HYPERCAPNIC RESPIRATORY FAILURE IS INFREQUENTLY REPORTED AS AN ADVERSE EVENT IN CLINICAL TRIALS

Dustin Anderson-Bell MD[1], Brian W Locke MD MSc[2]

University of Utah Health, Division of Pulmonary and Critical Care; Intermountain Medical Center, Division of Pulmonary and Critical Care

INTRODUCTION

- Many medications cause respiratory depression.
- This is often recognized only after their widespread adoption.
- Trials must report all life-threatening adverse events to clinicaltrials.gov.

Study Question:

- How often do trials report adverse events plausibly related to respiratory depression, hypercapnia, or hypoventilation?

METHODS

- Clinicaltrials.gov data through Dec 25th, 2022 parsed by Shi and Du (Scientific Data; 2024) who used BioBERT to extract trial elements from each registration.
- Adverse events were classified as not-related, possibly related, or definitively related to respiratory depression.
- Definite: Specific key words such as hypercapnia, hypercarbia, hypoventilation, respiratory acidosis.
- Possible: More general key words such as acute respiratory failure, respiratory arrest, dependence on ventilator.
- Studies were categorized by:
    - Condition under study
    - Class of medication or intervention
    - If the trial has finished (final outcomes)

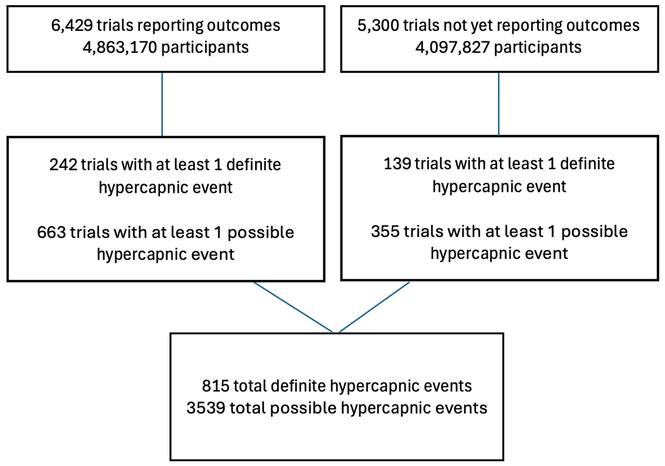

Figure 1: Source populations and event totals

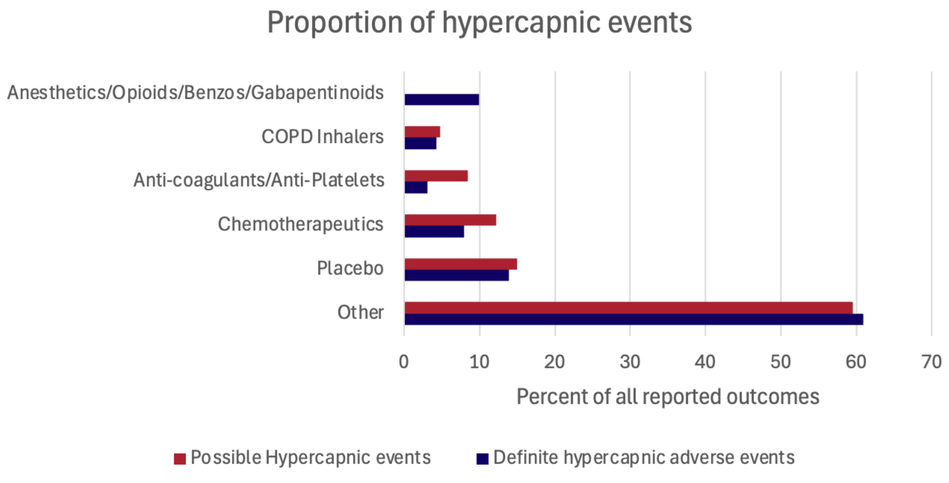

Figure 2: Relative contribution of each intervention class to reported hypercapnic events

RESULTS/DISCUSSION

- 6,429 finished trials (4,863,170 participants)
- 5,300 unfinished trials (4,097,827 participants)
- At least one definite hypercapnia event:
    - 242 (3.8%) of completed trials
    - 139 (2.6%) of unfinished trials
- At least one possible hypercapnia event:
    - 663 (10.3%) completed trials
    - 355 (6.6%) unfinished trials
- Total definite: 815 (0.02% of all events)
- Total possible: 3539 (0.1% of all events).
- Benzo, Opioid, Gabapentinoids, Anesthetics: 91 definite, 0 possible events.
- High-risk patients with low-risk medications (ie chemotherapeutics: 74 definite, 432 possible)
- Placebo arms: 113 definite, 2107 possible events.

CONCLUSIONS

- Hypoventilation-related adverse events are sporadically reported in clinical trials.
- Many reported adverse events are unlikely adverse drug reactions.
- Possible explanations include: studying healthy patients, insensitivity of passive data monitoring, under-representation of respiratory depressants
- **Reliable capture of hypoventilation events in trials might better identify risky medications sooner.**

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