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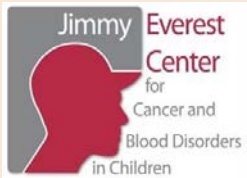
**Bill Meyer, MD**

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# Assessing the Efficacy of Inhaled Nitrous Oxide in Pediatric Oncology Patients Undergoing Repeated Invasive Procedures



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## Disclosure



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## Objectives



- Discuss the role of procedures in pediatric oncology patients and the need for procedural sedation
- Discuss the benefits and use of inhaled nitrous oxide
- Project development and design
- Preliminary Data

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## Acute Lymphoblastic Leukemia



- Most common pediatric cancer diagnosis
- 3,100 cases in the US each year
- 20 cases diagnosed at OU Children's last year
- The diagnosis and treatment of ALL requires multiple invasive procedures

Cancer.gov

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## Oncology Procedures

### Bone Marrow Biopsy/Aspirate



### Lumbar Puncture



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## Oncology Procedures

- Diagnosis
- Treatment Evaluation
- Treatment Administration
- Not unique to ALL patients

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## Current Standard of Practice

- IV Conscious Sedation
- Midazolam with Fentanyl OR Ketamine
- Effective sedation for most
- Fasting requirement (6 hours solids, 2 hours clear liquids)
- Recovery period 30-60 minutes and typically groggy rest of the day

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## Other Options

- Inhaled Nitrous Oxide (iNO)
- Decreases anxiety while providing mild analgesia and amnesia
- Noninvasive administration via the respiratory tract
- Quick onset and offset of action



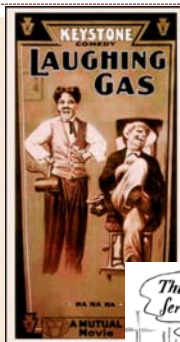
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## iNO

- Colorless, slightly sweet smelling gas
- Given in concentrations of 30-70%
- Peak effect in 1-2 minutes
- Offset of action within 1-2 minutes
- Patients back at mental status baseline within 3-5 minutes
- No fasting requirement
- No lasting effects throughout the day

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## History of iNO Use



- Discovered in 1772
- 1<sup>st</sup> gained popularity in the dental field 1800-1900s
- By late 1900s used widely in dental field with studies showing its effectiveness
- Early 2000s studies on its use in the emergency room emerged
- iNO was found to be effective for short painful procedures including laceration repairs, fracture reductions and lumbar punctures

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## iNO



- Over the past 20 years there have been multiple studies on the safety and effectiveness of iNO for procedural sedation in the pediatric population
- Primarily done in emergency rooms with little data on pediatric oncology patients or patients undergoing repeated procedures
- Some pediatric studies did include lumbar punctures, though they were few and not analyzed separately

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## Study Development



- Unique population of patients who would require repeated procedures
- Opportunity to directly compare two methods of sedation
- Alternative option of sedation that may be of benefit
- Obtain iNO in JEC clinic

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## Study Aims

- Primary Aims:

1. To compare the **efficacy** of iNO for sedation in pediatric oncology patients undergoing repeated lumbar punctures to current standard sedation.
2. To compare **patient and staff satisfaction** with iNO for sedation in pediatric oncology patients undergoing repeated lumbar punctures to current standard sedation.
3. To observe the **efficacy** of iNO for sedation in pediatric oncology patients undergoing bone marrow biopsy or aspirate.
4. To observe **patient and staff satisfaction** with iNO for sedation in pediatric oncology patients undergoing bone marrow biopsy or aspirate.

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## Study Aims

- Secondary Aim:

- To determine if patients **prefer** iNO or current standard sedation when undergoing lumbar puncture or bone marrow evaluation.

