# Increasing Patient Comfort - Based in the Classic Literature with Current Literature Updates

## Russell Bunting Periodontal Society

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# Topics:

- Oral Sedation (Nitrous Oxide)
- IV Sedation
- Local Anesthesia
- Post-Operative Analgesics

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# 75%

- of all medical emergencies in the dental office have a stress or anxiety component.

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# Medical History Review

- Determine sedation candidates at the evaluation appointment, not treatment appointment !!!

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# Choices:

- $N_2O/O_2$:
- Patients cannot get a ride home.
- Emergency patients.
- Very short time needed (just for the injection).
- Only light sedation needed.

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# Oral Sedation:

- Must have a ride home.
- Don't have $N_2O/O_2$ in the office.
- Patients (or practitioner) doesn't like the nasal hood.
- Amnesia (+/-).
- Only light sedation needed.



# IV Sedation:

- Precise control over the level of sedation.
- No extraneous equipment around the face (nasal cannula).
- Ability to reverse the drug.
- Amnesia
- Safety !!!!!

# General Anesthesia:

- Someone that doesn't want to be in the dental office:
- Extreme phobic
- Pre-cooperative children
- Intellectual disability

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# NOTICE:

- The use of sedation or anesthesia is **patient** driven, not **procedure** driven.

10

Oral sedation. Dionne R Compend Contin Educ Dent (1998 Sep) 19(9):868-70, 872, 874.

- "I fear a trip to the dentist more than I fear death."



# Oral Sedation:

- With Any Type of Sedation:
- Titration = Safety

# Oral Sedation

- With oral sedation, (safe) titration must be done on multiple appointments.
- Adding additional oral drug when the original amount has produced insufficient sedation may lead to extreme over sedation.

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# How and Why ?

- Drugs are not absorbed from the stomach, they must get to the intestine.
- With anxiety, there is delayed gastric emptying.
- Orally administrated sedatives may not be absorbed at the time anticipated.
- Both first and second doses may 'peak' at the same time leading to over sedation.

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## Alprazolam:

- Xanax®
- Onset: 45 minutes
- Peak: 1 to 2 hours
- Dose: 0.25 - 1 mg

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## Alprazolam:

- Clinical duration of action (NOT half-life): 4-6 hours.
- A reasonable choice when a long duration of action drug is needed.

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# Alprazolam

- XANAX Tablets (alprazolam) are indicated for the management of anxiety disorder . . . or the short-term relief of symptoms of anxiety.
- Treatment for patients with anxiety should be initiated with a dose of 0.25 to 0.5 mg.
- The elderly may be especially sensitive to the effects of benzodiazepines.

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# Lorazepam:

- Ativan®
- Onset of 1 hour
- Peak 2 hours
- Clinical duration of action = 6 - 8 hours
- Dose => 1 - 2 mg

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# Lorazepam

- For anxiety, most patients require an initial dose of 2 to 3 mg/day given b.i.d. or t.i.d.
- For insomnia due to anxiety or transient situational stress, a single daily dose of 2 to 4 mg may be given, usually at bedtime.
- For elderly or debilitated patients, an initial dosage of 1 to 2 mg/day in divided doses is recommended, to be adjusted as needed and tolerated.



# Zolpidem

- Ambien®
- Onset: 20 minutes
- Peak: 30 minutes
- Dose: 5 - 10 mg
- Duration: 2 - 3 hours

# Zaleplon

- Sonata®
- Onset: 30 minutes
- Peak: 1 hour
- Dose: 10 mg
- Clinical duration of action: 90 minutes

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Zaleplon (Sonata) Oral Sedation for Outpatient Third Molar Extraction Surgery. Ganzberg, S Dietrich, T Valerin, M Beck, FM Anesthesia Progress Volume 52, Number 4 December 2005 pages 128-131.

- Zaleplon (10 mg) was compared with triazolam (0.5 mg) for oral sedation in a third molar surgery model using a double-blind crossover design.
- Factors such as anxiolysis, amnesia, and quality of sedation were assessed.
- Of the 14 participants who completed the study, zaleplon sedation was found to be similar to triazolam sedation in all regards except that recovery from zaleplon was more rapid.

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## Triazolam:

- Halcion®
- Onset: 30 minutes
- Peak: 1 hour
- Duration: 2-3 hours

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## Triazolam (sublingual administration):

- Halcion®
- Onset: 20 minutes
- Peak: 45 minutes
- Duration: 2-3 hours
- 28% higher blood level than oral.

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# Halcion® Package Insert

- The recommended dose for most adults is 0.25 mg before retiring.
- A dose of 0.125 mg may be found to be sufficient for some patients (e.g., low body weight).
- A dose of 0.5 mg should be used only for exceptional patients who do not respond adequately to a trial of a lower dose since the risk of several adverse reactions increases with the size of the dose administered.
- **A dose of 0.5 mg should not be exceeded.**

25

Pharmacokinetics and Clinical Effects of Multidose Sublingual Triazolam in Healthy Volunteers. J Clin Psychopharmacol 2006;26:4-8
Jackson DL, Peter Milgrom P, Heacox GA, Kharasch ED

- This study was designed to determine the pharmacokinetics and sedative effects of incremental sublingual dosing of triazolam (total, 1.0 mg) in healthy adults.
- This study was funded by the Oral Sedation Research Fund of the Dental Organization for Conscious Sedation.

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# Jackson

- Ten healthy adult volunteers received sublingual triazolam (0.25 mg) followed by additional doses after 60 (0.50 mg) and 90 (0.25 mg) minutes.
- The timing and amount of the three predetermined incremental triazolam doses were based on conversations with networks of dentists who use incremental triazolam dosing strategies as part of their clinical practice.



# Jackson

- Plasma triazolam concentrations, clinical effects and bispectral index score (BIS) were measured intermittently for three hours.
- Triazolam concentrations gradually increased with time in all subjects and plasma triazolam concentrations and drug effects were greatest in all subjects at the end of the three hour evaluation period.
- Triazolam concentrations were still increasing at the time of the last measurement (180 minutes), thus no maximum triazolam concentration nor minimum BIS value could be determined.

