

TITLE: PARTIAL PARALYSIS WITH ATRACURIUM INDUCES SEGMENTAL CHANGES IN DIAPHRAGMATIC CONTRACTILITY

AUTHORS: E. Goldman, M.D., J. Walsh, M.D., and A.E. Grassino, M.D.

AFFILIATION: Ohio State University, Columbus, Ohio, 43210 and Notre-Dame Hospital and Meakins-Christie Laboratories, McGill University, Montreal, Canada

It has been shown¹ that during inspiratory resistive loading (IRL) and partial neuromuscular blockade (NMB) the rib cage is distorted. Whether this distortion induces a selective change in costal (co) or crural (cr) diaphragmatic contractility is not known. To examine this point, we studied separately the effect of IRL (60 cm H₂O/LPS) or NMB (atracurium) on co and cr shortening in seven ketamine anesthetized dogs breathing spontaneously. Tidal shortening (sonomicrometry) of co and cr (as percent of resting length Δ LFRC), tidal volume (VT), transdiaphragmatic pressure (Pdi), pressure-time index (TTDi), and ventilation (VE) were measured. After a sequence of baseline, IRL and again baseline measurements, atracurium was given until electromyographic activity of parasternal muscles was suppressed. During IRL, both segments (LFRCco and LFRCcr) increased shortening in the same proportion as compared to baseline. During NMB, however, LFRCco remained close to baseline while

LFRCcr increased almost twofold. Driving force (peak Pdi as percent of actual Pdi max), decrease in VT (70% from baseline) and increase in PaCO₂ were similar for both groups. These results suggest that when diaphragmatic segments were challenged with resistive loading they responded in synchrony while NMB induced inhomogeneity in shortening. The selective mechanism associated to this NMB effect is probably related to regional changes in rib cage and abdominal elastances or to variable sensitivity to NMB because of different fiber composition.

	Baseline	IRL	NMB
Δ Pdi peak cmH ₂ O	8.8±1	24.3±3*	5.7±1
Δ Pdi/Pdi max	9.4±2	28.6±4*	30.9±7*
Δ LFRC cr (%)	10.4±2	17.1±2*	17.9±2*
Δ LFRC co (%)	8.9±1	14.0±2*	8.4±2
VT ml	378±44	276±39*	248±22*
VE L/min	9.4±2	8.1±1	6.4±1*
PaCO ₂ mmHg	30.4±2	46.9±6*	46.7±4*
TTDi	0.013±.003	0.063±.011*	0.060±.014*

mean ± SEM
*p<0.01 (from baseline)

References:

1. Anesthesiology 71:A1119, 1989.

TITLE: ACETAZOLAMIDE IN THE TREATMENT OF ACUTE MOUNTAIN SICKNESS: CLINICAL EFFICACY AND EFFECT ON GAS EXCHANGE

AUTHORS: C.K. Grisson, F.H. Sarnquist, R.C. Roach, P.H. Hackett

AFFILIATION: Denali Medical Research Project, University of Alaska, Anchorage and Department of Anesthesia, Stanford University, Stanford, CA 94305

Acute mountain sickness (AMS) is a neurologic syndrome that occurs upon ascent to high altitude, and is associated with impaired pulmonary gas exchange. Acetazolamide prevents AMS when given prior to ascent, but has not been proven effective for treatment. We therefore set out to determine: 1) the efficacy of acetazolamide for treatment of AMS and 2) the effect of acetazolamide on pulmonary gas exchange in AMS.

After informed consent and with the approval of the University of Alaska Human Subjects Committee, twelve climbers with AMS at 4200m on Mt. McKinley were randomized in a double blind fashion to acetazolamide (n=6) or placebo (n=6) treatment groups. The dose of acetazolamide was 250 mg PO at 0 and 8 hours after inclusion in the study. Assessment of AMS and physical measurements were made at 0 hours and were repeated at 24 hours.

At 24 hours 5 of 6 acetazolamide-treated climbers were without AMS (symptom score <2), and all 6 placebo-treated climbers still had AMS (symptom score ≥2). No significant side-effects of acetazolamide

were reported. Acetazolamide improved pulmonary gas exchange and PaO₂ over 24 hours as compared to placebo. Change in A-a gradient for oxygen correlated significantly with change in symptom score for both groups (p<.005). Acetazolamide was associated with a decrease in A-a gradient and a greater improvement in symptoms, and placebo was associated with an increase in A-a gradient and less improvement in symptoms.

We conclude that acetazolamide is effective for the treatment of established cases of AMS, and is associated with an improvement in pulmonary gas exchange.

	PLACEBO (mean±SEM)	ACETAZOLAMIDE (mean±SEM)
Symptom Score*	n=6	n=6
Baseline	3.8 ± 0.7	3.8 ± 0.2
24 hours	2.5 ± 0.3	1.0 ± 0.2**
A-a Gradient mmHg	n=6	n=6
Baseline	8.8 ± 1.8	9.0 ± 1.6
24 hours	12.1 ± 1.7	8.2 ± 1.9
(change 0-24 hrs)	(+3.3 ± 0.9)	(0.8 ± 0.7)***
PaO₂ mmHg	n=6	n=6
Baseline	45.2 ± 1.3	44.2 ± 3.4
24 hours	43.8 ± 2.0	47.1 ± 2.9
(change 0-24 hrs)	(-1.4 ± 1.2)	(+2.9 ± 0.5)***

* A symptom score of 2 or greater indicated AMS.
** p<.01 acetazolamide versus placebo, Mann-Whitney U-test.
***p<.05 for change in A-a gradient and PaO₂ over 24 hours between groups, Mann-Whitney Rank-Sum test.