Cardiovascular Effects of i.v. MN-221 (bedoradrine) Administered with Nebulized Albuterol in Dogs

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Abstract

Background and Purpose

MN-221 is being developed as an i.v. adjunctive for the treatment of acute exacerbations of asthma. MN-221 is a novel, highly selective beta2-adrenoceptor agonist that is being developed as an i.v. adjuvant for the treatment of acute episodes of asthma. The high beta2 selectivity and partial beta1 action of MN-221 may explain the safety observed.

Methods

- Native Beagle dogs (n=4)
- Treatment groups:
  - Nebulized albuterol (5, 10, 20 µg/kg)
  - MN-221 (0, 0.3, 3, 30 µg/kg) iv for 15 min
  - Combination albuterol + MN-221
- Blood sampling for PK assessments (0, 5, 15, 30, 60, 120, and 240 min)
- Telemeter monitoring of MAP, HR, BP, and ECG up to 4 hr post-treatment

Results

- No significant effect of MN-221 alone on HR, MAP, BP, or ECG
- No additive nor synergistic effect of the combination treatment on HR. In fact, there were no statistical differences between:
  - 0.3 µg/kg MN-221 was significantly different than the 3 µg/kg and 30 µg/kg doses
  - 5 µg/kg Albuterol was significantly different from 10 and 20 µg/kg doses

Conclusions

- No significant elevation of HR by i.v. MN-221 concurrent with inhaled albuterol
- Effects of MN-221 or Albuterol Administration

- Effects of MN-221 or Albuterol on QTc Interval
- Effects of MN-221 or Albuterol on Mean Arterial Pressure
- Effects of MN-221 or Albuterol on Heart Rate