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## Study Design

- Randomized, non-blinded study with cross-over design, stratified based on standard sedation medications and procedure type

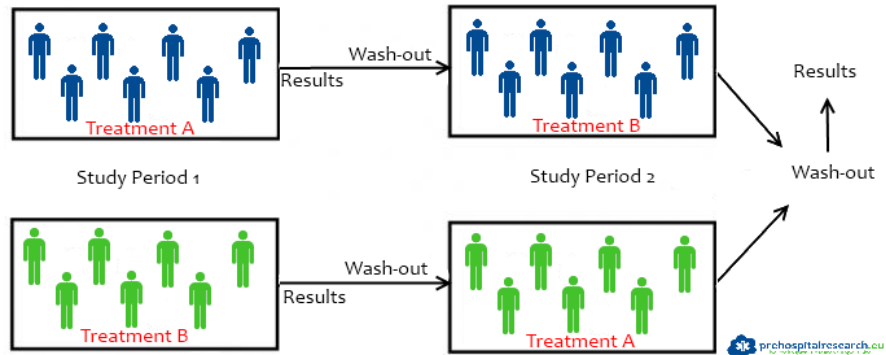
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## Study Design

- |                                                                                                                                                                                                                             |                                                                                                                                                                                                                                                                                                                                                                                                               |
|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"><li>• <b>Inclusion</b><ul style="list-style-type: none"><li>○ Ages 6mos-18yrs</li><li>○ Following a protocol that requires at least 2 LPs or 1 bone marrow evaluation</li></ul></li></ul> | <ul style="list-style-type: none"><li>• <b>Exclusions</b><ul style="list-style-type: none"><li>○ Prior adverse reactions to current standard sedation</li><li>○ iNO contraindications:<ul style="list-style-type: none"><li>✦ Pneumothorax</li><li>✦ Bowel Obstruction</li><li>✦ Middle ear disease</li><li>✦ Craniotomy</li><li>✦ Bleomycin</li><li>✦ Known Vit B12 deficiency</li></ul></li></ul></li></ul> |
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## Cross-over Design