## Jackson

- Eight of the subjects had Observer's Assessment of Alertness/Sedation scores consistent with the definition of deep sedation or general anesthesia.
- Four of the subjects had BIS scores less than 60.
- It should be noted that a bispectral index score of 60 is regarded as the threshold for general anesthesia.

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## Jackson

- **The current clinical application of incremental dosing with sublingual triazolam in dentistry has moved ahead of an adequate research foundation.**

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# My Recommendation:

- Fast Onset:
- Ambien®
- Administer 5-10 mg* orally, 30 minutes before the procedure
- Titrate nitrous oxide as needed



# My Recommendation:

- Fast Recovery:
- Sonata®
- Administer 10 mg* orally, 1 hour before the procedure
- Titrate nitrous oxide as needed
- *5 mg for the elderly

# My Recommendation:

- Long Appointment:
- Xanax®
- Administer 0.5 mg orally, 2 hours before the procedure
- Titrate nitrous oxide as needed

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# My Recommendation:

- Very Long Appointment:
- Ativan®
- Administer 1 - 2 mg orally, 2 hours before the procedure
- Titrate nitrous oxide as needed

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# My Recommendation:

- Typical Appointment:
- Triazolam®
- Administer 0.25 mg* sublingually, 1 hour before the procedure
- Titrate nitrous oxide as needed

* * upon failure, dose may be increased not to exceed 0.5 mg

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# IV Sedation

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# Versed

Versed® (midazolam) was FDA approved on December 20, 1985.

The brand name Versed® was withdrawn from the US market on July 28, 2003.

**Versed® has not existed for almost 15 years !!!**



# Package Insert

**Healthy Adults Below the Age of 60**: Titrate slowly to the desired effect, (e.g., the initiation of slurred speech). Some patients may respond to as little as 1 mg. No more than 2.5 mg should be given over a period of at least 2 minutes. Wait an additional 2 or more minutes to fully evaluate the sedative effect. If further titration is necessary, continue to titrate, using small increments, to the appropriate level of sedation. Wait an additional 2 or more minutes after each increment to fully evaluate the sedative effect. A total dose greater than 5 mg is not usually necessary to reach the desired endpoint.

If narcotic premedication or other CNS depressants are used, patients will require approximately 30% less midazolam than unpremedicated patients.

# Package Insert

**Patients Age 60 or Older, and Debilitated or Chronically III Patients**: Because the danger of hypoventilation, airway obstruction, or apnea is greater in elderly patients and those with chronic disease states or decreased pulmonary reserve, and because the peak effect may take longer in these patients, increments should be smaller and the rate of injection slower.

Titrate slowly to the desired effect, (e.g., the initiation of slurred speech). Some patients may respond to as little as 1 mg. No more than 1.5 mg should be given over a period of no less than 2 minutes. Wait an additional 2 or more minutes to fully evaluate the sedative effect. If additional titration is necessary, it should be given at a rate of no more than 1 mg over a period of 2 minutes, waiting an additional 2 or more minutes each time to fully evaluate the sedative effect. Total doses greater than 3.5 mg are not usually necessary.

If concomitant CNS depressant premedications are used in these patients, they will require at least 50% less midazolam than healthy young unpremedicated patients.



# Specific Agents:

- Opioids:
- Meperidine (Demerol®)
- Hydromorphone (Dilaudid®)
- Fentanyl (Sublimaze®)

# Meperidine

- Onset 1 minute, peak 5 minutes, duration 1 hour
- Other:
- - histamine release
- - euphoria
- - anticholinergic effects
- - MAO inhibitors

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# Meperidine

- Two Uses:
- As a one hour opioid during a procedure
- - dose: 20-100 mg
- BBG
- - dose: 25 mg

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# Hydromorphone

- Dilaudid®
- Onset 1 minute, peak 5 minutes, duration 2-3 hours
- A "rapid onset morphine"
- Dose 0.2 - 0.6; up to 1.0 mg



# Hydromorphone

- About 8-fold more potent than morphine (i.e. 1 mg hydromorphone = 8 mg morphine)
- No active metabolites, no histamine release
- **No APNEA !**

# Fentanyl

- Onset 1 minute, peak 2 minutes, duration 30 minutes
- Dose: 20 - 60; up to 100 ug
- Other:
- - Chest wall rigidity
- Receptor Types:
- - μ+++



