Reviewer’s report

Title: Use of Neuroleptics in a General Hospital

Authors:

raquel barba (rbarba@fhalcorcon.es)
javier bilbao (jbilbao@fhalcorcon.es)
helena martin-alvarez (hmartin@fhalcorcon.es)
carlos guijarro (cguijarro@fhalcorcon.es)
virgilio castilla (vcastilla@fhalcorcon.es)
isabel gonzalez-angiada (igonzalez@fhalcorcon.es)

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Reviewer: Dr Marek Brabec

Level of interest: A paper whose findings are important to those with closely related research interests

Advice on publication: Unable to decide on acceptance or rejection until the authors have responded to the compulsory revisions

The authors should be applauded for trying to draw attention to a practically important problem of neuroleptics use (or almost abuse, indeed) in a general hospital setting. Intrinsic nature of the problem together with the fact that it is set in routine hospital practice environment makes any assessment difficult. It is certainly more difficult than to study any effects testable in a regular environment, under strictly defined conditions etc. Consequently, the authors resorted to various observational study techniques. As is well known, such an approach has to be always very careful. Serious effort to eliminate all obvious and important sources of bias is always left to author's responsibility. Here, we can see some reserves which might lead to launching a more carefully designed and controlled future investigation as a continuation of the current one. Present study can be considered to be a first step (or a pilot study), focused on drawing attention to an important theme.

compulsory revisions

1. The authors state that they matched cases and controls ("by age and sex"). Any further information on how it was done is missing, however. It seems that they attempted 1:1 matching, but some cases probably could not be matched (resulting in 205 cases and 200 controls, see Page 8). That should be stated explicitly. Moreover, it seems that unmatched cases were rather extreme (age range of cases 20-102, and of controls 61-96, see Page 8). This is a HUGE imbalance which makes some further results potentially problematic. Nothing is stated about age matching details: for instance, was the matching done according to membership in some age interval? If so, how long the interval was (was it of equal length throughout age range)?
2. It might be questionable whether it is reasonable to include all cases without any restriction on age or whatever other conditions (like diagnosis, medical department doing the treatment etc.).
i) One unpleasant consequence of including cases of whatever age is the fact that matching is much easier for some age than other ("... patients ... received a neuroleptic drug. They were older and stayed longer than the rest of the population," on Page 2). This might lead to choosing randomly from a large number of potential controls for some age categories, while being forced to take whatever is left in other categories (with small or no randomness at all). At the extreme, this might lead to inability to match some cases - which is completely undesirable. Also, with small number of matching potential controls to choose from, it can happen that they come from only one department (or other systematically different "small pockets" of data). Did you check that this did not happen?
ii) One might suspect that some diagnoses could be a priori felt grossly different from others (showing possibly different relationship between neuroleptics use and several of the variables listed in Table 1). For instance, is not the chance of being prescribed neuroleptics when having fever very different between infectious diseases and others?
What about concentrating on a subset of cases (stating it explicitly) of certain age interval and certain diagnoses (whose comparison with respect to studying neuroleptics use and its relationship to chosen factors is medically meaningful).?

3. The phrase "independent predictor" repeats several times in the text. This is not entirely appropriate word. Other people use sometimes the notion of "independent variable" (not perfect) - explanatory variable is nicer. Even better would be to use only "predictor" (shorter and clearer). Even more contradictory phrases appear at some places: "independent correlates" (Page 6,10). These are completely unacceptable.

4. "Diagnostic criteria for dementia: ... based on the clinical judgment of the examining physician." (Page 6) Does it really mean that there was only one physician judging this? If not, how many of them were there (and was there any attempt to look at their classification differences e.g. by formal testing)? Same thing for "Follow up".

5. "To be accepted as demented there had to be documented evidence of decline of intellectual ... function that ..." (Page 6). Only in Discussion, one can learn, that no standard criteria were applied. This should be stated here clearly. Can there be any learning effect involved (so that physicians would have better sensitivity and specificity after some time) - if so, how severe the differences could be? Some reference is invoked on page 12 without stating any figures, however.

