

Research we can all use to Treat PONV *(Part I)*



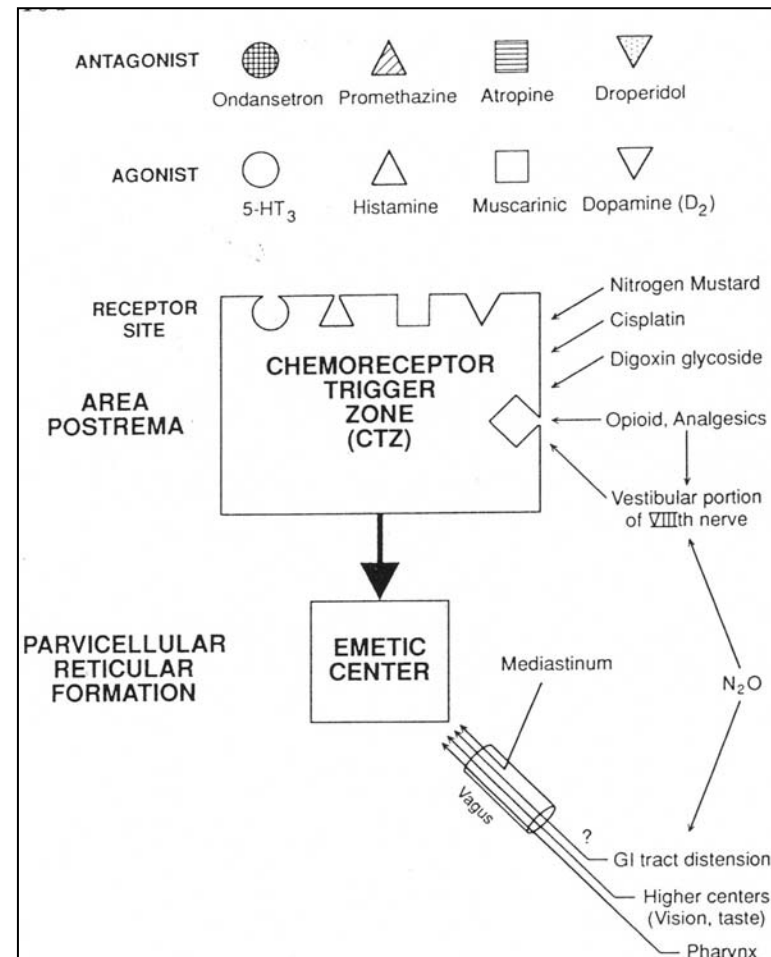
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SIGNIFICANCE

- ❑ Major problem facing patients and health care providers today.
- ❑ The incidence is as high as 75% (Thompson 1999).
- ❑ Average lost revenue to the institution of approximately \$415 per patient (Kenny 1994).
- ❑ Annual cost of \$253,270 - \$1,519,617
- ❑ Represents the lost revenue from performing 96,576 surgeries

BACKGROUND

- Nausea is initiated via chemo-receptor stimulation at the level of the CTZ which then transmits a signal to the emetic center when then stimulates a response via the Vagus nerve.
 - CTZ and emetic center located in the medulla
 - Primarily works in the area postrema
 - Typically therapy to treat and prevent PONV is administration of an agent that blocks this response at the level of the CTZ



CTZ Neurotransmitters

- Serotonin (5-HT₃) - ondansetron, dolasetron, granisetron
- Dopamine - metoclopramide, droperidol
- Histamine (H-1) - meclizine, hydroxyzine, promethazine
- Opioid antagonists - naloxone
- Cholinergic – scopolamine

PONV Treatment Modalities

- Conventional Treatments use medications that work specifically on the CTZ
 - Many possess characteristics that are unacceptable to many practices
 - Hypotension
 - Somnolence
 - Reversal of analgesia
 - Headache
 - Disinhibition
 - Expensive
- Problem
 - Finding an antiemetic that;
 - Is portable
 - Possesses a side effect profile that is acceptable and cost effective
 - *Is there a technique that could be widely used by everyone?*
- Possible Solution
 - Aromatherapy

Traditional Treatment/Prevention Methods

- Conventional Treatments
 - Anti-emetics
 - 5-HT3 Antagonists
 - HT-1 antagonists
 - Dopamine Antagonist
 - Dexamethasone
- TIVA
- Exclusion of N₂O from volatile admixture
- Non-conventional therapies
 - Acupressure
 - Aromatic Therapies
 - Folk Remedies

Aromatherapy

- Aromatherapy is the therapeutic use of plant-derived, aromatic essential oils to promote physical and psychological well-being
- Typical aromatherapy agents used to treat nausea and vomiting include
 - Peppermint- *relaxes smooth muscle in gut*
 - Ginger- *possible 5-HT3 blocker, works in CNS & GI*
 - Isopropyl Alcohol (IPA) - ?