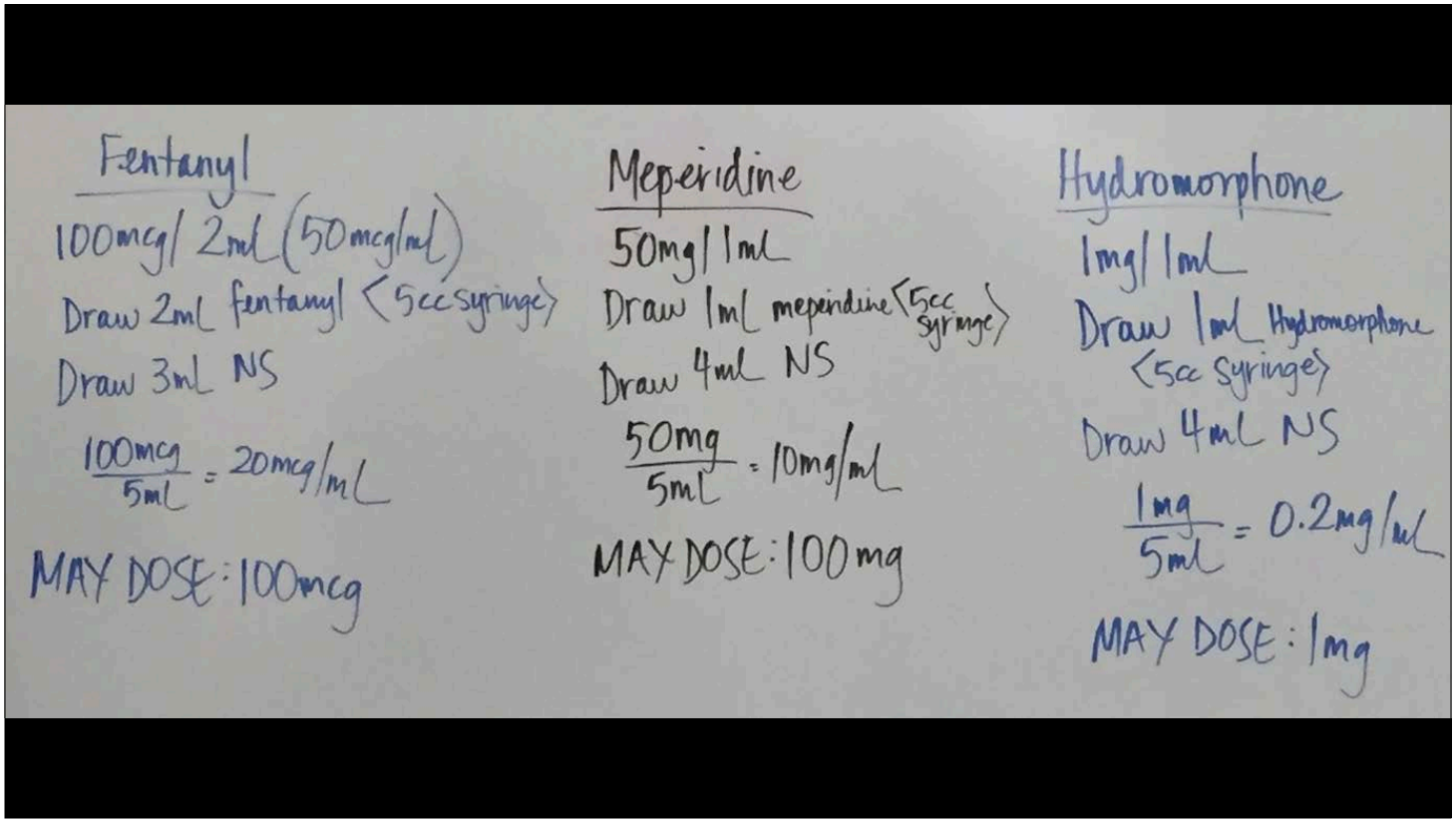
# Rate of Administration

- ALL SEDATIVE AGENTS (benzodiazepines and opioids) are administered at a rate of 1 mL/min

# Initial Titration

In your initial titration (first few minutes), if you get to 10 mg of midazolam plus the maximum opioid and the patient is still not properly sedated, in my opinion that has to be considered a failure





# Local Anesthesia



# Maximum Recommended Doses

- Articaine - 7mg/kg
- Bupivacaine - => 90 mg
- Lidocaine - 7mg/kg => 500 mg
- Lidocaine - 4.5 mg/kg => 300 mg
- Mepivacaine - 6.6 mg/kg => 400 mg
- Prilocaine - 8 mg/kg => 600 mg

## Needle Gauge

- Positive aspiration is directly correlated to needle gauge
- Larger gauge needles do not deflect
- Larger gauge needles do not break

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## Needle Gauge

- Patients cannot tell the difference between 25, 27 and 30 gauge needles.

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## Needle Dimensions

- Outside diameter:
- 30 gauge => 0.3 mm
- 27 gauge => 0.4 mm
- 25 gauge => 0.5 mm

53

Meechan, JG. Howlett, PC. Smith, BD. Factors influencing the discomfort of intraoral needle penetration. Anesth Prog 52:91–94 2005.

- A number of studies have shown that the gauge of dental needle is irrelevant in relation to injection discomfort.

54

Brownbill, JW. Walker, PO. Bourcy, BD. Keenan, KM. Comparison of inferior dental nerve block injections in child patients using 30-gauge and 25-gauge short needles. Anesth Prog 34:215-219 1987.

- Inferior dental nerve block injections are painful, and it is readily thought that thinner needles (30-gauge) may be less painful than thicker needles (25-gauge).
- With adult dentist subjects, no difference was found in the pain experienced by the penetration of thin and thick gauge needles.
- The large number of very low scores in both groups indicates that children do not think that inferior dental nerve block injections hurt very much.

55

Brownbill, JW. Walker, PO. Bourcy, BD. Keenan, KM. comparison of inferior dental nerve block injections in child patients using 30-gauge and 25-gauge short needles. Anesth Prog 34:215-219. 1987.

- Taking into consideration the three variables that were measured and reported, it can be concluded logically that the 25-gauge and the 30-gauge short needles exhibit little or no clinical differences when used to give inferior dental nerve block injections in children. There is no evidence to suggest that 30-gauge needles should be used in preference to 25-gauge needles.

56

## Malamed, SF. Reed, KL. Poorsattar, S. Needle Breakage: incidence and prevention. Dent Clin N Am 54:745–756. 2010.

- There is movement amongst dentists toward the use of smaller diameter needles on the assumption that they are less traumatic to the patient than larger diameter needles.
- Studies dating back to 1972 show this assumption to be unwarranted. Hamburg reported that patients are unable to differentiate among 23-, 25-, 27-, and 30-gauge needles.
- Fuller and colleagues reported no significant differences in perception of pain produced by 25-, 27- and 30-gauge needles during inferior alveolar nerve blocks in adults. Lehtinen compared 27- and 30-gauge needles and found that although insertion of the 30-gauge needle required significantly less force, the difference in pain perception was less remarkable.

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## Malamed, SF. Reed, KL. Poorsattar, S. Needle Breakage: Incidence and Prevention. Dent Clin N Am 54:745–756. 2010.

- Pogrel reported on 16 patients whom he evaluated following needle breakage in a 25-year period (1983–2008). Fifteen patients had received IANB and one a PSA. Thirteen of the 16 needles were 30-gauge short and 3 were 27-gauge short.
- Independent of the cited literature, two of the authors have seen a total of 51 cases; one has been involved in 34 cases that progressed to litigation in which broken dental needle fragments have remained within the soft tissues of the patient receiving the injection.