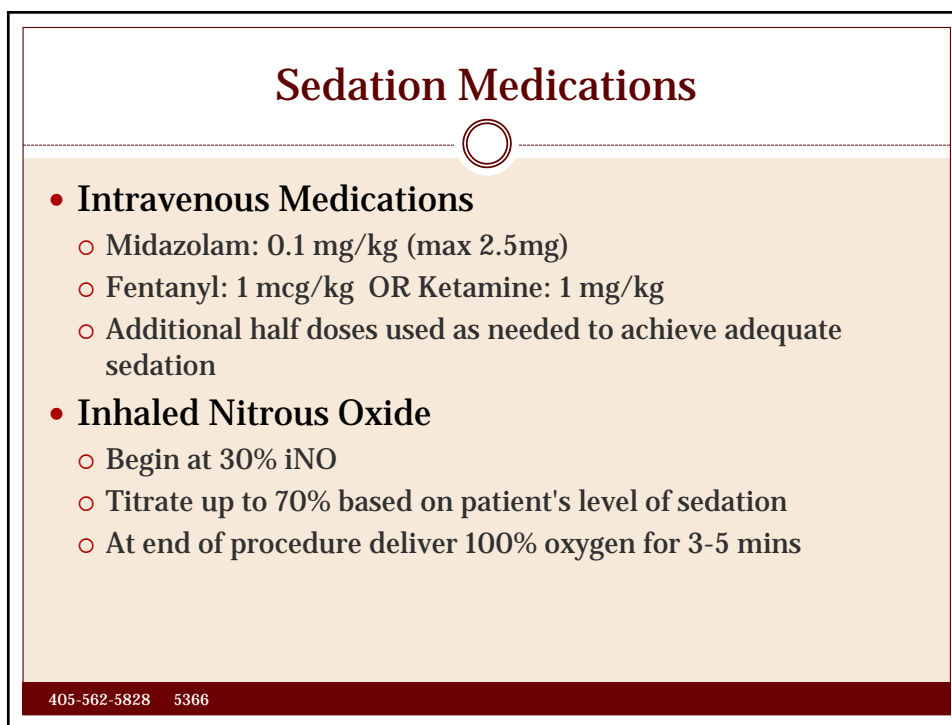
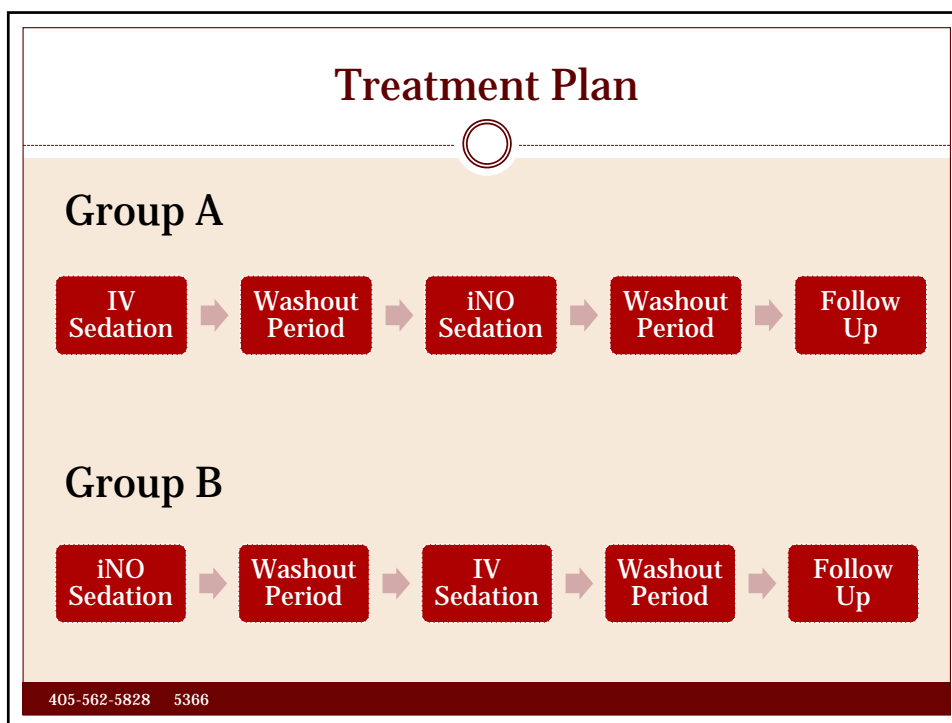


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## Rationale for Design

- **Randomized/Stratified**
  - To reduce bias of satisfaction scores based on order of drug administration, IV sedation meds and procedure type
- **Non-blinded**
  - Administration and fasting requirements are vastly different, preventing the ability to blind the intervention
- **Cross-over**
  - Decreases confounding factors by having each patient be their own control
  - Decreases the total number of patients needed to see a statistical difference

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## Supportive Care

- **Local anesthetics:**

- Topical lidocaine/prilocaine (EMLA) permitted
- Intradermal/subcutaneous lidocaine permitted
- Use of local anesthetics should be kept constant for both procedures

- **Child Life Specialist**

- Present for both procedures
- Helped prepare children for procedures and nitrous administration
- Offered distraction prior to and during procedures

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## Assessment

- **Survey**

- Used a previously validated Sedation Assessment Tool
- Questions about discomfort, procedure completion and side effects
- Permitted parental and nursing help with survey for younger patients

- **Follow-Up**

- Asked which method preferred and why

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**Appendix 2: PROcedural Sedation Assessment Survey (PROSAS)**

Study ID #: \_\_\_\_\_ Procedure Number: 1 2

**APPENDIX**

**Patient to complete the following survey by him- or herself with a family member or a nurse**  
How much discomfort did you experience during the procedure?

None		Slight discomfort		Moderate discomfort		Significant discomfort		Severe pain		
0	1	2	3	4	5	6	7	8	9	10

If having this procedure again in the future, how much sedation would you prefer to have?

