Intranasal Ketamine for Analgesia (INKA) in the Emergency Department: A Prospective Observational Series

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Background

- Timely analgesia is integral in the emergency department (ED).
- Intravenous (IV) opioids are used frequently, and their use is often delayed (e.g. cardiorespiratory monitoring required).
- Ketamine has shown efficacy as an analgesic in a variety of settings at sub-anesthetic doses, and obviates many of the concerns of opiates (e.g. no cardiorespiratory depression).
- The intranasal route has demonstrated excellent absorption and has many advantages vs IV therapy (e.g. shorter time to administration).

Methods

- **Design:**
  - Open-label, non-randomized, uncontrolled trial.
  - Patients recruited as convenience sample (10/2012-01/2013).
- **Sample size**: 40
  - To detect a change in visual analog scale (VAS) of ≥ 13mm with a power of 80% (alpha = 0.05), 34 subjects were needed.
    - 13mm reduction in VAS pain score previously shown to be clinically significant in an ED population
  - Six patients were added to offset potential dropouts.

Inclusion:

- ≥6 years of age with moderate or severe pain (VAS ≥50mm).

Exclusion:

- Pregnancy, history of schizophrenia, need for immediate IV access, uncontrolled hypertension (SBP> 180mmHg), nasal occlusion, or Glasgow Coma Scale <15.

Intervention:

- 0.5mg/kg INK given via mucosal atomization device.
- A single, repeat dose of 0.25 mg/kg of INK could be given after 10 minutes if the recorded VAS was ≥50 mm.

Outcomes measurements:

- Pain scores and vital signs were taken every 5 minutes for the first 30 minutes, then every 10 minutes for up to 1 hour.
- Patients were screened for adverse events every 10 minutes.
- Satisfaction and nasal irritation were assessed at 30 minutes.
- Follow-up interviews were performed at 24 and 72 hours.

Statistical Analysis:

- Wilcoxon Signed-Ranks Test.

Table 1. Characteristics of ED patients (n = 40) receiving INK for analgesia.

Characteristic	Subjects (n=40)
Age, y	
Median	48
(IQR)	(36 to 57)
Age distribution, No. (%)	
11 – 21	3 (8)
22 – 49	19 (47)
50 – 74	17 (42)
75 or older	1 (3)
Male, No. (%)	13 (33)
Weight, kg	
Median	72
(IQR)	(59 to 87)
Baseline pain VAS (0-100), mm	
Median	77
(IQR)	(68 to 86)
Medical conditions, No. (%)	
Non-fracture musculoskeletal pain	21 (53)
Fracture	9 (22)
Abdominal pain *	4 (10)
Other **	4 (10)
Dental pain	2 (5)

* Conditions were: small bowel obstruction, diverticulitis, gastritis, biliary colic.
** Conditions were: migraine, shingles, renal colic, gout.

Table 2. Outcomes in patients receiving intranasal ketamine. * p <0.0001

Measured Parameter	Subjects(n=40)
≥13mm reduction in VAS pain score within 30 minutes. No. (%) [95% CI]	35 (88)* [74-95]
Maximum reduction in VAS pain score within 30 minutes (mm) Median (IQR)	47 (28 to 56)
No. minutes to achieve a ≥13mm reduction in VAS pain score (n = 35) Median (IQR)	9.5 (5 to 13)
Patient-reported satisfaction (1 to 10) Median (IQR)	7 (5 to 9)

Table 3. Adverse events in patients receiving INK (n=40) *

	Mild Adverse Effects No. (%)	Bothersome Adverse Effects No. (%)
Patients experiencing an adverse effect †	22 (55)	9 (23)
Incidence of adverse effects §		
Dizziness	15 (38)	6 (15)
Feeling of unreality	10 (25)	4 (10)
Nausea	3 (8)	1 (3)
Fatigue	4 (10)	0
Headache	0	0
Changes in hearing	1 (3)	0
Mood change	3 (8)	0
General discomfort	0	0
Hallucination	0	0
Median patient-reported nasal irritation (1 to10 scale)	2 (IQR 1 to 4)	Range: 1 to 10

* 14 subjects reported no adverse effects
† Some subjects experienced both mild and bothersome adverse effects
§ Some subjects experienced more than one adverse effect.

Results

- Twenty-three subjects (58%) required 2 doses of INK.
- A clinically significant reduction in pain (i.e. VAS reduction of ≥ 13mm) was attained by 88% of this study population within 30 minutes.
- Nineteen of 40 subjects (48%) achieved this reduction by 5 minutes.
- The maximum reduction in VAS within 30 minutes was a median of 47mm.
- Bothersome adverse effects were noted in 9 patients (23%).
- No significant changes in O_2 saturation, blood pressure, or respiratory rate.
- All adverse effects were transient and did not require intervention.

Limitations

- Open-label: performance and detection bias.
- No comparison group: unable to assess magnitude of placebo effect, compare to standard care.
- Small sample size: limits generalizability and ability to identify uncommon adverse reactions.

Conclusions

- INK given at doses of 0.5 to 0.75 mg/kg reduces VAS pain scores to a clinically significant degree (i.e. ≥13mm reduction in VAS) within 30 minutes
- Adverse effects were mild and transient.
- INK may have a role in the provision of expedited, non-invasive analgesia to ED patients.

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