

# Hangi durumlarda sedasyon; hangi ajan?

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Acil Tıp AD

# Sunu planı

- ◎ GS hakkında genel bilgiler
- ◎ GS ilaçları
- ◎ Hangi durumlarda hangi ilaç (ilaç stratejileri)

# Kısa tarihçe

- ◎ Cerrahi anestezinin gelişimi tıp tarihindeki en önemli olaylardan biridir.
- ◎ İnhaler anestezikler;
  - › W. Long ve William E. Clark ilk kez 1842’de eter kullanmışlar. (cerrahi ve diş çekiminde)
- ◎ Lokal ve rejyonal anestezi;
  - › Carl Koller 1884’de topikal kokainin gözde cerrahi anestezi oluşturduğunu göstermiş.

# Kısa tarihçe

## © İntravenöz anestezi;

- › 1855’de Alexander Wood’un hipodermik şırınga ve iğneyi icat etmesinden sonra gelişmiştir.
- › İndüksiyon ajanları, nöromusküler blokerler, opioidler
  - Kloral hidrat 1872
  - Tiyopental 1932
  - Klordiazepoksit 1955
  - Ketamin 1962
  - Etomidat 1964
  - Propofol 1986

# Giriş

- ◎ Acil pratiğinin en önemli konularından biridir.
- ◎ Genellikle sedasyon ve analjezi kavramları birlikte.

# GS- tanımı

- © Hastanın kardiyο-respiratuar fonksiyonlarını korurken, sedatif ve/veya disosiyatif anestetik ajanlar kullanarak bilincinin baskılanmasıdır.

# GS-tanımlamalar

## Sedasyon düzeyleri (minimalden derine) ve genel anestezi tanımı

|                                                                                      | Minimal<br>sedasyon,<br>anksiyolizis | Moderate<br>sedasyon               | Derin<br>sedasyon                             | Disosiatif<br>sedasyon                                 | Genel<br>anestezi           |
|--------------------------------------------------------------------------------------|--------------------------------------|------------------------------------|-----------------------------------------------|--------------------------------------------------------|-----------------------------|
| ●  |                                      |                                    |                                               |                                                        |                             |
| <b>Yanıt</b>                                                                         | Sözel uyarıya normal yanıt           | Sözel veya dokunmaya anlamlı yanıt | Tekrarlanan veya ağrılı uyarıya anlamlı yanıt | Derin analjezi ve amnezi (katalepsi benzeri trans hali | Ağrılı uyarana yanıt yok    |
| <b>Havayolu</b>                                                                      | Etkilenmez                           | Müdahale gerekmez                  | Müdahale gerekebilir                          | Müdahale gerekmez                                      | Müdahale genellikle gerekli |
| <b>Spontan solunum</b>                                                               | Etkilenmez                           | Yeterli                            | Yetersiz olabilir                             | yeterli                                                | Sıklıkla yetersiz           |
| <b>Kardiyo-vasküler fonksiyon</b>                                                    | Etkilenmez                           | Genellikle korunur                 | Genellikle korunur                            | Genellikle korunur                                     | Bozulabilir                 |

# GS-endikasyonları

- ◎ Anksiyetesi ön planda olan hastalar,
- ◎ Ağrısı olmayan yada tolere edilebilir düzeyde olan hastalar,
- ◎ Mevcut ağrısı lokal anastetikler veya topikal ilaçlarla kontrol edilebilen hastalar.

# GS-kontraendikasyonlar

- ◎ Mutlak kontraendike olduğu bir durum yok,
  - > Aşırı uç yaşlar (<6 ay veya >70 yaş)
  - > Kusmaya meyil oluşturabilecek durumlar
  - > Zor havayoluna sahip hastalarda
  - > Mental durumunda değişiklik olanlar
  - > ASA III ve yukarısı olanlar.

# GS-işlem öncesi değerlendirme

## ◎ Risk değerlendirilmesi,

### > İleri yaş

- Spesifik bir **yaş sınırı** yoktur. Ancak yaşlılarda istenmeyen olayların gelişmesi çok daha sıktır.

