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Fentanyl-Induced Chest Wall Rigidity after Tracheal Resection

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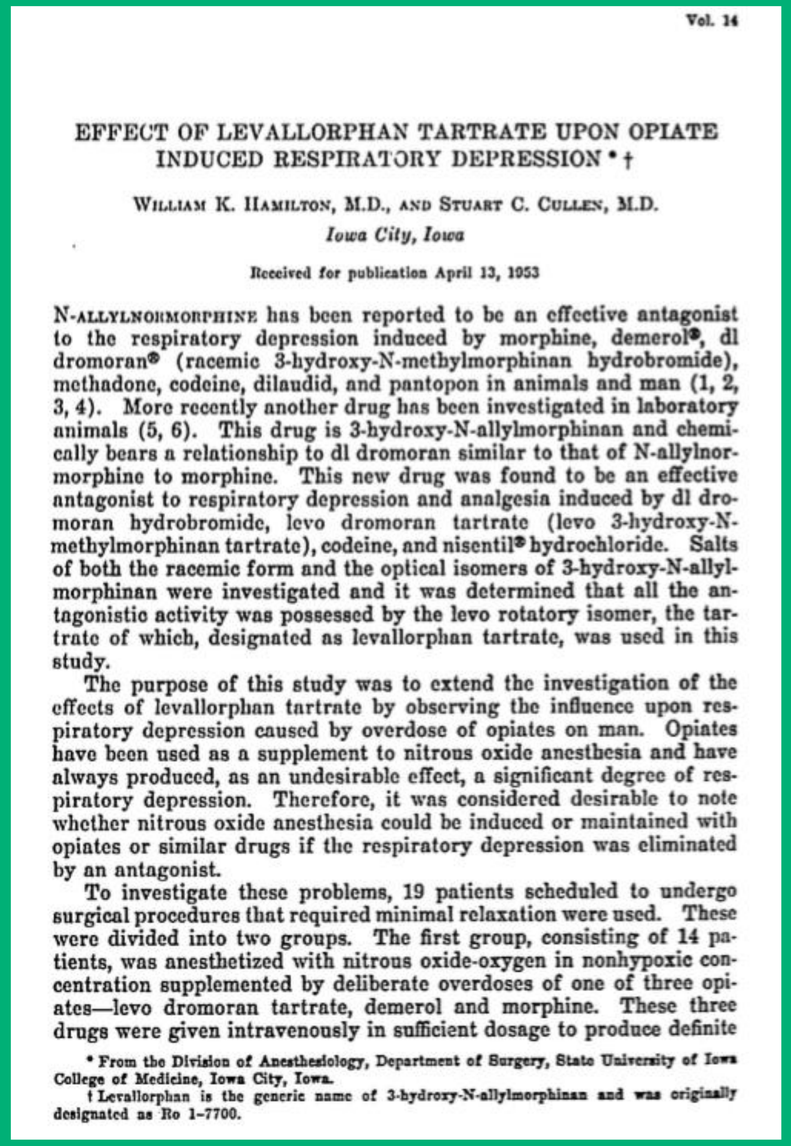

Vol. 14

EFFECT OF LEVALLORPHAN TARTRATE UPON OPIATE INDUCED RESPIRATORY DEPRESSION *†

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N-ALLYLNORMORPHINE has been reported to be an effective antagonist to the respiratory depression induced by morphine, demerol®, dl dromoran® (racemic 3-hydroxy-N-methylmorphinan hydrobromide), methadone, codeine, dilaudid, and pantopon in animals and man (1, 2, 3, 4). More recently another drug has been investigated in laboratory animals (5, 6). This drug is 3-hydroxy-N-allylmorphinan and chemically bears a relationship to dl dromoran similar to that of N-allylnormorphine to morphine. This new drug was found to be an effective antagonist to respiratory depression and analgesia induced by dl dromoran hydrobromide, levo dromoran tartrate (levo 3-hydroxy-N-methylmorphinan tartrate), codeine, and nisentil® hydrochloride. Salts of both the racemic form and the optical isomers of 3-hydroxy-N-allylmorphinan were investigated and it was determined that all the antagonistic activity was possessed by the levo rotatory isomer, the tartrate of which, designated as levallorphan tartrate, was used in this study.

