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Antiemetic prophylaxis for Temozolomide: Monotherapy vs. combination?

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Introduction: Temozolomide>75 mg/m^2 has moderate emetogenic potential and 5HT3 antagonist monotherapy is recommended as antiemetic prophylaxis. However, NCCN, ESMO and other international guidelines recommend multi-drug combinations for intravenous chemotherapy of moderate emetogenicity but antiemetic prophylaxis for oral chemotherapeutic agents is not well defined. Further Temozolomide has potential for causing delayed emesis. We hypothesize the need for combination antiemetic prophylaxis for adjuvant Temozolomide and compared 5HT3 antagonist monotherapy with combination regimens.

Methods: We maintain a prospective chemotherapy database of patients diagnosed with central nervous system tumors. This database was used for selection of cases for the current practice audit. Patients included in study were receiving adjuvant Temozolomide for gliomas from October 2017 to June 2018. Antiemetic prophylaxis was administered for five days along with Temozolomide (150–200 mg/m^2) under three subsets: Ondansetron 8 mg BD, Ondansetron 8 mg BD+Domperidone 10 mg BD and Ondansetron 8 mg BD+Olanzapine 5 mg BD. CINV (graded as per CTCAE 4.03) was defined as either nausea or vomiting occurring within 120 hours of last dose of TMZ. Statistical Analysis was performed using SPSS version 20 and R Studio version 1.1.456. The CINV, nausea, vomiting were compared using chi-square test with Bonferroni correction. A p value of below 0.025 was considered significant.

Results: 360 patients were selected with 91 (25.3%), 113 (31.4%) and 156 (43.3%) patients in Ondansetron, Ondansetron+Domperidone and Ondansetron+Olanzapine group respectively. The overall incidence of CINV, nausea and Vomiting was 25.0% (n=90), 25.0% (n=90) and 7.2% (n=26) respectively. The incidence of ≥Grade 2 nausea [17(18.7%), 13(11.5%) and 10(6.4%) p:0.012] and ≥Grade 2 vomiting [5(5.5%), 5(5.3%) and 0; p:0.015] was reduced with combination antiemetic regimes which was statistically significant. Olanzapine+Ondansetron were most efficacious antiemetic prophylactic combination.

Conclusions: The CINV rates with Temozolomide at 150-200 mg/m^2 are high with Ondansetron monotherapy. The combination of Ondansetron with Olanzapine leads to statistically significant decrease in the rate of moderate to severe emesis and nausea and offers a cost effective steroid sparing antiemetic regimen.

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