- Bu ilaca karşı artmış hassasiyetten ya da yaşlılarda ilacın dağılımı değiştiğinden uygulanan ilacın yüksek serum düzeylerine ulaşmasından olabilir.

# GS-işlem öncesi değerlendirme

- ◎ Risk değerlendirilmesi,
  - > İleri yaş
  - > Komorbid hastalıkların varlığı

| American Society of Anesthesiologists (ASA) Physical Status Classification System |                                                                                 |
|-----------------------------------------------------------------------------------|---------------------------------------------------------------------------------|
| ASA 1                                                                             | A normal healthy patient                                                        |
| ASA 2                                                                             | A patient with mild systemic disease                                            |
| ASA 3                                                                             | A patient with severe systemic disease                                          |
| ASA 4                                                                             | A patient with severe systemic disease that is a constant threat to life        |
| ASA 5                                                                             | A moribund patient who is not expected to survive without the operation         |
| ASA 6                                                                             | A declared brain-dead patient whose organs are being removed for donor purposes |

| CLASS | DESCRIPTION                                               | EXAMPLES                                        | SEDATION RISK  |
|-------|-----------------------------------------------------------|-------------------------------------------------|----------------|
| I     | Normal and healthy patient                                | No past medical history                         | Minimal        |
| II    | Mild systemic disease without functional limitations      | Mild asthma, controlled diabetes                | Low            |
| III   | Severe systemic disease with functional limitations       | Pneumonia, poorly controlled seizure disorder   | Intermediate   |
| IV    | Severe systemic disease that is a constant threat to life | Advanced cardiac disease, renal failure, sepsis | High           |
| V     | Moribund patient who may not survive without procedure    | Septic shock, severe trauma                     | Extremely high |

# GS-işlem öncesi değerlendirme

- ◎ Risk değerlendirilmesi,
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  - > Komorbid hastalıkların varlığı

**Yaşlı ve komorbid** hastalığı olanlarda istenmeyen olay riskini azaltmak için;

- Başlangıç dozunu daha düşük tutmak,
- İlacı daha yavaş uygulamak,
- Tekrarlayan doz sıklığını geniş tutmak.

# GS-işlem öncesi değerlendirme

- ◎ Risk değerlendirilmesi,
  - > İleri yaş
  - > Komorbid hastalıkların varlığı
  - > Aspirasyon riski

ACEP önerisi; (**Öneri düzeyi B**)

- Acil serviste çocuk ve erişkinlerde açlık durumu gözetilmeksizin GSA'nın geciktirilmemesini önermektedir.

## Düşük riskli hastalarda açlık durumu ve GSA ile ilgili konsensus önerileri

| Açlık durumu                      | Aciliyet      | Aspirasyon riski | Önerilen sedasyon seviyesi          |
|-----------------------------------|---------------|------------------|-------------------------------------|
| >3 saat oral alım yok             | Herhangi biri | Düşük            | Kısıtlama yok                       |
| < 3 saat herhangi bir berrak sıvı | Acil          | Yüksek           | Kısıtlama yok                       |
| <3 saat herhangi bir berrak sıvı  | Acil değil    | Yüksek           | Moderate sedasyon için kısıtlama    |
| <3 saat hafif aoperatif           | Acil          | Yüksek           | Kısa, derin sedasyon için kısıtlama |
| <3 saat hafif aoperatif           | Acil değil    | Yüksek           | Moderate sedasyon için kısıtlama    |
| <3 saat yemek                     | Acil          | En yüksek        | Moderate sedasyon için kısıtlama    |
| <3 saat yemek                     | Acil değil    | En yüksek        | Minimal sedasyon için kısıtlama     |

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| <3 saat yemek                     | Acil          | En yüksek        | Moderate sedasyon için kısıtlama    |
| <3 saat yemek                     | Acil değil    | En yüksek        | Minimal sedasyon için kısıtlama     |

# GS-işlem öncesi değerlendirme

- ◎ Risk değerlendirilmesi,
  - > İleri yaş
  - > Komorbid hastalıkların varlığı
  - > Aspirasyon riski
  - > Zor havayolu

# GS-genel hususlar

## ◎ GS için minimum kişi sayısı

ACEP önerisi; (**Öneri düzeyi C**)

- Hastayı devamlı monitörize eden bir hemşire veya başka bir sağlık görevlisi ve işlemi gerçekleştiren hekim olmak üzere en az 2 kişi.