58

## Malamed, SF. Reed, KL. Poorsattar, S. Needle Breakage: Incidence and Prevention. Dent Clin N Am 54:745–756. 2010.

- Thirty-three of these events involved 30-gauge short needles; a 27-gauge short was involved in the other case. All but one involved administration of an IANB. The other case was a PSA nerve block.
- The second author has been involved with 17 cases, all of which were both IANB and 30-gauge short needles.
- A manufacturer of dental local anesthetic needles reported that in a 6-year period (1997–2002) 27 doctors contacted them reporting instances of broken dental needles. All involved 30-gauge short needles.

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## Malamed, SF. Reed, KL. Poorsattar, S. Needle Breakage: Incidence and Prevention. Dent Clin N Am 54:745–756. 2010.

**Table 3**
**Needle purchases, US dentistry, 2006**

| | | Data Provided by | | | |
|---|---|---|---|---|---|
| Gauge | Length | Sullivan-Schein Inc. (2006) | | Septodont Inc. (2006) | |
| 25 | Short | <1% | 1% | 0.6% | 3% |
| | Long | 1% | | 2.3% | |
| 27 | Short | 10% | 42% | 13% | 38% |
| | Long | 32% | | 25% | |
| 30 | Short | 50% | 56% | 51% | 59% |
| | Extra short | 6% | | 8% | |

60

Malamed, SF. Reed, KL. Poorsattar, S. Needle Breakage: Incidence and Prevention. Dent Clin N Am 54:745–756. 2010.

- Although rare, dental needle breakage can, and does, occur. Review of the literature and personal experience of the authors brings into focus several commonalities which when avoided can minimize the risk of needle breakage with the fragment being retained from occurring. These include:

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Malamed, SF. Reed, KL. Poorsattar, S. Needle Breakage: Incidence and Prevention. Dent Clin N Am 54:745–756. 2010.

- Do not use short needles for IANB in adults.
- Do not use 30-gauge needles for IANBs in adults or children.
- Do not bend needles when inserting them into soft tissue.
- Do not insert a needle into soft tissue to its hub, unless it is absolutely essential for the success of the injection.
- Observe extra caution when inserting needles in younger children or in extremely phobic adult or child patients.

62

Gordon, SM. Brahim, JS. Dubner, R. McCullagh, LM. Sang, C. Dionne, RA. Attenuation of pain in a randomized trial by suppression of peripheral nociceptive activity in the immediate postoperative period. Anesth Analg 95:1351–7. 2002.

- Subjects were randomly allocated to one of four groups: preoperative 2% lidocaine, postoperative 0.5% bupivacaine, both, or placebo injections.
- General anesthesia was induced and third molars extracted. Pain was assessed over 4 h and at 24 and 48 h.

63

Gordon, SM. Brahim, JS. Dubner, R. McCullagh, LM. Sang, C. Dionne, RA. Attenuation of pain in a randomized trial by suppression of peripheral nociceptive activity in the immediate postoperative period. Anesth Analg 95:1351–7. 2002.

- Pain was decreased in the immediate postoperative period in the bupivacaine groups, whereas it increased in the lidocaine group over time.
- Pain intensity was less 48 h after surgery in the groups whose postoperative pain was blocked by the administration of bupivacaine, but no effect was demonstrated for the preoperative administration of lidocaine alone.

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# "That local anesthetic didn't work very long; he metabolized it quickly."

- Distribution (Onset): The time from administration to the site of action (sodium channel).
- Duration: The time the drug is bound to the receptor site.
- Redistribution: The drug comes off the receptor site and travels to other areas of the body.
- Metabolism (Biotransformation): The drug is changed or broken down by the body.

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# "You should use a drug with a short half-life so it won't last very long."

- Half-Life
- Alpha = Distribution
- Beta = Elimination
- Gamma = discussed only with radioactive agents.
- Context Sensitive = the time taken for blood plasma concentration of a drug to decline by one half after an infusion designed to maintain a steady state (i.e. a constant plasma concentration) has been stopped. The "context" is the duration of infusion.

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# Beta Half-Life

- Articaine: 43.8 minutes with 1:100,000 epinephrine; 44.4 minutes with 1:200,000 epinephrine.
- Lidocaine: 1.5 to 2.0 hours.

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# Clinical Duration of Action

- Articaine: Complete anesthesia lasts approximately one hour for infiltrations and up to approximately two hours for nerve block.
- Lidocaine: Xylocaine™ dental injections with epinephrine 1:100,000 or 1:50,000 provide an average pulp anesthesia of at least 60 minutes with an average duration of soft tissue anesthesia of approximately 2.5 hours.

68

Kanaa, MD. Meechan, JG. Corbett, IP. Whitworth, JM. Speed of injection influences efficacy of inferior alveolar nerve blocks: A double-blind randomized controlled trial in volunteers. JOE Volume 32, Number 10, October 2006.

- Depositing 2 mL of solution, either slowly over 60 seconds or rapidly over 15 seconds. To blind the patient to the procedure, the needle remained in place for 45 seconds before depositing solution in the case of rapid injection.
- Overall, slow IANB injection produced significantly more episodes of no pulp response than rapid IANB injection in first molars, premolars and lateral incisors.
- In the present study, IANB injections were significantly more comfortable when given slowly than rapidly.

69

Kanaa, MD. Meechan, JG. Corbett, IP. Whitworth, JM. Speed of injection influences efficacy of inferior alveolar nerve blocks: A double-blind randomized controlled trial in volunteers. JOE Volume 32, Number 10, October 2006.

**TABLE 1.** Onset of pulpal anesthesia for first molars, first or second premolars, and lateral incisors after slow and rapid IANB

| Injection speed | Onset of pulpal anesthesia (min) | | | | | |
|---|---|---|---|---|---|---|
| | First molar | | Premolar | | Lateral incisor | |
| | Mean | SD | Mean | SD | Mean | SD |
| Slow IANB | 5.4 | 3.2 | 8.9 | 8.2 | 13.3 | 9.8 |
| Rapid IANB | 6.7 | 7.1 | 11.1 | 9.7 | 11.6 | 10.1 |
| Wilcoxon signed ranks | $p = 0.98$ | | $p = 0.30$ | | $p = 0.42$ | |

IANB, inferior alveolar nerve block.