The purpose of this study was to extend the investigation of the effects of levallorphan tartrate by observing the influence upon respiratory depression caused by overdose of opiates on man. Opiates have been used as a supplement to nitrous oxide anesthesia and have always produced, as an undesirable effect, a significant degree of respiratory depression. Therefore, it was considered desirable to note whether nitrous oxide anesthesia could be induced or maintained with opiates or similar drugs if the respiratory depression was eliminated by an antagonist.

To investigate these problems, 19 patients scheduled to undergo surgical procedures that required minimal relaxation were used. These were divided into two groups. The first group, consisting of 14 patients, was anesthetized with nitrous oxide-oxygen in nonhypoxic concentration supplemented by deliberate overdoses of one of three opiates—levo dromoran tartrate, demerol and morphine. These three drugs were given intravenously in sufficient dosage to produce definite

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† Levallorphan is the generic name of 3-hydroxy-N-allylmorphinan and was originally designated as Ro 1-7700.

The first published case of opioid induction was in 1953 when it was called:

“Wooden chest syndrome”

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General Floors

Procedural Areas

Peroperative Area

Operating Rooms

Outpatient surgical area

Post-anesthesia Care Unit

Intensive care unit

Fentanyl is utilized for pain control and sedation throughout numerous hospital settings.

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- Sedation and analgesia in the intensive care setting is highly variable
- Most practitioners utilize opioids in some form or another
- Any lipophilic synthetic opioid can cause muscle rigidity**

Table 2—*IV Sedative and Opioid Analgesic Medications Used in Adult ICU Patients

Drug/Class	Elimination	Onset/Duration	Dosing (IV)	Concentration	Advantages	Disadvantages	Relative Daily Cost†
Lorazepam/ benzodiazepine	Hepatic conjugation to inactive metabolite	5–20 min/6–8 h; up to 24–72 h in elderly/cirrhosis/ ESRD	LD: 2–4 mg IV push MD: 2–6 mg IV q4h-q6h; infusion: 1–10 mg/h; start low in elderly	100 mg/100 mL D5W only	Inexpensive, longer half-life	Propylene glycol toxicity at high doses (anion gap metabolic acidosis, renal insufficiency)	$$
Midazolam/ benzodiazepine	Cytochrome P450 3A4; active metabolite excreted renally	5–10 min/1–4 h (longer in ESRD/ CHF/liver failure)	LD: 2–5 mg IV push MD: 1–20 mg/h; start low in elderly	100 mg/100 mL NS or D5W	Shorter acting if preserved organ funct ion; fast onset	Many drug interactions, may increase midazolam levels, active metabolite accumulates in renal failure	$$$
Propofol	Conjugation	30–50 s/ approximately 3–10 min (dose dependent)	MD: 5–150 μg/kg/min	Premixed (10 mg/mL)	Short acting	↓ BP, increase serum triglyceride, pancreatitis, propofol infusion syndrome, zinc depletion	$$$$
Dexmedetomidine	Hepatic Cytochrome P450 and glucuronidation	Immediate/ approximately 6 min (longer in liver failure)	LD: 0.5–1 μg/kg over 10 min; MD: 0.2–0.7 μg/kg/h for 24 h	100 μg/50 mL NS only	Very short duration; has some analgesic properties	↓ BP, ↓ HR; not approved for use > 24 h, some studies use longer	$$$$$
Morphine sulfate/opioid analgesic	Conjugation; active metabolite excreted renally	5–10 min/2–4 h	LD: 2–4 mg IV push MD: 2–30 mg/h for ventilated patients	100 mg/100 mL NS or D5W	Reduces tachypnea	↓ BP, respiratory depression, accumulation in hepatic/renal failure	$
Fentanyl/opioid analgesic	Cytochrome P450 3A4	1–2 min/2–4 h (longer in liver failure)	LD: 25–50 μg IV push MD: 0.7–10 μg/kg/h for ventilated patients	1.25 or 2.5 mg/ 250 mL NS or D5W	Less hypotension than morphine	3A4 inhibitors may increase fentanyl; fever will increase patch fentanyl levels by 30%	$$
Hydromorphone/opioid analgesic	Hepatic	5–10 min/2–4 h	LD: 0.2–0.6 mg IV push MD: 0.5–3 mg/h	100 mg/100 mL NS or D5W	May work if patients are tolerant to morphine/fentanyl	Respiratory depression, caution in nonventilated patient; highly addictive	$
Alfentanil/opioid analgesic	Hepatic; active metabolites excreted renally	1 min/30–60 min (dose dependent)	LD: 50–75 μg/kg slowly over 3–5 min; MD: 0.5–3 μg/kg/ min (usual 1–1.5 μg/kg/min)	10 mg/250 mL NS or D5W	Very short-acting agent	↓ HR, ↓ BP, ↑ ICP; 3A4 inhibitors may increase levels of alfentanil	$$
Remifentanil/opioid analgesic	Tissue esterases	1–3 min/10–20 min	LD: 1 μg/kg over 1 min MD: 0.6–15 μg/kg/h for MV (unlabeled use); use ideal body weight if > 30% over ideal body weight	5 mg/250 mL NS or D5W	No accumulation in hepatic or renal failure	↓ HR, ↓ BP, ↑ ICP	$$$
Sufentanil/opioid analgesic	Hepatic	1–3 min/dose-dependent duration	LD: 1–2 μg/kg slowly over 3–5 min; MD: 8–50 μg as needed	250 μg/250 mL D5W; variable stability in NS		↓ HR, ↓ BP, ↑ ICP	$