Emerg Med J. 2006 Dec;23(12):922-3.

## **The safety of single-physician procedural sedation in the emergency department.**

Hogan K<sup>1</sup>, Sacchetti A, Aman L, Opiela D.

### **⊕ Author information**

#### **Abstract**

**BACKGROUND:** Previous research has shown the safety of procedural sedation in the emergency department in university settings involving multiple emergency physicians.

**OBJECTIVE:** To examine sedation in the emergency department conducted by a single emergency physician with monitoring by the emergency nurse.

**METHODS:** The Procedural Sedation in the Community Emergency Department Registry is a prospective observational database of procedural sedation cases directed by the emergency physicians. Among other parameters, the registry tracks whether emergency physicians or emergency nurses monitored patient sedation. The incidence of complications and outcomes were compared between these two monitoring groups.

**RESULTS:** 1028 procedural sedations were performed on 977 patients at 14 sites. In 885 (86.1%) cases the emergency physician directed the sedation, and performed the procedure with monitoring by the emergency nurse. Complications occurred in 42 (4.1%) patients, 35 (4.0%) EN monitored patients and 6 (4.2%) EP monitored patients ( $p>0.7$ ). Procedures were successful in 863 (97.5%) cases monitored by emergency nurses and in 140 (97.9%) patients monitored by emergency physicians ( $p>0.7$ ).

**CONCLUSION:** Procedural sedation in the emergency department performed by a single emergency physician is safe and effective.

# GS-genel hususlar

- ◎ GS için minimum kişi sayısı
- ◎ Monitörizasyon

## ACEP önerisi; (**Öneri düzeyi B**)

- Acil serviste GSA uygulamalarında gelişebilecek hipoventilasyon ve apneyi klinik değerlendirme ve/veya pulse oksimetreden daha erken tanımda bunlara yardımcı bir cihaz olarak kapnografinin kullanımını önermektedir.

[J Clin Anesth](#). 2011 May;23(3):189-96. doi: 10.1016/j.jclinane.2010.08.012. Epub 2011 Apr 14.

## **Capnography enhances surveillance of respiratory events during procedural sedation: a meta-analysis.**

[Waugh JB<sup>1</sup>](#), [Epps CA](#), [Khodneva YA](#).

### **Author information**

#### **Abstract**

**STUDY OBJECTIVE:** To determine if capnography, in addition to standard monitoring, identified more respiratory complications than standard monitoring alone.

**DESIGN:** Meta-analysis.

**SETTING:** University medical center.

**MEASUREMENTS:** The electronic databases PubMed, CINAHL, and Cochrane Library (Cochrane Reviews, CENTRAL) were searched for studies published between 1995-2009 reporting adverse respiratory events during procedural sedation and analgesia (PSA) with clearly defined end-tidal carbon dioxide threshold, adult population, clear study design, P-value calculation, similar outcome and predictor variable definitions, and binary independent and dependent variable raw data. Five such studies were evaluated independently. A meta-analysis of these studies was performed.

**MAIN RESULTS:** During PSA, cases of respiratory depression were 17.6 times more likely to be detected if monitored by capnography than cases not monitored by capnography (95% CI, 2.5-122.1;  $P < 0.004$ ).

**CONCLUSION:** End-tidal carbon dioxide monitoring is an important addition in detecting respiratory depression during PSA.

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# GS-genel hususlar

- ◎ GS için minimum kişi sayısı
- ◎ Monitörizasyon
- ◎ Oksijenizasyon

•Özellikle uzun yada uzamış girişimlerde yüz maskesiyle birlikte yüksek akım oksijen verilmesi önerilmektedir.

[Ann Emerg Med.](#) 2011 Oct;58(4):360-364.e3. doi: 10.1016/j.annemergmed.2011.05.018. Epub 2011 Jun 15.

## **The utility of high-flow oxygen during emergency department procedural sedation and analgesia with propofol: a randomized, controlled trial.**

[Deitch K<sup>1</sup>](#), [Chudnofsky CR](#), [Dominici P](#), [Latta D](#), [Salamanca Y](#).