70

## Kudo, M. Initial injection pressure for dental local anesthesia: Effects on pain and anxiety. Anesth Prog 52:95–101. 2005.

- The operator used approximate injection speeds of either 30 or 160 s/mL to inject 0.5 mL of local anesthetic solution submucosally. The mean injection time was 16.35 seconds for the high-speed group and 94.57 seconds for the low speed group.
- There was a significant correlation between the intensity of pain and pressure at the start of injection.
- It is therefore recommended that the local anesthetic should be injected under low pressure to minimize pain and anxiety among patients.

71

## Kafalias, MC. Gow-Gates, GAE. Saliba, GJ. The Gow-Gates technique for mandibular block anesthesia. A discussion and a mathematical analysis. Anesth Prog 34:142-149. 1987.

- It is claimed that depositing 2 mL of an anesthetic solution at the lingula in 18.3 sec increases hydrostatic pressure from 14.5 to 469 mm Hg.
- Such a great imbalance between intra and extravascular pressure and the resulting loss of the anesthetic through the pores of the capillary walls affects its concentration at the nerve membrane and may result in a partial or complete failure of the block.

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## Second Division

- Greater palatine approach
- The V2 injection anesthetizes:
- - the maxillary teeth and periodontium.
- - hard and soft palate.
- - sinuses, portions of the nose, orbit, upper cheek, lower eyelid, and side of the face.



## Second Division

- The entrance to the foramen is located at the distolateral aspect of the depression felt during palpation before the greater palatine injection.
- This foramen generally is located halfway between the gingival margin and midline of the palate, approximately 5 mm anterior to the junction of hard and soft palate.

## Second Division

- After a 'good' greater palatine injection is administered and has taken effect, a long needle is used to probe the canal entrance gently.
- Angulation is mostly superior, with slight distal and lateral components.



## Second Division

- The most effective position of the needle for administration of the V2 block injection generally is such that a $45^0$ angle exists between the needle and soft tissue.
- The needle is inserted to a depth of approximately 30 mm.

# Second Division

- After aspiration, the contents of the cartridge is slowly deposited.
- Up to 15 percent of patients have anatomical deviations that make this approach ineffective.
- The most common complication is anesthesia of CN VI.

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Second Division photography by Dr. Ray Voller

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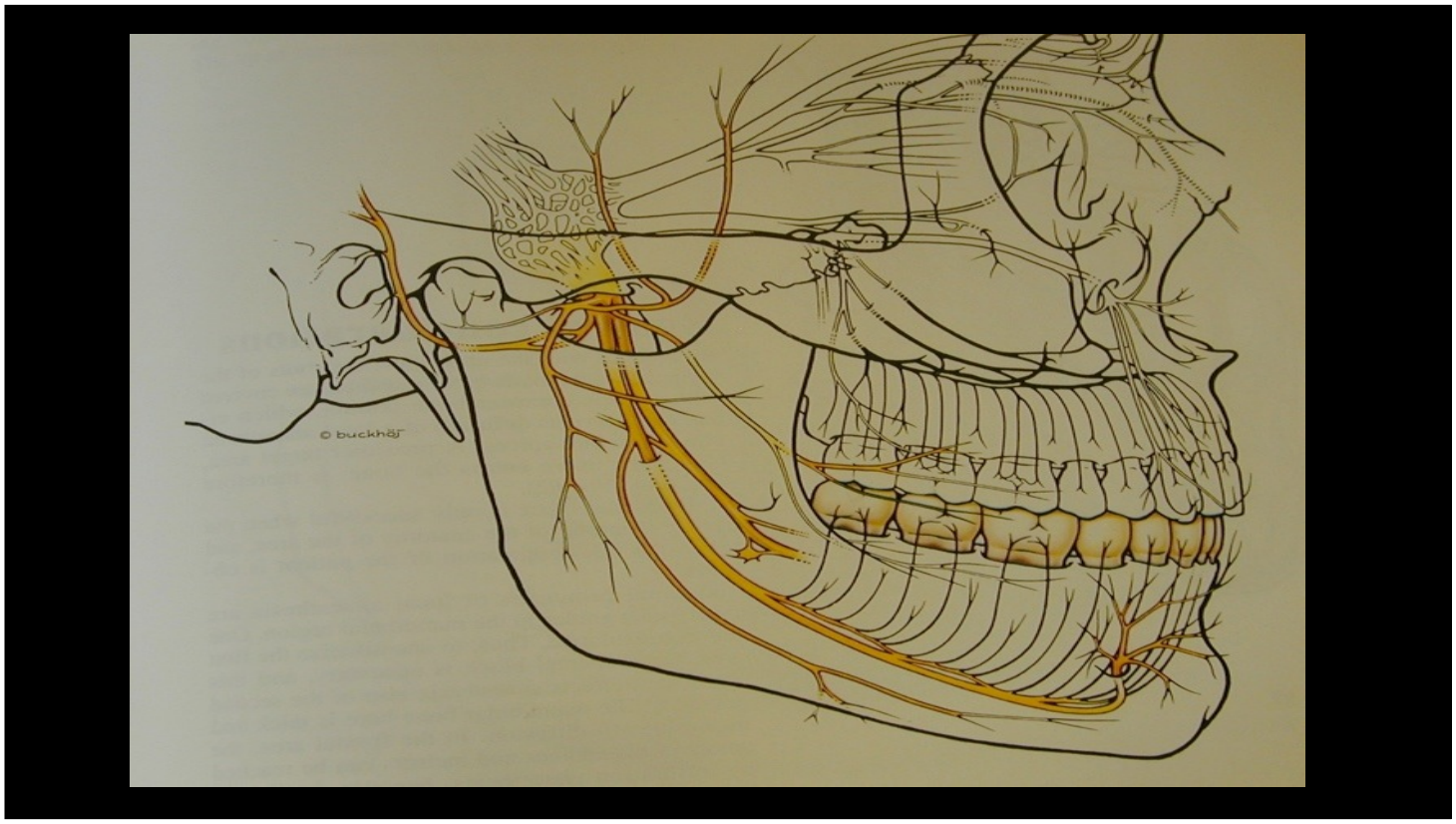
80

81

# My Mandibular Block

Local Anesthesia Part 2: Technical Considerations. Reed, KL., Malamed, SF., Fonner, AM. Anesth Prog 59:127-137, 2012.

