Publication

Automated analysis of delayed emesis in the telemetered ferret: detection of synergistic effects of aprepitant and ondansetron.

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Abstract

Nausea and vomiting are common side effects of cancer chemotherapy. We have previously described a model in the ferret where delayed emesis can be measured automatically using telemetry. This study was designed to examine the sensitivity of this automated emesis model for detecting moderate and/or additive pharmacological effects by investigating low-dose effects of aprepitant alone or in combination with ondansetron. Ferrets implanted with telemetry devices (Data Sciences International) were orally treated with aprepitant (0.03 mg/kg) and/or ondansetron (0.3 mg/kg) and then challenged with cisplatin (8 mg/kg, i.p.). Abdominal pressure was recorded in unrestrained animals from 18 to 72 h post-challenge, and the pressure signals were automatically analyzed using adapted software (Emka Technologies). Ondansetron administered alone 1 h before cisplatin challenge had no significant effects on the delayed emesis phase. Once-daily treatment with aprepitant (2 h before cisplatin and then 24 and 48 h after cisplatin challenge) slightly reduced the total number of emetic events (-32%, NS). When administered together, aprepitant and ondansetron exhibited synergistic effects on delayed-phase emesis. The combined treatment markedly and significantly decreased the mean number of emetic events recorded between 24 and 54 h after cisplatin dosing (-75%, $P < 0.05$) and the total number of emetic events (-56%, $p < 0.05$). Our results demonstrate that the automated cisplatin-induced emesis model in the ferret is sensitive enough to detect the synergistic effects of aprepitant and ondansetron in combination, creating new and important perspectives for the evaluation of combined therapy in the reduction of side effects of cancer chemotherapy.