Markedly less sedation		Somewhat less sedation		Same amount of sedation		Somewhat more sedation		Markedly more sedation		
-5	-4	-3	-2	-1	0	1	2	3	4	5

On a scale of 0-10, how much pain were you feeling before the procedure?

None		Slight pain		Moderate pain		Significant pain		Severe Pain		
0	1	2	3	4	5	6	7	8	9	10

On a scale of 0-10, how much pain are you feeling now?

None		Slight pain		Moderate pain		Significant pain		Severe Pain		
0	1	2	3	4	5	6	7	8	9	10

Do you have any nausea now?

☐ Yes  
☐ No

Other comments about your experience?

**Procedure Nurse (Name):** \_\_\_\_\_

Any episodes of O<sub>2</sub> desaturation <90% or leading to intervention?

☐ Yes  
☐ No

Any problematic changes in heart rate or blood pressure during intervention? (eg. systolic blood pressure <90, >160; heart rate <50, >120)

☐ Yes  
☐ No

Any hemodynamic or respiratory conditions that interrupted the procedure?

☐ Yes  
☐ No

**Physician (Name):** \_\_\_\_\_

Please rate the patient's cooperation during the procedure:

☐ Procedure aborted due to lack of cooperation  
☐ Procedure delayed/interrupted due to lack of cooperation  
☐ Adequately cooperative

Was the exam interrupted in any way due to patient discomfort?

☐ Yes  
☐ No

Did the patient report any pain during recovery?

☐ Yes  
☐ No

Did the patient report any nausea during recovery?

☐ Yes  
☐ No

Leffler et al

## Study Progress

- Enrolled 27 patients
- 25 Lumbar Punctures
- 2 Bone Marrow Biopsies
- 2 Deceased prior to study procedures
- Completed data collection on 2 bone marrow patients and 13 lumbar puncture patients

## Preliminary Data

Variable	Mean	Std Dev	Minimum	Lower Quartile	Median	Upper Quartile	Maximum
Nitrous	3.08	2.50	0.00	0.00	3.00	5.00	8.00
IV	1.15	1.95	0.00	0.00	0.00	1.00	6.00
Nitrous -IV	1.92	2.78	-1.00	0.00	0.00	4.00	8.00

Mean	Std Dev	Statistic	Pr >  S
1.92	2.78	15	0.03

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## Preference

- 10 patients preferred IV
  - 3 willing to try iNO again with higher concentration
  - 2 willing to try iNO again when older
- 6 patients preferred iNO

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## IV Preference



- “I could feel the poke with the NO.”
- “She seemed more anxious during the NO procedure, however the recovery was much easier. We would be willing to try NO again when she is older and better able to understand.”
- “I had a feeling of being trapped during the NO procedure. The recovery was great though, and I was able to drive that afternoon.”
- “I did not sedate well with the NO. I would be willing to try again at a higher concentration.”

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## iNO Preference



- “I didn’t have to be NPO and I didn’t have the hallucinations I had with the IV meds”
- “Eating the morning of the procedure is important to him. And the recovery was much better. He didn’t stumble all day like he does with the IV meds.”
- “She was awake more throughout the day following the procedure.”
- “She was awake right after the procedure.”

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## Bone Marrow Biopsy Results

- Low enrollment due to low numbers done in outpatient setting
- Compared iNO to prior procedures
- Neither preferred iNO
- One procedure was delayed due to difficulty with sedation

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## Limitations

- **Recruitment**
  - 27 enrolled, 16 declined
- **iNO new to clinic**
  - Nurses and providers uncomfortable increasing iNO concentration
  - Comfort level improved over the course of a few weeks
- **Number of prior procedures high**
  - Mean 8.9, Range 1-21
  - IV preference mean 12 (3-21)
  - iNO preference mean 8 (5-15)

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