### **Author information**

### **Abstract**

**STUDY OBJECTIVE:** We determine whether high-flow oxygen reduces the incidence of hypoxia by 20% in adults receiving propofol for emergency department (ED) sedation compared with room air.

**METHODS:** We randomized adults to receive 100% oxygen or compressed air at 15 L/minute by nonrebreather mask for 5 minutes before and during propofol procedural sedation. We administered 1.0 mg/kg of propofol, followed by 0.5 mg/kg boluses until the patient was adequately sedated. Physicians and patients were blinded to the gas used. Hypoxia was defined a priori as an oxygen saturation less than 93%; respiratory depression was defined as an end tidal CO(2) greater than 50 mm Hg, a 10% absolute change from baseline, or loss of waveform.

**RESULTS:** We noted significantly less hypoxia in the 59 patients receiving high-flow oxygen compared with the 58 receiving compressed air (19% versus 41%;  $P=.007$ ; difference 23%; 95% confidence interval 6% to 38%). Respiratory depression was similar between groups (51% versus 48%; difference 2%; 95% confidence interval -15% to 22%). We observed 2 adverse events in the high-flow group (1 hypotension, 1 bradycardia) and 2 in the compressed air group (1 assisted ventilation, 1 hypotension).

**CONCLUSION:** High-flow oxygen reduces the frequency of hypoxia during ED propofol sedation in adults.

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# GS- ideal bir ilaç nasıl olmalı?

- Hızlı etki başlangıcı,
- Kısa etki süresi,
- Hemodinamiye en az etki,
- Major yan etkisi en az olmalı.



| AGENT         | ROUTE         | ONSET (min) | DURATION (min) | ADVANTAGES                                                                 | ADVERSE EFFECTS                                                      |
|---------------|---------------|-------------|----------------|----------------------------------------------------------------------------|----------------------------------------------------------------------|
| Midazolam     | Intravenous   | 1-2         | 30-60          | Rapid onset                                                                | Respiratory depression                                               |
|               | Intramuscular | 10-15       | 60-120         | Short duration                                                             |                                                                      |
|               | Oral          | 15-30       | 60-90          | Easy to titrate                                                            |                                                                      |
|               | Rectal        | 10-30       | 60-90          | Multiple routes                                                            |                                                                      |
|               | Intranasal    | 10-15       | 45-60          |                                                                            |                                                                      |
| Methohexital  | Intravenous   | <1          | 4-7            | Rapid onset                                                                | Respiratory depression<br>Apnea<br>Hypotension                       |
|               | Rectal        | 5-10        | 20-60          | Short duration<br>Airway reflexes maintained                               |                                                                      |
| Pentobarbital | Intravenous   | 1-2         | 30-60          | Rapid onset<br>Airway reflexes maintained                                  | Respiratory depression<br>Apnea<br>Hypotension<br>Prolonged recovery |
| Ketamine      | Intravenous   | 1           | 15             | Airway reflexes maintained                                                 | Emergence phenomena<br>Emesis<br>Laryngospasm<br>↑ICP and ↑IOP       |
|               | Intramuscular | 5           | 15-30          | No respiratory depression                                                  |                                                                      |
|               | Oral          | 30-45       | 120-240        | Predictable                                                                |                                                                      |
|               | Rectal        | 5-10        | 15-30          |                                                                            |                                                                      |
|               | Intranasal    | 5-10        | 30-120         |                                                                            |                                                                      |
| Etomidate     | Intravenous   | <1          | 5-10           | Rapid onset<br>Short duration<br>Minimal CV effects<br>Cerebral protective | Respiratory depression<br>Myoclonus<br>Adrenal suppression           |
| Propofol      | Intravenous   | <1          | 8-10           | Rapid onset<br>Short duration<br>Antiemetic<br>Cerebral protective         | Respiratory depression<br>Hypotension<br>Injection pain              |

