Journal Watch

Lack of Benefit from Paracetamol (Acetaminophen) for Palliative Cancer Patients Requiring High-Dose Strong Opioids: A Randomized, Double-Blind, Placebo-Controlled, Crossover Trial

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Abstract:

Objective: The study aim was to investigate potential analgesic benefits of 4 g of paracetamol daily for palliative cancer patients requiring high-dose opioids.
Methods: Thirty-one patients, using at least 200 mg of oral morphine equivalent daily, were recruited to a prospective, double-blinded, randomized, crossover trial. Patients received usual medications plus 4 g of paracetamol or placebo for five days each in random order. Primary outcome, effect on pain, was assessed using daily diaries, including numerical rating scale (NRS) from zero (no pain) to 10 (unbearable) and recording numbers of breakthrough analgesics. Secondary outcomes – nausea, vomiting, cognitive impairment, constipation, and overall well-being – were assessed using the NRS. Data from the last four days of each treatment were analyzed. Patients also indicated in which part of the study their pain was better controlled.
Results: Twenty-two patients, requiring a median dose of 255 mg of oral morphine equivalent daily, completed the trial. There were no significant order or treatment-by-order interaction effects for any variable; paired t-tests were conducted to investigate change in mean levels on outcome variables with placebo vs. paracetamol. For none of the variables was there a statistically significant difference when assessed with placebo compared with paracetamol. No change approached clinically significant levels, with a mean difference in rated pain of 0.16, and mean difference of 0.42 for a number of breakthrough medications. Fifteen patients were undecided whether paracetamol improved pain.
Conclusions: These data do not support the common practice of adding regular paracetamol daily as an adjunct to high-dose opioids for pain control in cancer patients receiving palliative care.

Comments:

Strength/Uniqueness:

1. This sample size was small but adequately powered.
2. The primary and secondary outcomes of this study were clearly stated and adequately measured.
3. In previous similar studies acetaminophen was mentioned to have an opioid-sparing effect but in those studies the outcome was unclear and they also reported a relatively small difference in analgesic effects between the acetaminophen and placebo groups. The current study has rectified the aforementioned deficiencies of the previous literature on this topic.

Weakness:

1. The result indicated that there is a trend for lower numerical ratings of pain, a lower number of breakthrough analgesic doses, less drowsiness, unclear thinking, and constipation in the acetaminophen group compared with the placebo group. Although the multivariate analysis showed that these differences were statistically non-significant (small sample size might have been a contributing factor)
2. This is a single institute study with the majority of participants being in the community. The result may not be applicable to different settings and different populations.
3. No information on baseline daily opioid doses in either placebo or acetaminophen group was provided.

Relevance to Palliative Care:

This study provides awareness for clinicians in regards to potential harm of high dose acetaminophen in management of cancer pain while using relatively high dose opioids.