to placebo.

Discretionary Revision:

There is no reason to perform the t-tests on patient characteristics in Table 1. This is just testing the randomisation which at the 5% level will be significant 5% of the time.

The reason for stopping data collection for eight patients is unclear. Did they or their surgeon become aware of their randomisation. In the latter case was this a reason for their withdrawal? Did it disqualify them from the intention-to-treat population? Was an analysis population defined?

Despite the numerous criticisms given above the analysis described should be straight forward to perform and will produce easily interpretable results showing if there are differences in pain scores between treatment groups. It is encouraging to see that both the authors and editor considered a paper with largely non-significant results suitable for publication which helps to reverse the usual reporting bias.

**Competing interests:**

None declared.