| AGENT         | ROUTE                                                        | ONSET (min)                             | DURATION (min)                             | ADVANTAGES                                                                 | ADVERSE EFFECTS                                                      |
|---------------|--------------------------------------------------------------|-----------------------------------------|--------------------------------------------|----------------------------------------------------------------------------|----------------------------------------------------------------------|
| Midazolam     | Intravenous<br>Intramuscular<br>Oral<br>Rectal<br>Intranasal | 1-2<br>10-15<br>15-30<br>10-30<br>10-15 | 30-60<br>60-120<br>60-90<br>60-90<br>45-60 | Rapid onset<br>Short duration<br>Easy to titrate<br>Multiple routes        | Respiratory depression                                               |
| Methohexital  | Intravenous<br>Rectal                                        | <1<br>5-10                              | 4-7<br>20-60                               | Rapid onset<br>Short duration<br>Airway reflexes maintained                | Respiratory depression<br>Apnea<br>Hypotension                       |
| Pentobarbital | Intravenous                                                  | 1-2                                     | 30-60                                      | Rapid onset<br>Airway reflexes maintained                                  | Respiratory depression<br>Apnea<br>Hypotension<br>Prolonged recovery |
| Ketamine      | Intravenous<br>Intramuscular<br>Oral<br>Rectal<br>Intranasal | 1<br>5<br>30-45<br>5-10<br>5-10         | 15<br>15-30<br>120-240<br>15-30<br>30-120  | Airway reflexes maintained<br>No respiratory depression<br>Predictable     | Emergence phenomena<br>Emesis<br>Laryngospasm<br>↑ICP and ↑IOP       |
| Etomidate     | Intravenous                                                  | <1                                      | 5-10                                       | Rapid onset<br>Short duration<br>Minimal CV effects<br>Cerebral protective | Respiratory depression<br>Myoclonus<br>Adrenal suppression           |
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|               | Oral          | 30-45       | 120-240        |                                                                            |                                                                      |
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| AGENT         | ROUTE                                                        | ONSET (min)                             | DURATION (min)                             | ADVANTAGES                                                                 | ADVERSE EFFECTS                                                      |
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- ◎ IV olarak 1-2 dakikada ve 0.02-0.03 mg/kg olarak ya da 0.5-1.0 mg titre ederek verilir.
- ◎ Tek doz 2.5 mg geçmemelidir.
- ◎ Tekrar dozlarında adipoz dokuda birikerek uzamış sedasyona neden olabilir.

| AGENT         | ROUTE                                                        | ONSET (min)                             | DURATION (min)                             | ADVANTAGES                                                                 | ADVERSE EFFECTS                                                      |
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| Methohexital  | Intravenous<br>Rectal                                        | <1<br>5-10                              | 4-7<br>20-60                               | Rapid onset<br>Short duration<br>Airway reflexes maintained                | Respiratory depression<br>Apnea<br>Hypotension                       |
| Pentobarbital | Intravenous                                                  | 1-2                                     | 30-60                                      | Rapid onset<br>Airway reflexes maintained                                  | Respiratory depression<br>Apnea<br>Hypotension<br>Prolonged recovery |
| Ketamine      | Intravenous<br>Intramuscular<br>Oral<br>Rectal<br>Intranasal | 1<br>5<br>30-45<br>5-10<br>5-10         | 15<br>15-30<br>120-240<br>15-30<br>30-120  | Airway reflexes maintained<br>No respiratory depression<br>Predictable     | Emergence phenomena<br>Emesis<br>Laryngospasm<br>↑ICP and ↑IOP       |
| Etomidate     | Intravenous                                                  | <1                                      | 5-10                                       | Rapid onset<br>Short duration<br>Minimal CV effects<br>Cerebral protective | Respiratory depression<br>Myoclonus<br>Adrenal suppression           |
| Propofol      | Intravenous                                                  | <1                                      | 8-10                                       | Rapid onset<br>Short duration<br>Antiemetic<br>Cerebral protective         | Respiratory depression<br>Hypotension<br>Injection pain              |

- ◎ 0.75-1.0 mg/kg başlangıç dozu. (ek dozlar 0.5 mg/kg)
- ◎ Diğer barbitüratların aksine epileptik nöbetleri tetikleyebilir.

