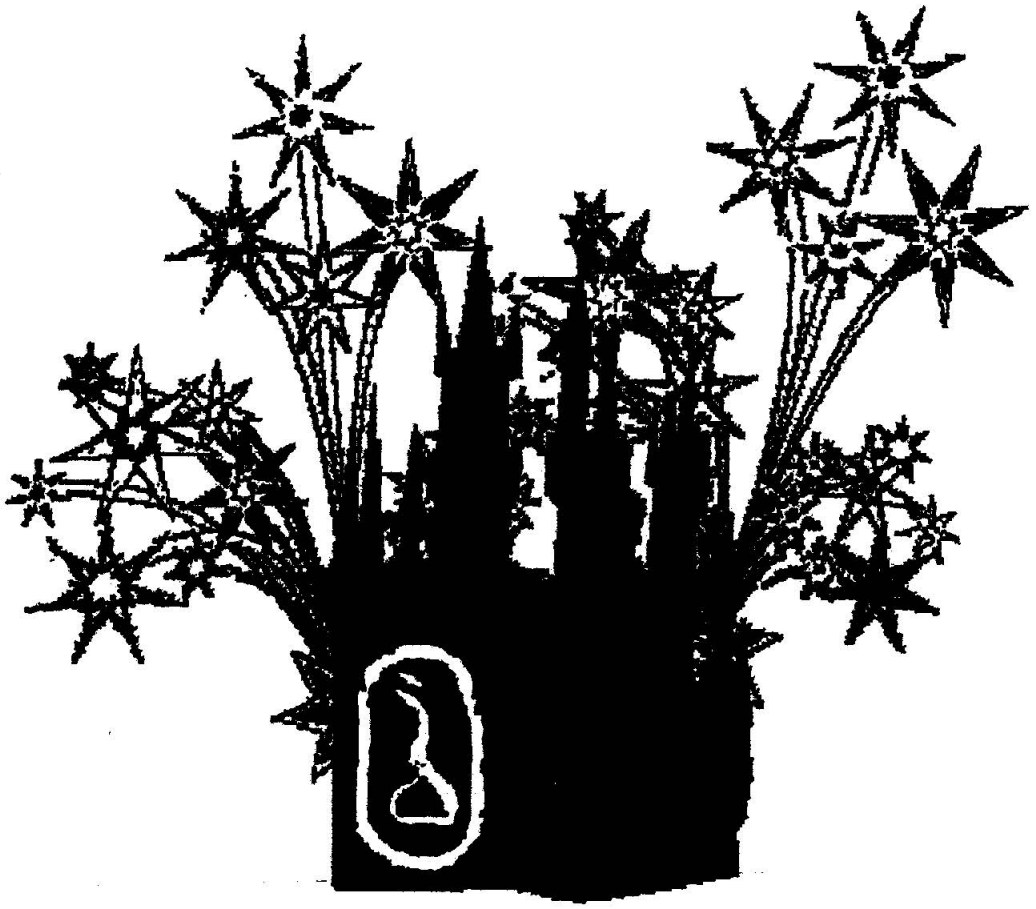
14TH INTERNATIONAL CONFERENCE OF RACING ANALYSTS AND VETERINARIANS

CONFERENCE HANDBOOK



JULY 3 - 8, 2002

DISNEY'S CORONADO SPRINGS RESORT

ORLANDO, FLORIDA

PHARMACODYNAMICS OF GUANABENZ AND RELATED β_2 AGONISTS[§]

JD Harkins and T Tobin

Department of Veterinary Science, The Maxwell H. Gluck Equine Research Center, University of Kentucky, Lexington, KY 40506 USA

In human medicine, β_2 receptor agonists are used primarily for the treatment of systemic hypertension. In veterinary medicine, β_2 agonists are primarily used for large animal control. These agents are used in equine medicine as short-acting sedatives/tranquilizers to render animals more compliant and safer to handle. Indeed, the advent of these agents is credited with greatly increasing the safety of equine practice. The objective of this study was to determine the pharmacological effects of guanabenz and other β_2 adrenergic agonists including xylazine, detomidine, medetomidine, clonidine, romifidine, and amitraz.

The sedative/analgesic effects of these agents were compared using various methods for measurement. Head ptosis and heart rate (HR) were used as a measure of sedation. The heat lamp/hoof withdrawal method was used to measure analgesia. Blood and urine analyses were performed to detect hyperglycemia or elevated urine glucose after dosing.

Guanabenz produced a 3-4 h sedative effect, which was the longest produced by any of the drugs tested in this study. Xylazine and clonidine produced dose-dependent durations and depths of head ptosis. The durations of head ptosis following detomidine, romifidine, and medetomidine were of shorter durations. In separate experiments, clonidine and guanabenz were injected and followed by intravenous yohimbine (60 mg) 30 min later. Head ptosis was immediately reversed and approached control values within 5 min.

Guanabenz also provided maximal analgesia (defined as >280% of control HWRL) of approximately 1h duration, with an analgesic effect that persisted for about 5 h, which was by far the longest effect of all the β_2 agonists. Medetomidine, romifidine, and xylazine provided maximal analgesia for shorter durations. Detomidine and clonidine provided only limited analgesia. The decreased HR following guanabenz administration had the longest duration of approximately 3 h. The other β_2 agonists decreased HR for shorter durations.

Urine production increased dramatically following administration of the β_2 agonists, with a concomitant decrease in specific gravity. Guanabenz had the longest duration for increased urine volume, lasting approximately 3 h. Xylazine had the shortest polyuric effect, persisting for about 1 h. Urine glucose remained negative following medetomidine, clonidine, and xylazine administrations. With guanabenz, amitraz, romifidine, and detomidine administrations, urine samples were positive for glucose at some time during the subsequent 8 h. Following guanabenz administration, blood glucose concentrations increased to >250 mg/dL by 1 h after injection.

Guanabenz, an β_2 agonist similar to clonidine, detomidine, and xylazine, provided a more intense and longer-lasting analgesic response than any other β_2 agonist evaluated in the horse.

[§]Supported by grants entitled "Thresholds and clearance times for therapeutic medications in horses" funded by The Equine Drug Council and The Kentucky Racing Commission, Lexington, KY and by research support from the National, Florida, Kentucky, Nebraska, Arkansas, Pennsylvania, Ohio, and Canadian Horsemen's Benevolent and Protective Associations, and Mrs. John Hay Whitney.