452258 - SAFETY OF CHLORPROMAZINE FOR POSTOPERATIVE NAUSEA AND VOMITING

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Introduction: Chlorpromazine (CPZ), the only drug active at all nausea and vomiting brain receptor sites, (acetylcholine, dopamine, histamine, and serotonin), [1,2] is used extensively in cancer chemotherapy [3,4], but has been studied for postoperative nausea and vomiting (PONV) only once [5,6], in 1963, using a dose of 50mg intramuscularly. The study was stopped because of hypotension, now known to be caused by CPZ-induced vasodilation. In 1963, induction anesthetic was administered directly into a vein without a running IV. A recent trial of IV chlorpromazine for migraine found 0.1mg/kg safe and effective [7]. However, both anesthetic agents and phenothiazines can prolong the electrocardiogram QT interval, which may lead to dangerous arrhythmias. Duration from T-wave peak to end (Tp-e) may be a better measure of the danger of arrhythmia than rate-corrected QT (QTc). A small dose of CPZ was therefore studied to assess the safety of combining CPZ with general anesthesia.

Methods: A double-blind randomised controlled trial with full concealment, with N = 120, in laparoscopic surgery, with University of Saskatchewan Research Ethics Board approval and informed consent. Null hypothesis: CPZ 10mg IV at anesthetic induction is not different from saline in prevention of PONV or in side effects. PONV was assessed in Post-anesthetic Care Unit (PACU) and next day. Electrocardiograph strips before and after study drug were randomised and measured by a blinded assistant.

Results: Demographics: Females: 104, males: 15; age (mean $\pm$ standard deviation): 38 ± 13 years; height: 165 ± 9 cm; weight: 72 ± 15 kg; type of surgery: 91 gynecology, 21 cholecystectomy, and 8 other. One drug-group subject was lost to follow-up. **Efficacy:** see table; not significantly different from placebo for incidence or severity of PONV in PACU or next day. **Safety:**, one subject in the drug group was sleepier than expected in PACU. One had lower blood pressure than anticipated after induction, which was easily corrected. There was no difference in QTc or Tp-e intervals between NS and CPZ. Although the anesthetic prolonged the QTc (pre-induction 429 ± 34 ms; later 448 ± 39 ms; $P < 0.00001$), it had no effect on Tp-e (pre-induction 80 ± 18 ms, later 78 ± 18 ms; $P = 0.35$).

Discussion: A remarkably low incidence of PONV in both groups, especially in PACU, may confound the results. We attribute this to the use of midazolam in the standard anesthetic. The small dose of CPZ chosen for this study did not show a statistically significant difference from NS, but there is a less than 10% probability that the better outcome with CPZ is due to chance. Thus, a study with larger doses is indicated. Chlorpromazine is inexpensive and appears to be safe in the context of anesthesia practice.

References: 1.Lancet 1982;1(8273):658. 2.Cancer Chemother Pharmacol 1989; 24:307. 3.Cancer 1998; 83:1214. 4.Support Care Cancer 1997 ; 5:500. 5.Br J Anaes 1965; 332. 6

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	NS Group	CPZ Group	P-value
Patients vomiting in PACU	2	1	0.98
Patients with rescue meds in PACU	20	11	0.09
Patients with an emetic event	15	12	0.66
Total emetic events (counts*)	38 [26 to 50]	28 [17 to 38]	
QT_c (ms)	435 ± 36	441 ± 40	0.28
Tp-e (ms)	79 ± 19	79 ± 16	0.91

*Poisson analysis of counts: total events (vomit or retch)[95% confidence intervals]