Scheduled Prophylactic Ondansetron Administration Did Not Improve Its Antiemetic Efficacy In Children Undergoing Craniotomy For Tumor Resection

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Introduction: Postoperative nausea and vomiting (PONV) after craniotomy can increase intracranial pressure, bleeding and pulmonary aspiration. Ondansetron, a $5HT_3$ antagonist is very useful in the prevention and treatment of PONV after various surgical procedures including neurosurgical operations in adult patients (1,2). However, ondansetron has not been shown to be effective in children for prophylaxis of post craniotomy emesis (3). Ondansetron's terminal half-life is shorter in younger patients compared to adults (4). We hypothesized that repeating ondansetron after 6 hours of initial dose may improve its efficacy in children undergoing craniotomy for various tumor resection surgeries.

Methods: After Institutional Review Board approval and informed consent from parents, 75 children, aged 2-18 years, of both sexes who underwent intracranial tumor resection under general endotracheal anesthesia were included in the study. Computer generated random numbers randomly allocated children to three treatment groups: Group 1, received saline placebo at dural closure and after 6 hours, Group 2 received ondansetron 150 μg/kg at dural closure and saline after 6 hours and Group 3, received ondansetron 150 μg/kg, at dural closure and after 6 hours of the initial dose. Drugs were prepared in identical syringes of same volume by an anesthesiologist not involved in the follow-up of patients. A standard anesthesia technique (oxygen, nitrous oxide and isoflurane) was used along with morphine IV 0.2 mg/kg for intraoperative analgesia. Children were extubated at the end of surgery. They were admitted to postoperative neurosurgical intensive care unit and followed up for 24 hours after surgery. Nurses who were aware of the protocol but unaware of the drugs given recorded each episode of nausea, vomiting and retching that occurred in the first 24 hours. Emesis is defined as an episode of vomiting or combined nausea and vomiting. Rescue antiemetic, metoclopramide 250 μg/kg was given for > 2 emetic episodes in 5 minutes. Postoperative pain was managed with diclofenac and IVmorphine as needed. Adverse events such as excessive sedation, extra pyramidal reactions, reintubation and re-exploration were noted. Data were analyzed by SPSS 12.0 using unpaired - t – test, Chi-square test and Fisher exact test wherever appropriate. $P < 0.05$ was considered statistically significant.

Results: Five children in group1, three in group 2 and six from group 3 were excluded because they could not be extubated at the end of surgery. Demographic data, duration of surgery and perioperative morphine requirements were comparable in all groups. More children in Group 3 underwent supratentorial craniotomy (95%) compared to Group 1 (58%, P=0.02) and Group 2 (70%, P=0.05). The incidence of PONV was similar in all three groups at 0-6, 6-24 and 0-24 hours postoperatively. Two patients in group 3 had excessive sedation. None of the children had extra pyramidal reactions, needed reintubation or re-exploration

	Group 1 (n=19)	Group 2 (n=23)	Group 3 (n=19)
0-24 hours			
Nausea	1 (5%)	4 (17%)	1 (5%)
Emesis	5 (26%)	2 (9%)	6 (32%)
Rescue	3 (16%)	1 (4%)	3 (16%)
PONV	6 (32%)	6 (26%)	7 (37%)
0-6 hours PONV	5 (26%)	5 (22%)	5 (26%)
6-24 hours PONV	3 (16%)	4 (17%)	4 (21%)

Discussion: Furst et al administered ondansetron 150 μg/kg at induction and at the end of surgery and reported no benefit in post craniotomy emesis in children (3). Ondansetron's lack of efficacy in children is not related to its short terminal half-life, since we did not find any increase in its efficacy even after repeating the dose after 6 hours. The reason why post craniotomy nausea and vomiting in children is resistant to ondansetron is not clear because the studies have shown its efficacy in adult craniotomy patients. The risk of PONV is moderate (32%) for craniotomy in children indicating the need for combination antiemetic therapy according to consensus guidelines (5). More research is needed with other class of antiemetic drugs and combination of drugs.

Conclusion: Ondansetron is not effective in the prophylaxis of PONV after pediatric craniotomy.

References: 1. J Neurosurg Anesthesiol 2002; 14:102-7. **2**. J Neurosurg Anesthesiol. 2001; 13:207-12. **3**. Anesth Analg 1996; 83:325-8. **4**. Clin Pharmacol Ther. 1995; 58:316-21. **5**. Anesth Analg 2003; 97:62-71