Aromatherapy

- Multiple trials show effectiveness and ineffectiveness of aromatic regimens
 - Ginger
 - Morin AM, Betz O, Kranke P. et al. Is ginger a relevant antiemetic for PONV? *Anesthesiol Intensivmed Notfallmed Schol* 2004; 39(5): 281-5.
 - Pooled data from 6 randomized trials showed ineffectiveness from ginger application to control PONV
 - Peppermint & IPA
 - Anderson LA, Gross JB. Aromatherapy with peppermint, isopropyl alcohol or placebo is equally effective in relieving PONV. *J Perianesth Nurs* 2004; 19(1): 29-35.
 - Sample size of 33 patients
 - No perioperative or intraoperative controls indicated
 - Showed effectiveness from inhalation alone & failed to isolate effective treatment regimen

Aromatherapy

- ❑ Isopropyl Alcohol- unclear pharmacokinetics
 - Multiple flaws noted in earlier studies performed or studies performed exclusively on pediatric populations
- ❑ Studies:
 - Langevin P, Brown M. A simple, innocuous, and inexpensive treatment for PONV. (*abstract*). *Anes Analg* 1997; 84 (suppl): S15
 - Smiler BG, Srock M. Isopropyl alcohol for transport-related nausea (letter). *Anes Analg* 1998; 87: 1214
 - Wang S, Hofstadter M, Zain A. An alternative method to alleviate PONV in children. *J Clin Anesth* 1999; 11:231-34
 - **Winston AW, Rinehart RS, Riley GP, Vacchiano CA, Pellegrini JE. Comparison of inhaled isopropyl alcohol and intravenous ondansetron for treatment of PONV. *AANA J* 2003; 71(2): 127-32.**
 - **Cotton JW, Rowell LR, Hood RR, Pellegrini JE. A comparative analysis of isopropyl alcohol and ondansetron in the treatment of PONV from the hospital to the home setting. *AANA J* 2007; 75(1): 21-26**
 - **Pellegrini JE, Deloge J, Bennett J, Kelly J. Comparison of isopropyl alcohol inhalation versus promethazine in the treatment of patients identified as high risk for PONV. *AANA J* (April 2009 issue). (to be discussed in Part II)**

*Winston AW, Rinehart RS, Riley GP, Vacchiano CA, Pellegrini JE.
Comparison of inhaled isopropyl alcohol and intravenous ondansetron for
the treatment of PONV. AANA J 2003; 71(2): 127-32.*

- ❑ *Randomized, prospective IRB approved study*
- ❑ *100 ASA I-II women scheduled for laparoscopic GYN surgery under GETA*
 - *Demographic Variables*
 - ❑ *Age, weight, ASA Status, Medication History, Type of surgical procedure*
 - ❑ *Time Requirements*
 - *TOTAL*
 - *Anesthesia*
 - *Surgical*
 - *PACU*
 - *SDSU*
 - *Measured 0-10 Verbal Numeric Rating Scale for Nausea*
 - *"0" indicated "no nausea" and "10" indicated "worst imaginable nausea"*
 - *Measured at baseline, immediately upon nausea complaint and every 5 minutes following treatment regimen (IPA or ondansetron)*
 - *Administered IPA treatments every 5 minutes (up to 3 applications) and ondansetron 4 mg IV every 15 minutes (up to 8 mg total)*
 - *IPA subjects instructed to take 3 deep inhalations from a standard alcohol prep pad*



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- Measured Variables (*cont.*)
 - Incidence of Nausea
 - In PACU only
 - Time to 50% reduction in VNRS Scores
 - Calculated from VNRS score reported at onset of nausea
 - Incidence of Emesis
 - Emetic events separated by at least 1 minute
 - Analgesic Requirements
 - Overall perioperative requirements
 - Preoperative, Intraoperative & Postoperative