6. "The odds-ratios and ... estimated from regression coefficients." (Page 6) Is it really the logistic regression coefficient what is meant?

7. "Patients did not differ from controls in terms ..." (also at further places on Page 9 and later) It should read: did not differ significantly from ... Note huge difference in information content of statistically significant result and something which is not significant. The fact that no significant difference is found does not mean (by far) that no difference is proven.
8. "... (TABLE 1). There were no differences between groups in the complementary data" (Page 9) What is meant by that? E.g. Incontinent OR is significantly different from 1 (as well as previous dementia, death).

9. "We used a multiple logistic regression ... adjusting for age ..." Was the age taken linearly (on logistic scale), or as a higher order polynomial, or was it dicretized?

10. "This study confirms the high rate of neuroleptics use ..." (Page 12) Is not it actually LOWER than in other studies? Here, 7.7% was found, while quoting 9.4-42.8% from other studies (Page 4).

discretionary revisions

1. To make reading easier, it would be nice to improve organization of the paper a little bit. For instance, a reader can find bits of important information scattered throughout the paper (e.g. information about how data were collected, about missing data problems etc. appear in several sections: both Methodical and Results). Description of the whole study design should be more concentrated. It would be much more convenient to have all this information at the beginning (in Methods paragraph). For a quick orientation, it would also help to state explicitly short one-sentence definitions like: Case is defined as .... at the very beginning (e.g. in Methods section of Abstract on page 2).

3. It might be convenient to speak about cases and controls all the time (and not to switch between case/control and patient/control).

2. Some formulations can (and should) be made more precise. Consider statements like "All demographic, clinical and complementary data were compared between cases and controls." (on page 2). Clearly, this cannot be true. By far, not all such information was available. On the contrary, amount of available information was quite limited due to practical considerations. It seems that convenience (accessibility of the information in standard medical records) was an important factor when choosing variables to consider. This should be stated openly (perhaps motivating further, more controlled investigations).

3. i) As mentioned before, we would consider the presented investigations to be rather a pilot study, which might motivate future work. One important deficiency is that there is no notion of replication in the paper (other than reporting results of various patients). To be of general practical interest, the results should be compared to data from other hospitals. It remains to be seen in future how stable the findings are from center to center. Is the suggested neuroleptics overuse only an isolated problem of several hospitals, or is it typical? These (and other) questions cannot be answered without having data from different hospitals (obtained via similar methodology). Further, even within one center, one can think of testing potential interesting differences (among physicians, among departments etc.).

ii) A further study in future might try to use more stringent formal criteria of assessment (e.g. explicitly stated checklists for certain classifications etc.) to suppress subjectivity as much as possible.
It is not surprising to find (Page 8) that “Twenty-two cases ... did not complete a clinical neurological examination and were not tested.” One would be curious about why they did not complete the examination? Could it be because they tended to be more/less ill than the rest? In such a case, some further results could be somewhat problematic.

In this context, note the difference in attrition of cases and controls due “lost follow up” mentioned on page 9 (and TABLE 2). Not surprisingly, larger attrition is observed among cases.

5. What is "hospitalised average length of stay" on page 8? Is it some kind of long-term average for the particular hospital?

6. "... while the diagnosis of dementia three months after admission is probably related with a high rate of previous unrecognised dementia." Why do you think so? Is this because sensitivity of the 3-months-after-admission is (much) higher than sensitivity previous assessment? Are there any arguments for this?

7. "... approaches ... patients should be research." (Page 13) language

Level of interest

BioMed Central is willing to publish any scientifically sound paper. However, we would like to draw particular attention to the more interesting papers. Could you therefore indicate which of the four categories below best describes the paper (when responding to these questions, simply delete those options that do not apply).

A paper whose findings are important to those with closely related research interests

**Competing interests:**

None declared.