*ESRD = end-stage renal disease; LD = loading dose; MD = maintenance dose; D5W = 5% dextrose in water; CHF = congestive heart failure; NS = normal saline solution; ↓ BP = hypotension; ↓ HR = bradycardia; ↑ ICP = increased intracranial pressure.

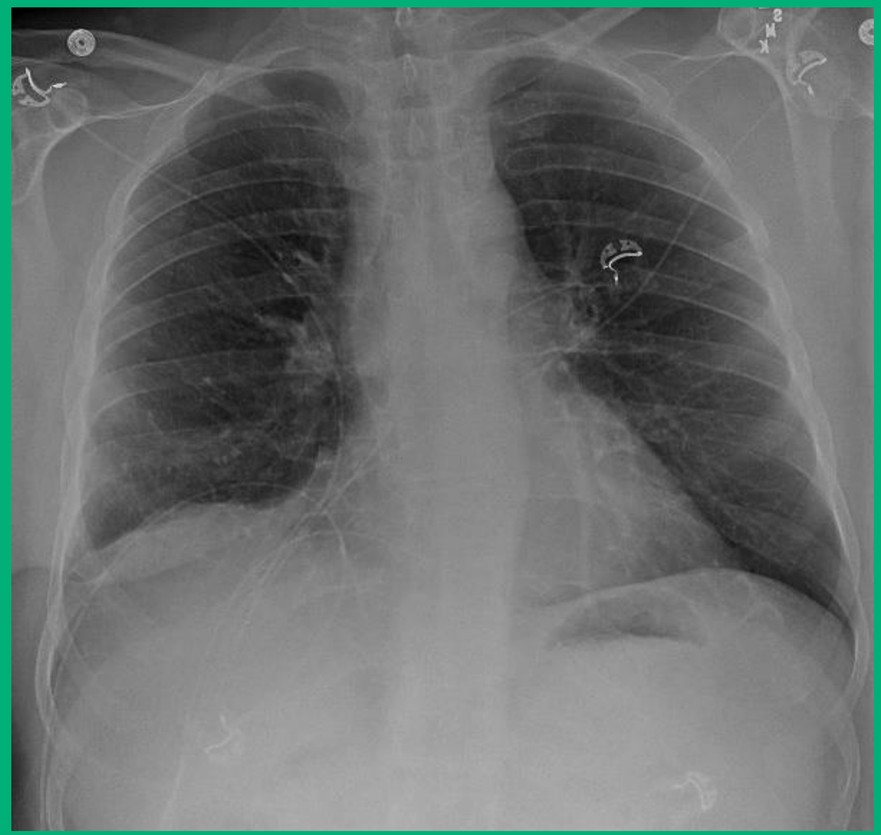
†Dollar signs represent arbitrary scale of medication costs, ranging from $ = very low cost, to $$$$$ = very high cost.