Hypothesis

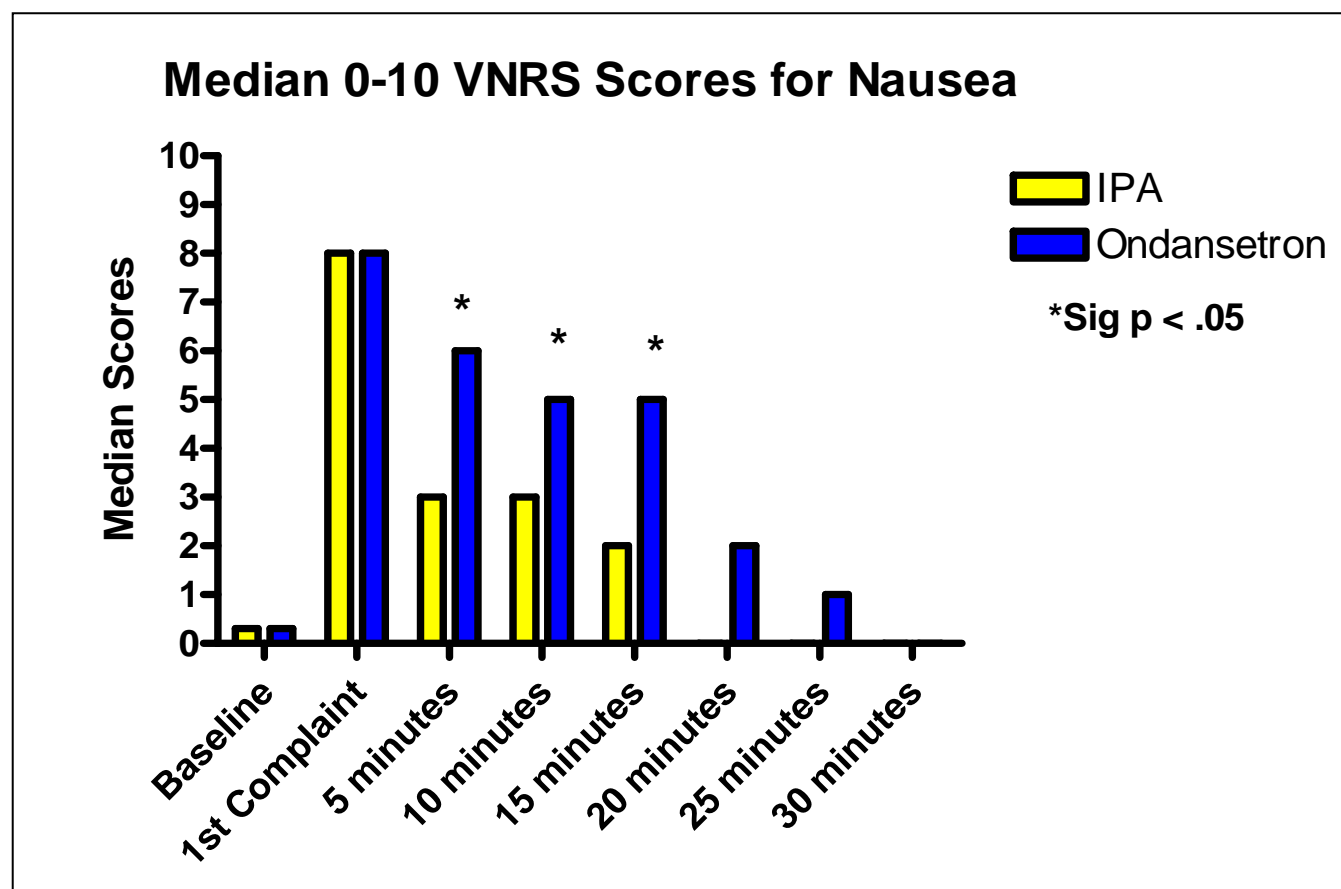
Subjects treated with inhaled isopropyl alcohol vapors will experience relief of PONV equal to that of subjects treated with intravenous ondansetron