| AGENT         | ROUTE         | ONSET (min) | DURATION (min) | ADVANTAGES                                                                 | ADVERSE EFFECTS                                                      |
|---------------|---------------|-------------|----------------|----------------------------------------------------------------------------|----------------------------------------------------------------------|
| Midazolam     | Intravenous   | 1-2         | 30-60          | Rapid onset                                                                | Respiratory depression                                               |
|               | Intramuscular | 10-15       | 60-120         | Short duration                                                             |                                                                      |
|               | Oral          | 15-30       | 60-90          | Easy to titrate                                                            |                                                                      |
|               | Rectal        | 10-30       | 60-90          | Multiple routes                                                            |                                                                      |
|               | Intranasal    | 10-15       | 45-60          |                                                                            |                                                                      |
| Methohexital  | Intravenous   | <1          | 4-7            | Rapid onset                                                                | Respiratory depression<br>Apnea<br>Hypotension                       |
|               | Rectal        | 5-10        | 20-60          | Short duration<br>Airway reflexes maintained                               |                                                                      |
| Pentobarbital | Intravenous   | 1-2         | 30-60          | Rapid onset<br>Airway reflexes maintained                                  | Respiratory depression<br>Apnea<br>Hypotension<br>Prolonged recovery |
| Ketamine      | Intravenous   | 1           | 15             | Airway reflexes maintained<br>No respiratory depression<br>Predictable     | Emergence phenomena<br>Emesis<br>Laryngospasm<br>↑ICP and ↑IOP       |
|               | Intramuscular | 5           | 15-30          |                                                                            |                                                                      |
|               | Oral          | 30-45       | 120-240        |                                                                            |                                                                      |
|               | Rectal        | 5-10        | 15-30          |                                                                            |                                                                      |
|               | Intranasal    | 5-10        | 30-120         |                                                                            |                                                                      |
| Etomidate     | Intravenous   | <1          | 5-10           | Rapid onset<br>Short duration<br>Minimal CV effects<br>Cerebral protective | Respiratory depression<br>Myoclonus<br>Adrenal suppression           |
| Propofol      | Intravenous   | <1          | 8-10           | Rapid onset<br>Short duration<br>Antiemetic<br>Cerebral protective         | Respiratory depression<br>Hypotension<br>Injection pain              |

- ◎ Yetişkinlerde genellikle IV olarak 1-2 dakikada 1-2 mg/kg dozunda verilir.
- ◎ Tekrar dozu 5-10 dakikada bir  $\frac{1}{4}$  kadarı.

## **Adverse events associated with ketamine for procedural sedation in adults.**

Strayer RJ<sup>1</sup>, Nelson LS.

### **+ Author information**

#### **Erratum in**

*Am J Emerg Med.* 2009 May;27(4):512.

#### **Abstract**

**STUDY OBJECTIVES:** Ketamine is widely used as a procedural sedation agent in pediatrics, where its safety and efficacy are supported by numerous studies. Emergency physicians use ketamine infrequently in adults, as it is believed to have a more significant side effect profile in this population. However, adult data on ketamine use in the emergency medicine literature are sparse. **Our objective was to determine ketamine's adverse effect profile in adults when used for procedural sedation.**

**METHODS:** We performed a literature review based on adverse effect research methodology recommendations. PubMed, EMBASE, TOXNET, and a variety of specialized databases were queried without regard to publication date or language. Experts were contacted to locate additional data. Inclusion criteria included adult study; ketamine used to facilitate the performance of painful procedures; dose of at least 1 mg/kg intravenous or at least 2 mg/kg intramuscular; original data and adverse events reported; spontaneously breathing patient, and no continuous cotherapies. Studies that met inclusion criteria were abstracted onto structured forms and their results qualitatively summarized.

**RESULTS:** Of the 5512 unique citations that were evaluated, 87 met criteria for inclusion. Most studies were performed in the 1970s and published in the anesthesia literature. Contexts, end points, and methodological quality varied widely across studies. Ketamine reliably produces conditions that facilitate the performance of painful procedures. Pharyngeal reflexes are generally preserved and cardiovascular tone stimulated, including a rise in blood pressure and myocardial oxygen demand. