

Cisapride decreases gastric content aspiration in mechanically ventilated patients

ABSTRACT

Our study demonstrates that patients who are kept in a semirecumbent position still experience aspiration of gastric contents. Furthermore, cisapride decreases the amount of air in their abdomen during intubation and mechanical ventilation, potentially preventing ventilator-associated pneumonia. Gastric content aspiration was not completely prevented by cisapride, even with the patient in the semirecumbent position.

INTRODUCTION

Retinoic acid receptors (RAR-, -Aceast^{ne}, and Serrano) are transcription factors that regulate various endocrine metabolic pathways. In contrast, anti-estrogens like tamoxifen or raloxifene have been shown to possess anticancer activity in both estrogen receptor positive and negative breast tumor cells, when ligands are targeted specifically for these RAR isoforms. Hence, such molecules could form a new class of drugs targeting breast cancer; because both agonists and antagonists of RAR can exhibit anti-tumor activity against breast or prostate cancer as well as lung cancer or leukemia respectively, the development of both types of ligands may have important biomedical applications. Our recent work has shown that antagonists can be discovered logically using a model of the antagonist-bound conformation of their receptors. We aim to identify novel molecular structures that have RAR agonist activity, as several retinoid and non-retinoid ligands have been described, which activate one or fewer RAR isoforms simultaneously. Several compounds, including the all-trans retinoic acid (all-trans RA), have been clinically tested and exhibit unacceptable side effects, such as skin dryness, cheilitis, hypertriglyceridemia, and conjunctivitis (Fig. 1a). However, the compounds examined so far belong to a small series of related structures. With the increasing evidence, it seems likely that the RAR- isoform, which is under the transcriptional control of RAR α , suppresses cell growth and tumorigenicity, suggesting potential therapeutic properties. New molecules with both receptors on the epitope and an active RAR antagonist may therefore present more favorable toxicity than pan-agonists. Using a flexible virtual screening algorithm (Molsoft ICM, virtual library screening module), we quickly docked hundreds of thousands of different flexible compound structures into the ligand binding pocket of RAR and identified two novel RAR- selective agonists. The ligands that exhibit unique structural and chemical traits could be utilized to create novel compounds for cancer prevention and treatment.

CONCLUSION

The AITDs examined in the ER gene did not appear to have any association with a dinucleotide repeat polymorphism, as our data indicated otherwise. However, this does not necessarily rule out the existence of other polychromatic variants within the gene; they may still be associated with AITB. Using microsatellite markers with multiple alleles in case-control studies is problematic due to limitations in this study. Although our results suggest significant diversity in the genetic backgrounds of AITDs, further investigation needs to be conducted in a larger group of patients. Despite the need for further research to confirm its impact on BMD and risk of osteoporosis, we suggest that the ER microsatellite polymorphism may have a minimal pathogenic significance in predicting osteoarthritis as

complication of GD.