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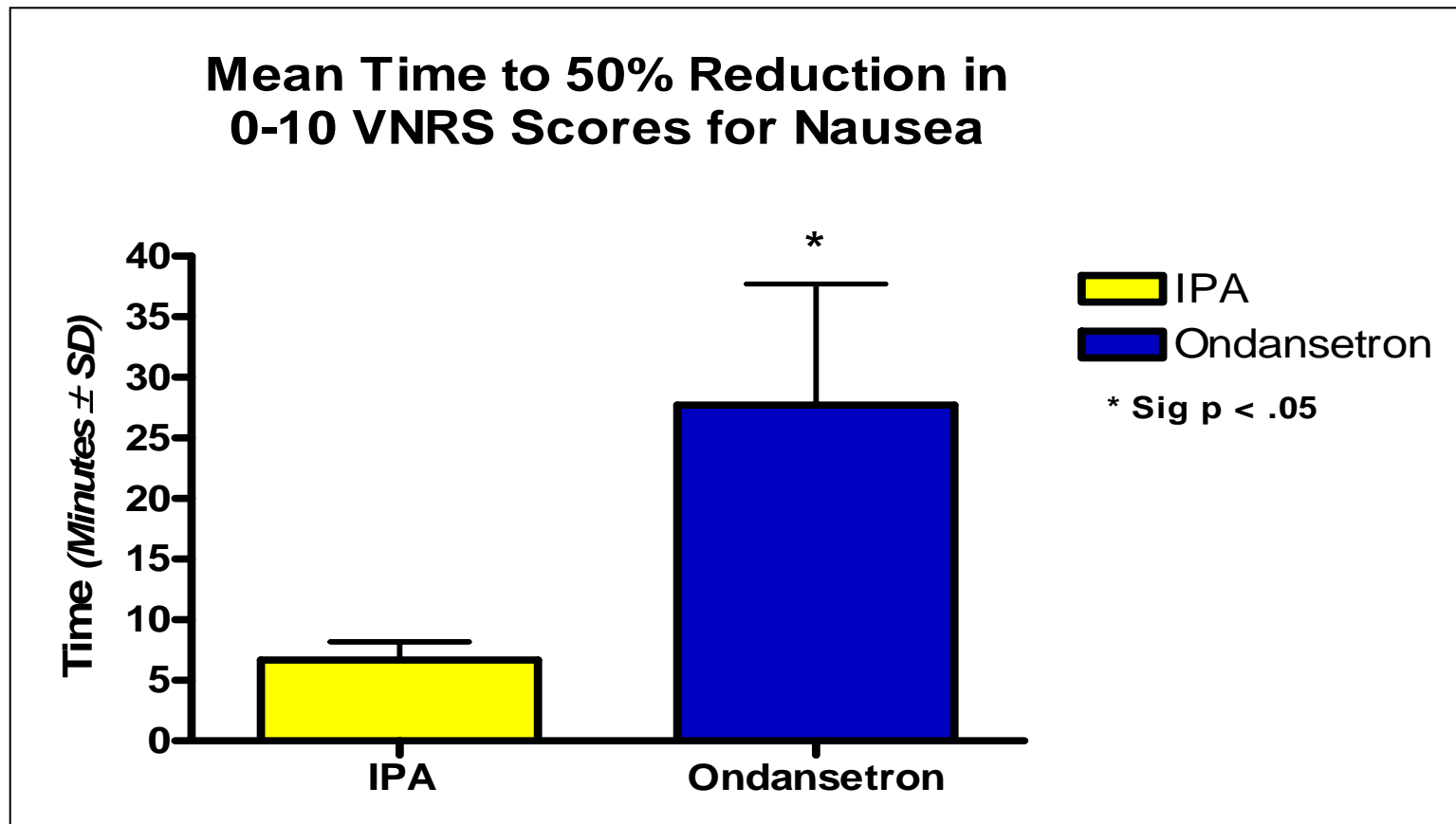
□ Results

- 100 subjects enrolled (50/group)
 - Nausea experienced disproportional between groups
 - 29 subjects in **IPA group** reported PACU nausea
 - 8 subjects required ondansetron rescue in PACU
 - 12 subjects in **Ondansetron group** reported PACU nausea
 - 2 subjects required promethazine rescue in PACU
- No differences in demographic variables, surgical or anesthesia times
- No differences in amount of analgesia administered at any time interval
 - Total Postoperative opioid use (Morphine Equiv)
 - IPA Group – 4.8 ± 1.45 mg
 - Ondansetron Group – 5.0 ± 2.0 mg
- Same anesthesia induction and maintenance used for all subjects

