DEM Journal Club

Article Appraisal

Article: A randomized controlled trial of intravenous haloperidol vs. intravenous metoclopramide for acute migraine therapy in the emergency department.
Gaffigan ME, Bruner DI, Wason C, Pritchard A, Frumkin K. J Emerg Med. 2015 Sep;49(3):326-34.

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Background and Study Objective(s):

Previous literature has shown both haloperidol and metoclopramide to be effective in the treatment of migraine headaches. Typical first-line ED migraine therapy includes metoclopramide with diphenhydramine while the use of haloperidol alone is limited by akathisia. This study's objective was to compare the safety and efficacy of metoclopramide and haloperidol in treatment of acute migraine headaches in the ED.

Study Design:

This study was a double-blind, randomized head-to-head comparison conducted at 3 United States Department of Defense teaching hospital ED's. Patients were included based on meeting the Modified International Headache Society's migraine criteria. The study's exclusion criteria were extensive including hypersensitivity to study drugs, history of heart disease, electrolyte abnormalities and signs that would indicate further investigation for a headache cause other than migraine. All 64 study participants were given 1L IVNS, 25mg diphenhydramine, and then randomized to receiving either 5mg haloperidol or 10mg metoclopramide. There was no control arm to compare the effects of haloperidol and metoclopramide to.

The primary outcome was pain relief measured using the visual analog scale within 80 minutes or at the time of discharge (if sooner than 80 minutes) after administration of trial medications. A difference of 13 mm on the visual analog scale was used as being clinically significant perhaps based on previous research (Todd et al, Annals of EM, 27:4, April 1996), though this was not referenced. Secondary outcomes were nausea, restlessness, sedation, the need for rescue medications, side effects and QTc change at 80 minutes or time of discharge. Patients were also followed up with 48-hour call back for further secondary outcomes of satisfaction with study drug and persistence of symptoms.

Results:

Similar visual analog scale results were found for pain relief, side effects and satisfaction with equal times to maximum improvement. The mean reduction from baseline pain was statistically and clinically significant for both haloperidol and metoclopramide ($p<0.01$ for both) but there was no statistical difference in comparison to each other ($p>0.05$).

In terms of secondary outcomes at 80 minutes or the time of discharge, both drugs had no difference in reducing nausea, causing restlessness, patient satisfaction or QTc change. Haloperidol required fewer rescue medications ($p<0.02$) but resulted in more restlessness on follow-up phone calls ($p<0.015$). The authors concluded that haloperidol is at least as safe and effective as metoclopramide for the ED treatment of migraine headache.

Validity of Results:

The opinion of Journal Club attendees was that although patient characteristics, treatment, randomization and blinding were well done, there were major flaws in the paper's internal validity especially with regards to sample size. The paper's hypothesis was not clearly stated and therefore, statistical analysis was difficult to apply not knowing whether this was a non-inferiority study or not. Furthermore, though the authors mentioned that the study was set for a power of 0.81, it is difficult to believe that such a small sample size (n=64) would be enough to detect a difference between the two drugs, especially given the range (variance) of migraine headache pain and subjective variability in improvement. Given that this is a negative study, a larger sample size becomes exceedingly important in order to detect a difference between the two drugs. A non-inferiority study would have lowered the sample size needed to adequately power the study but again, no hypothesis was stated and we cannot know if this is what the authors did.

Generalizability of Results:

Generalizability of the paper is limited potentially by the relatively young age of subject participants, but more so by the extensive exclusion criteria which would limit the paper's findings (even if they were felt to be valid) to a small portion of migraine headache sufferers.

The Bottom Line:

The overall sentiment of Journal club attendees was that this study had too small a sample size to realistically detect a difference between the performance of both drugs in terms of acute migraine pain relief in the ED.