82




83

# My mandibular block

- Anatomical location of the lingula:
  - At or below 1.0 cm above the mandibular occlusal plane 84% of the time.
  - At or below 1.5 cm above the mandibular occlusal plane 96% of the time.
  - 60% distally of the mesiodistal length of the ramus.

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# My mandibular block

- Approach from the contralateral premolars.
- 1.5 cm above the mandibular occlusal plane - and parallel to it.
- With a needle endpoint 60% of the mesiodistal length of the ramus, distally.



# My mandibular block

- Advance a 25 gauge long needle until you hit bone (required).
- - withdraw 1 mm.
- - aspirate.
- - inject 3/4 of the cartridge of local anesthetic over two minutes.

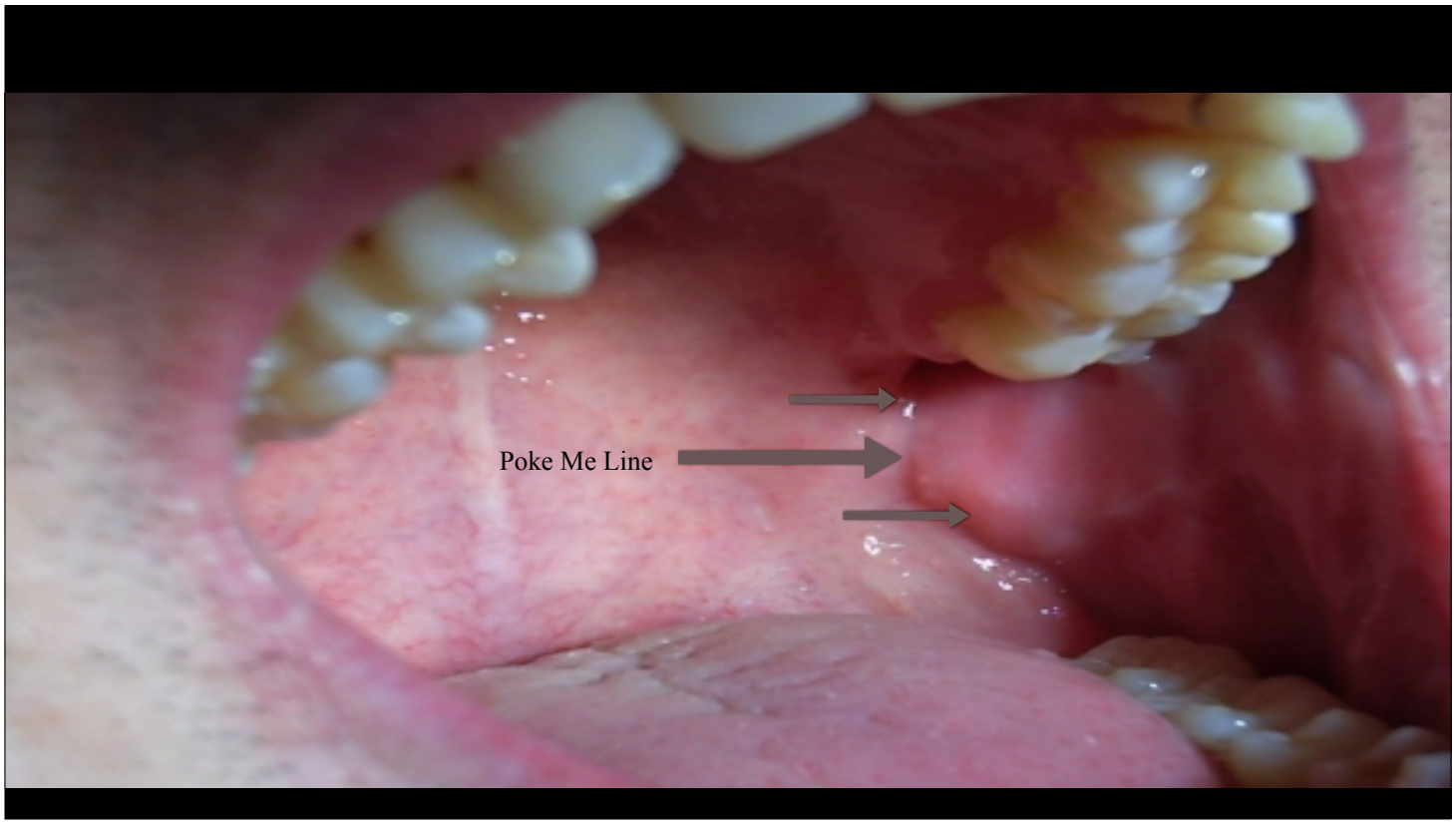
# My mandibular block

- - withdraw the needle 1/2 way.
- - aspirate.
- - slowly inject the lingual nerve.
- - save a few drops of anesthetic for the buccinator.

87


88

89




90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# Post-Operative Analgesics

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# The Dental Pain Model

- Dionne R and Cooper SA: Evaluation of preoperative ibuprofen for postoperative pain after removal of third molars. Oral Surg, Oral Med, Oral Path 45:851-856, 1978.
- Reproducible moderate to severe dental pain model
- Impacted third molars

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# Ceiling Analgesic Doses:

- Aspirin - 1000 mg
- Acetaminophen - 1000 mg*
- Ibuprofen - 400 mg**
- Codeine ~ 60 mg
- Hydrocodone ~ 10 mg
- Oxycodone ~ 10 mg

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# Opioids

- The most important aspect of the opioids in medicine
- Separate pain from suffering

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# http://www.bandolier.org.uk/booth/painpag/Acutrev/Analgesics/Leagtab.html

- Numbers needed to treat (NNT) are calculated for the proportion of patients with at least 50% pain relief over 4-6 hours compared with placebo in randomised, double-blind, single-dose studies in patients with moderate to severe pain.
- Because these NNT comparisons are against placebo, the best NNT of 2 means that 50 of 100 patients will get at least 50% relief specifically because of the treatment.