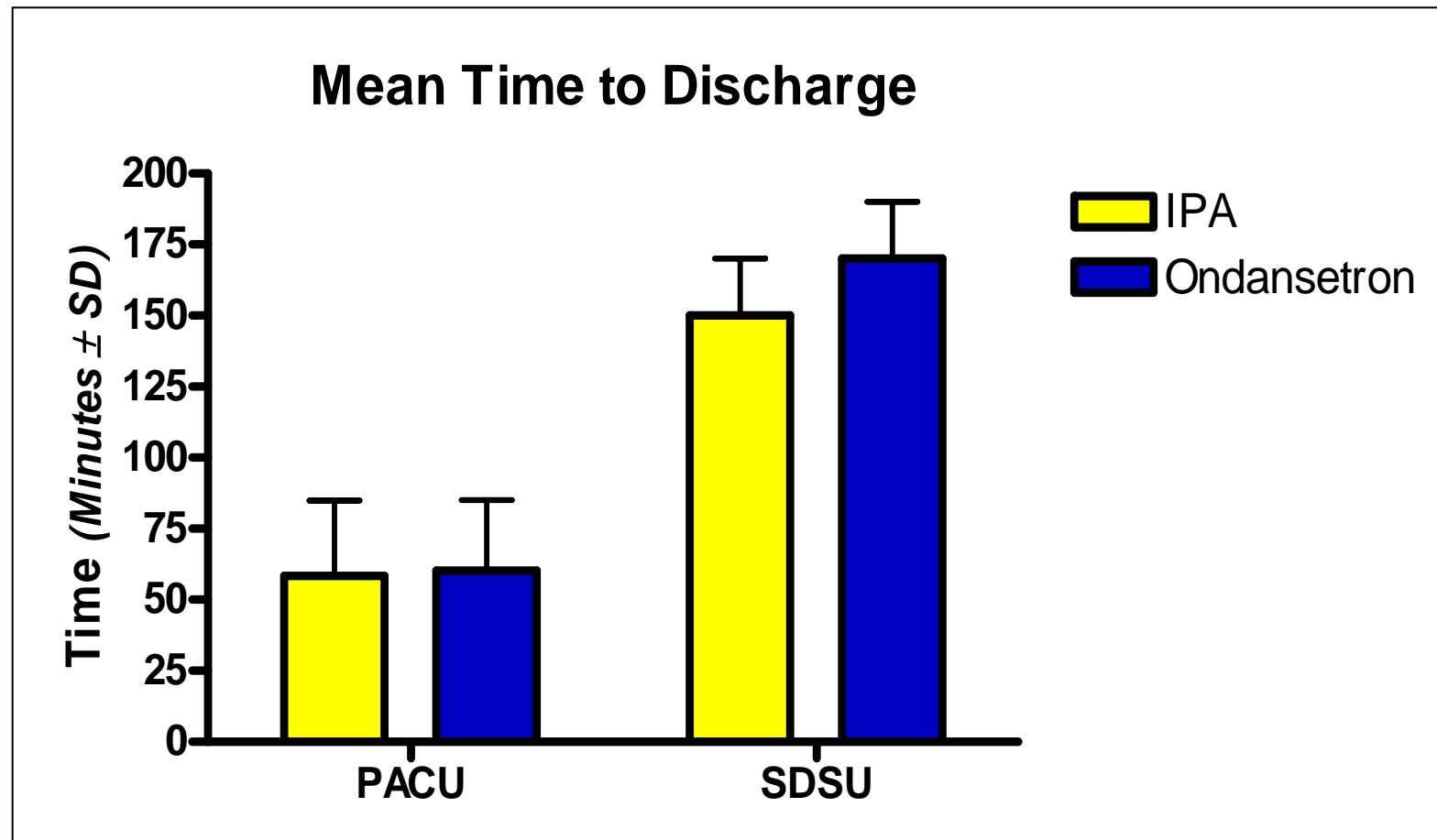
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□ Discussion

- Relief of symptoms comparable to ondansetron
 - Equality at 30 minutes
- Difficulty with controlling treatment regimens
 - PACU nurses resistant to administer IPA
 - Required continuous monitoring by investigators
 - *Possible respondent/practitioner bias*
 - *May have impacted use of IPA earlier than ondansetron*
- No data beyond PACU
 - Nausea reported to return following discharge in IPA group (*anecdotal*)
 - No use of IPA in SDSU and no determination if it would be useful following discharge to home
 - Plans made to repeat Winston et al study (*to validate results of study*) but incorporated IPA treatment regimen into 24 hour design

Cotton JW, Rowell LR, Hood RR, Pellegrini JE. A comparative analysis of isopropyl alcohol and ondansetron in the treatment of PONV from the hospital to the home. AANA J 2007; 75(1): 21-26.

- ❑ Study performed to address shortcomings of 1st clinical trial done by Winston et al.
- ❑ Research design same but time of treatment extended to 24 hours (*to measure utility in SDSU & Home settings*)
 - Same demographic profiles
 - ❑ 100 ASA I-II Female GYN patients enrolled
 - Same treatment regimens used for in-hospital
 - Treatment regimens added to facilitate home treatment
 - ❑ IPA group – primary Tx modality for both inpatient and outpatient use
 - 25 mg promethazine suppositories used for outpatient rescue
 - ❑ Ondansetron group – Ondansetron used for inpatient treatment; 25 mg promethazine suppositories used for outpatient treatment
- ❑ Research performed at same clinical site as Winston et al. study

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- Hypothesis – will an IPA antiemetic treatment regimen be effective in treating PONV beyond the PACU setting
 - 100 subjects randomized to receive IPA or ondansetron treatment in hospital
 - Those randomized to receive IPA provided with IPA pads for home use and instructed to “self-administer” IPA if nausea occurred in home setting
 - 25 mg promethazine suppository used for breakthrough PONV
 - Those randomized to receive ondansetron in the hospital setting were instructed to “self-administer” promethazine 25 mg suppository if nausea occurred in home setting
 - Protocol violations noted (*to be discussed separately*)