The patient is a 52yo gentleman with a history of:

- **HTN**
- **Asthma**
- **Seizure disorder**
- **Bipolar disorder**
- **Subglottic tracheal stenosis complicated by prolonged previous intubation after trauma**

He presented for tracheal resection and reanastomosis. Intraoperatively he received:

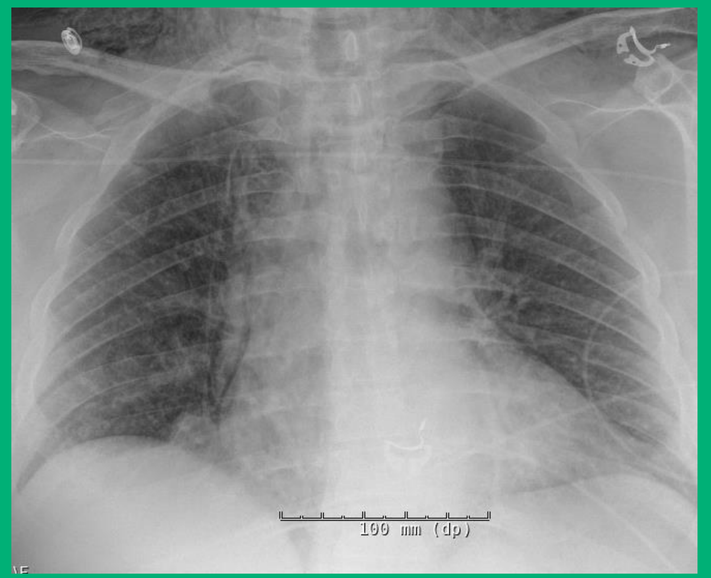
- **Midazolam 2mg**
- **Fentanyl 100mcg**
- **Propofol 200mg**
- **Succinylcholine 200mg**
- **Remifentanil infusion at 0.2mcg/kg/min (3365mcg in total)**
- **Sevoflurane**



Pre-operative chest radiograph

- Arrived intubated and in hemodynamically stable condition to the Surgical Intensive Care Unit.
- Fentanyl and propofol infusions were initiated.
- Immediately after the fentanyl infusion began, the patient developed:
  - severe hypoxemia
  - ventilator dyssynchrony
  - elevated peak and plateau ventilator pressures
  - muscular rigidity of the extremities, masseters, thoraco-abdominal wall
  - severe respiratory acidosis
- There was no wheeze, elevated lactate or abnormal chest radiograph findings.
- FIMR was regconized
  - the fentanyl infusion was stopped
  - intravenous rocuronium was administered
  - resolution of FIMR occurred rapidly
- The patient was then sedated with midazolam and paralyzed with cis-atricurium.
- He was successfully extubated the following day.

	1 3/6/2020 0305	2 3/6/2020 0113	3 3/5/2020 1113
ARTERIAL BG			
PH ARTERIAL	*7.349*	*7.139 **	*7.369*
PCO2 ARTERIAL	*48*	*86*	*37*
PO2 ARTERIAL	*86*	*95*	*124*
ART BICARB	*25.9*	*28.0*	*21.0*
CO2 TOTAL ARTERIAL	*27.3*	*30.7*	*22.2*
BASE EXCESS ARTERIAL	*0.3*	*-3.6*	*-3.6*
ART O2 SAT	*96.0*	*93.2*	*98.4*
FIO2	*Not Provided*	*Not Provided*	*43.0%*
ART TEMP			*36.0*
TEMPERATURE	*Not Provided*	*Not Provided*	
ART BAROM PRESSURE	*765*	*764*	*762*
IONIZED CALCIUM			*1.06*
LACTIC ACID ART	*1.4*	*1.5*	*0.7*



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Fentanyl-Induced Chest Wall Rigidity: an overview

Proposed mechanism of action: central activation of mu opioid receptors

- Non-N-methyl-D-aspartate (NMDA) and NMDA receptor activation leads to disinhibition of spinal motor neurons
- Activation of spinal motor neurons at the level of the locus ceruleus in the pons
- Modulation of gama-aminobutyric acid (GABA) pathways at the spinal cord and basal ganglia level

Known risk factors include:

- Large dose administration
- Increased rate of administration
- Extremities of age
- History of critical illness
- Neurologic illness
- Metabolic derangements
- Use of dopaminergic agents

Differential Diagnosis includeS:

- Acute bronchospasm
- Tension pneumothorax
- Seizure/Status epilepticus
- Mucus plug
- Severe agitation

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Fentanyl-Induced Chest Wall Rigidity: Clinical Impications

RECUSCITATION!
- **AIRWAY**
- **BREAHTING**
- **CIRCULATION**

RECUSCITATION!

1. **Secure the airway via endotracheal intubation**
2. **Provide agents to counter the fentanyl:**
   - ***Naloxone***
   - ***Neuromuscular blockade***
3. **Supportive care**

Thank you!

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