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# Codeine

# Tylenol #3

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# Tylenol #

- APAP (300 mg)
- Codeine
  - #1 - 7.5mg
  - #2 - 15mg
  - #3 - 30mg
  - #4 - 60mg

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## Tylenol #3

- (300/30) NNT = 5.7
- (300/30x2) NNT = 4.2



## Acetaminophen

- (325 mg x 2): NNT = 4.6
- (500 mg x 2): NNT = 3.8

## Codeine

- Codeine (60 mg): NNT = 16.7

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## Placebo

- Placebo: NNT = 18

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# Hydrocodone



Wolfe S. Hydrocodone: testimony for the Health Research Group of Public Citizen before the U.S. Food and Drug Administration Drug Safety and Risk Management Advisory Committee, January 25, 2013. www.citizen.org/documents/2092.pdf

- The United States consumes 99 percent of the world's hydrocodone.
- Hydrocodone consistently ranks among the most-abused medicines in the US, according tot he DEA.

## Norco

- 7.5 mg/325 mg
- 10 mg/325 mg

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## Zohydro ER

- 10, 15, 20, 30, 40 & 50 mg capsules
- Twice daily dosing
- Approved for up to 100 mg BID !!!

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# Oxycodone



# Percocets

- Each have acetaminophen 325 mg & varying amounts of oxycodone
- 2.5
- 5.0
- 7.5
- 10

## Percocets

- (325/5) NNT = 5.5
- (325/5x2) NNT = 2.6

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## Meperidine

- 100 mg IM = 2.9

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# Morphine

- 10 mg IM = 2.9

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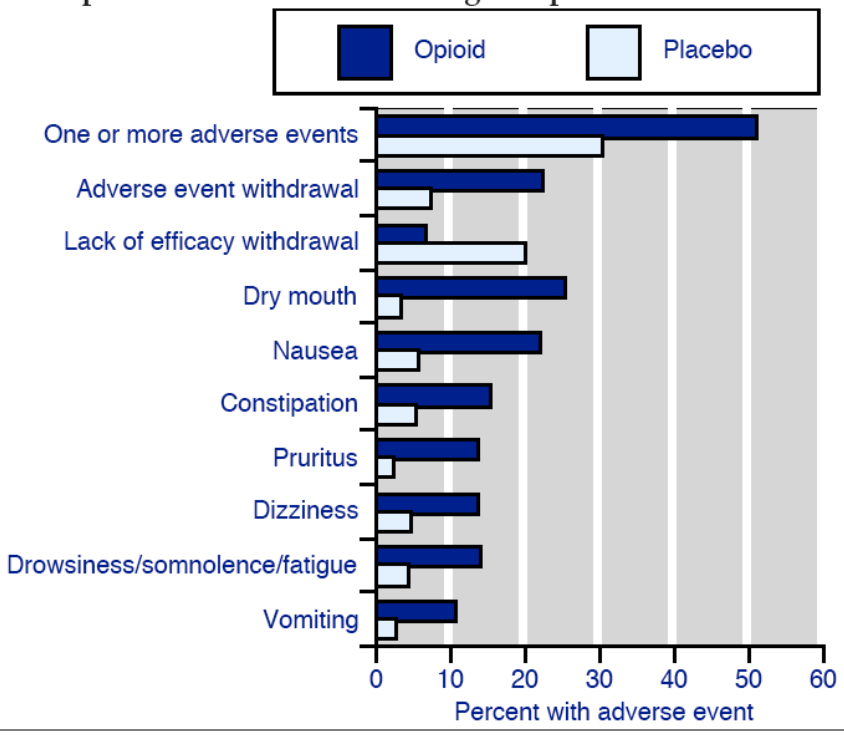
**Figure 7: Comparison of adverse event rate of oral opioid and placebo in chronic non-malignant pain**

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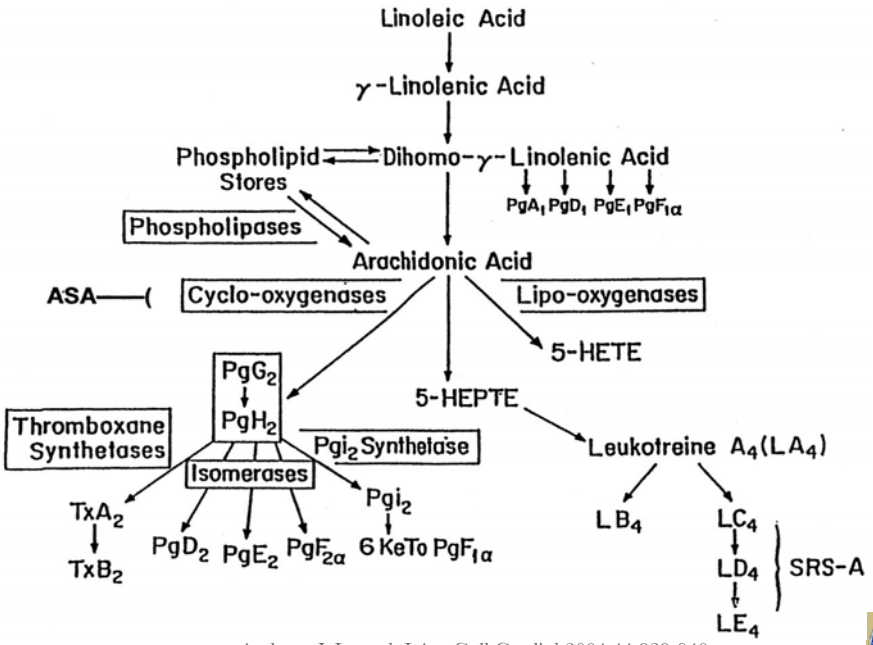
# NSAIDs