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	IPA	Ondansetron	Significance *p < .05
	N = 38	N = 34	
Age (y)	30.47 ± 5.7	31.15 ± 5.0	0.32*
Height (in)	68.74 ± 2.4	64.82 ± 2.5	0.266
Weight (kg)	78.87 ± 17.3	73.29 ± 12.6	0.245
Anesthesia Time (min)	95 ± 39.0	95.24 ± 36.9	0.684
Surgical Time (min)	47.97 ± 31.93	48.39 ± 30.29	0.895
PACU Time (min)	63.23 ± 30.2	62.62 ± 29.7	0.959

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- 100 subjects enrolled
 - 28 subjects disenrolled
 - Protocol violations
 - 12 subjects in ondansetron group administered IPA treatments in PACU/SDSU (*nurse driven*)
 - 6 subjects in IPA group administered other antiemetic agents in PACU before IPA treatments (*anesthesia provider driven*)
 - 10 subjects in IPA group that reported losing IPA pads in home prior to use
 - Only 1 subject required promethazine rescue in home
 - 72 subjects included in final analysis
 - 38 subjects in IPA group
 - 34 subjects in ondansetron group

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□ Incidence of Nausea

■ PACU

- 5 subjects (15%) had nausea requiring tx in ondansetron group
- 8 subjects (21%) had nausea requiring tx in IPA group

■ SDSU

- 15 subjects (44%) had nausea requiring tx in ondansetron group
- 21 subjects (55%) had nausea requiring tx in IPA group

■ Home

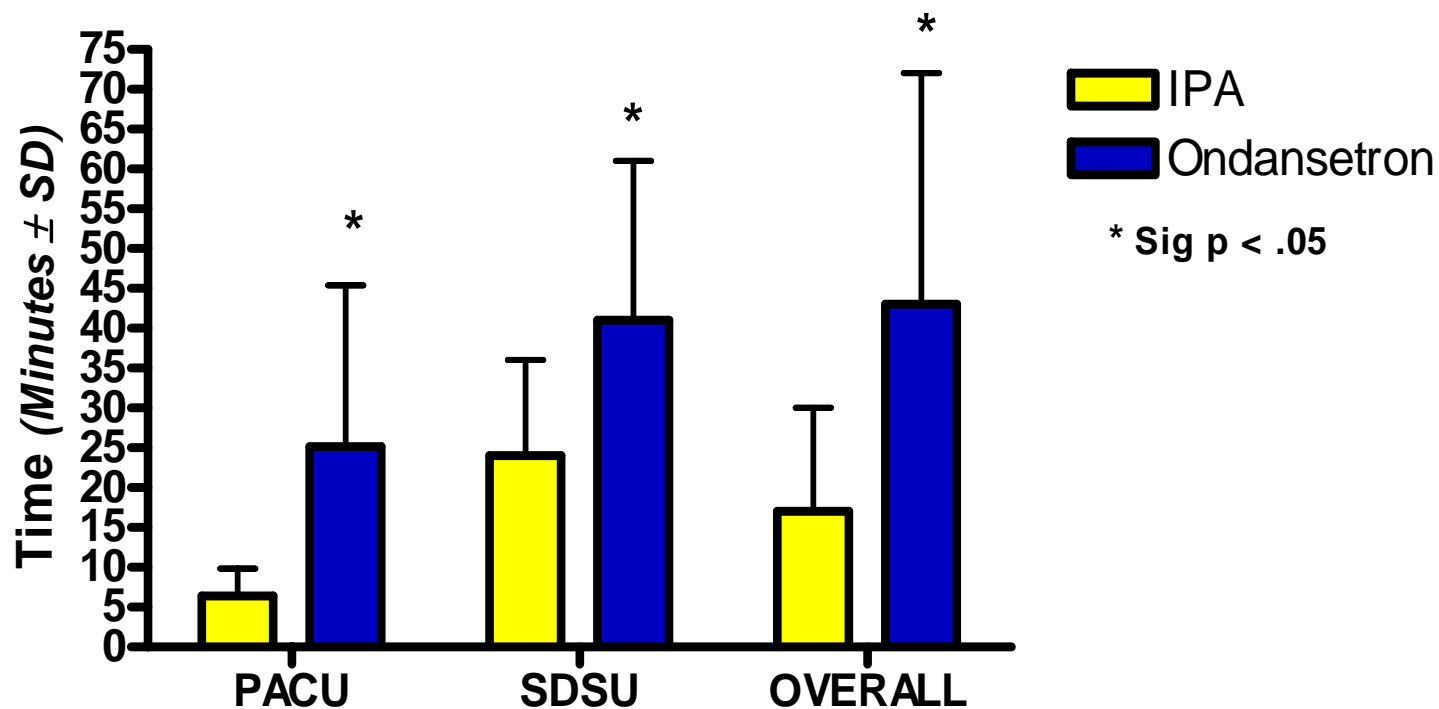
- Ondansetron group - 10 subjects (29%) reported nausea at home
 - 5 subjects (15%) required promethazine treatment for control of nausea
 - 4 subjects required both suppositories
- IPA group - 12 subjects (31%) reported nausea at home
 - 11 subjects reported using IPA for treatment at home
 - 1 subject used promethazine for treatment in deference to IPA

□ VNRS scores

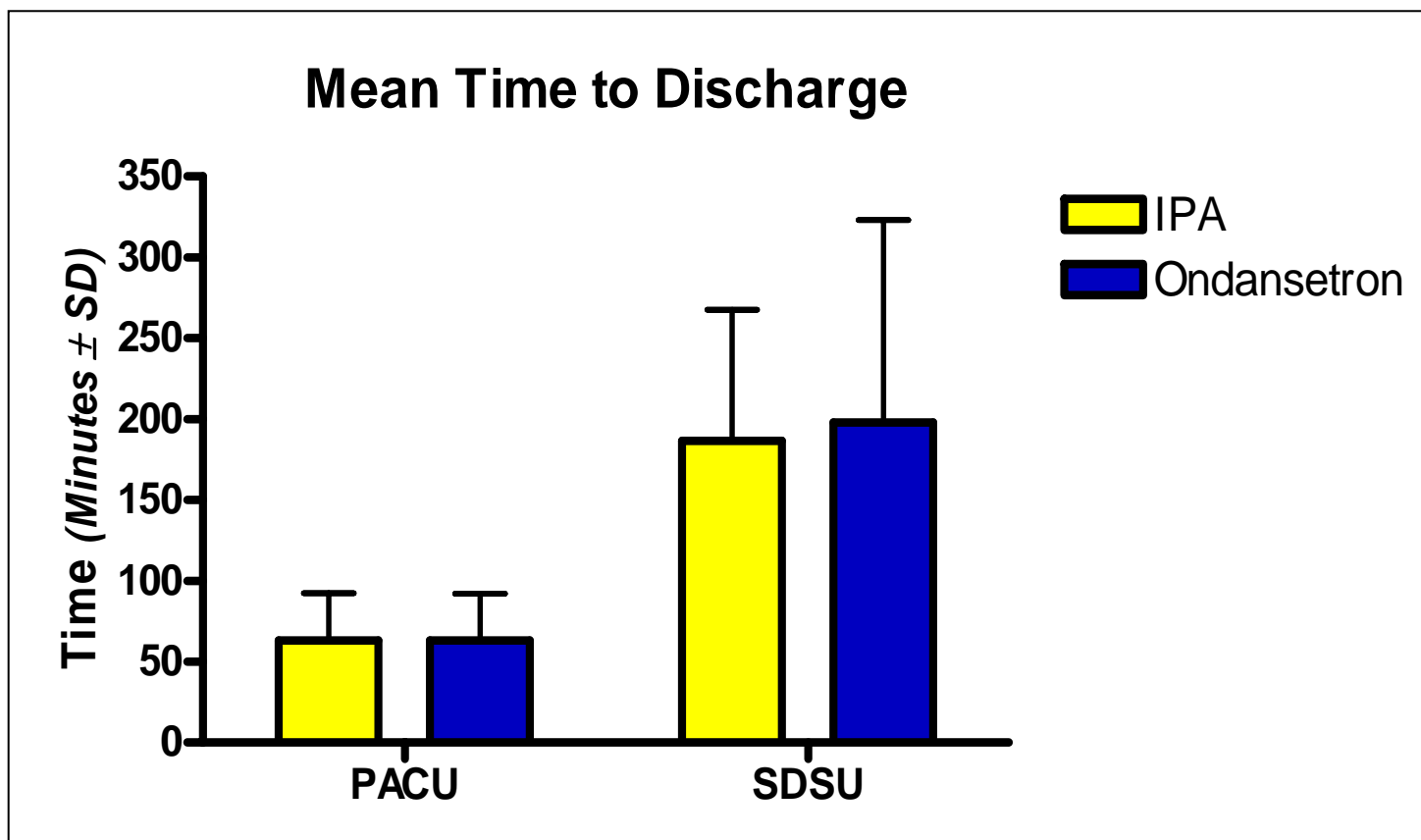
- Noted similar baseline and initial complaint scores between groups
 - Disproportionate time interval measurements used
 - Every 5 minutes in PACU Setting
 - Every 15 minutes in SDSU Setting
 - Subjective measurement used in HOME setting

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Time to 50% reduction in VNRS scores for Nausea