- Non Steroidal Anti-Inflammatory Drugs



The arachidonic acid cascade and its lipo-oxygenase branch, determinants of aspirin side effects




Ambrus, J. L. et al. J Am Coll Cardiol 2004;44:939-940

# NSAIDs

- Anaprox
  - Naproxen sodium
  - Aleve
  - Maximum Daily Dose: 1650 mg
  - Rx: Anaprox DS, TID

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# Naproxen Sodium

- Naproxen 220: NNT = 3.4
- Naproxen 440: NNT = 2.3

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# NSAIDs

- Motrin
  - Ibuprofen
  - Maximum Daily Dose: (acutely) 3200 mg, (chronically) 2400 mg
  - Ceiling Analgesic Dose: 400 mg*
  - Rx: 600 mg QID

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# Ibuprofen

- 200 mg: NNT = 2.7
- 400 mg: NNT = 2.4
- 600 mg: NNT = 2.4
- 800 mg: NNT = 1.6*

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# Ibuprofen 800 mg

- In practice any comparison with more than 250 or so patients is probably adequate.
- For instance, ibuprofen 800 mg is at the top of the league, with an NNT of 1.6 and with 100% of patients achieving at least 50% pain relief.
- But only 76 patients have ever been involved in comparative trials with placebo.
- This makes the apparent wonderful result less so, and you should treat it cautiously.



# NSAIDs

- Toradol Oral
  - Ketorolac
  - Maximum Daily Dose: (PO) 40 mg, (parenterally) 120 mg
  - Ceiling Analgesic Dose: IM 60 mg, IV 30 mg, PO 10 mg*
  - Rx: 10 mg q4-6 hours, not to exceed 40 mg/day

# Ketorolac

- 10 mg (PO): NNT = 2.6
- 20 mg (PO): NNT = 1.8
- 30 mg (IM): NNT = 3.4
- 60 mg (IM): NNT = 1.8



# NSAIDs

- Ketoprofen
- Maximum Daily Dose: 300 mg
- Ceiling Analgesic Dose: 100 mg
- Rx: 50 mg (x2) TID

# Ketoprofen

- 12.5 mg NNT = 2.4
- 100 mg NNT = 1.6

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Akural EI, Järvimäki V, Länsineva A, Niinimaa A, Alahuhta S. Effects of Combination Treatment With Ketoprofen 100 mg + Acetaminophen 1000 mg on Postoperative Dental Pain: A Single-Dose, 10-Hour, Randomized, Double-Blind, Active- and Placebo-Controlled Clinical Trial. Clinical Therapeutics react-text: 50 31(3):560-8 February 2009.

- Single-dose randomized, double blind, active and placebo controlled study.
- Patients aged 18 to 40 years with moderate or severe pain after surgical removal of impacted third molars were randomly assigned to receive one of the following drugs in single oral doses: ketoprofen 100 mg + acetaminophen 1000 mg, ketoprofen 100 mg, acetaminophen 1000 mg, or placebo tablets.
- The results from this study suggest that combination treatment with ketoprofen + acetaminophen provided a significantly more rapid onset of analgesia than either of the 2 agents used alone in the treatment of these patients with moderate to severe acute pain re- sulting from oral surgery.

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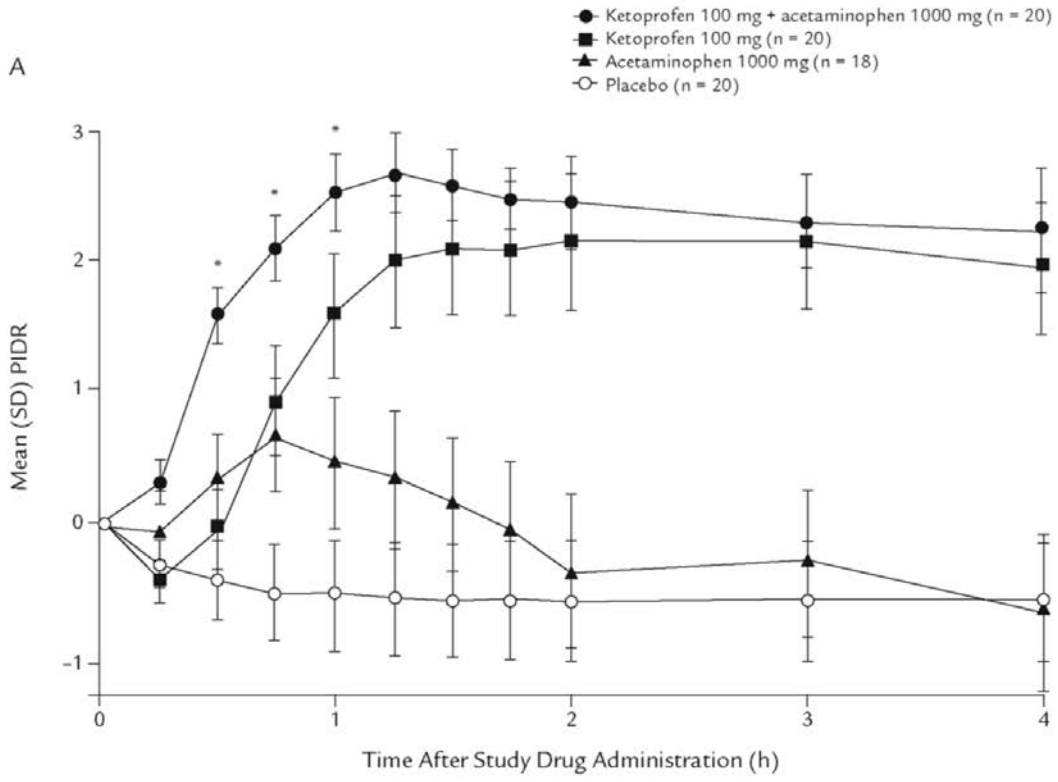


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# Combinations

- Ibuprofen 200 mg with APAP 500 mg NNT = 1.6
- Ibuprofen 400 mg with APAP 1000 mg NNT = 1.5

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