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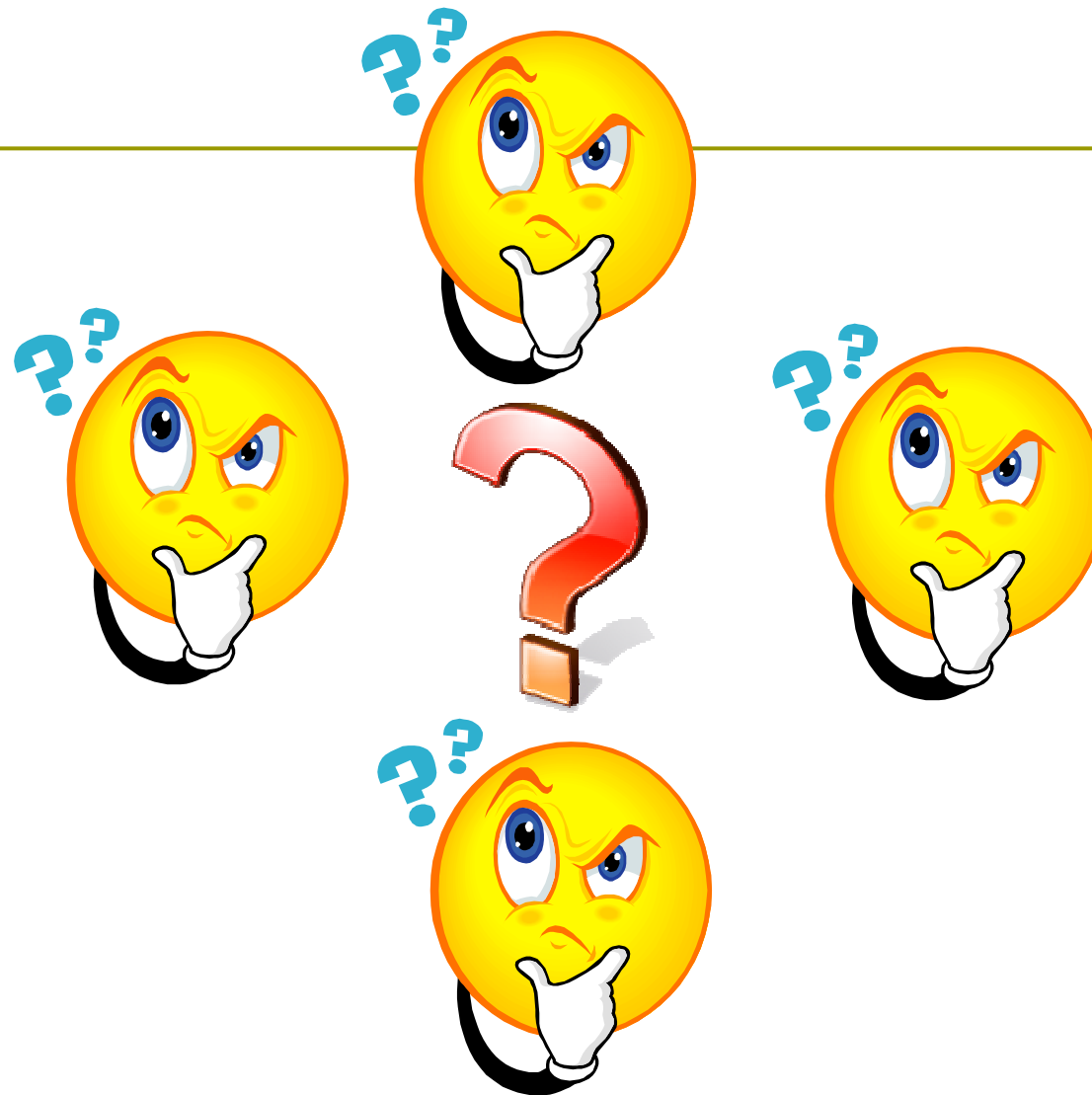
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□ Discussion

- No impact on discharge times
 - Departmental policy?
- Logistical problems encountered
 - Inverse to Winston et al study
 - Nurses preference for IPA over ondansetron
 - Anesthesia providers reluctance to use IPA
 - Winston study most anesthetics performed by investigators
- High satisfaction scores for IPA users in home setting
- Possible reluctance to self-administer promethazine suppositories in home setting
 - Consider SL ondansetron

Conclusion

- ❑ IPA data validated by noted similarities in time to 50% reduction in PACU VNRS scores between studies
- ❑ IPA is a viable option for treatment in any setting
- ❑ IPA is safe to use concurrently with other antiemetics
- ❑ IPA is easy to apply, safe to use and very inexpensive
 - IPA shown to be safe, reliable and inexpensive
 - ❑ Conclusion that IPA should possibly be considered a first line drug
 - Viable to use in home setting
 - ❑ Possible discharge treatment regimen
- ❑ No data regarding use with concomitant antiemetics in high risk population
 - ❑ Future study planned
 - Study performed & results will be discussed in Part II



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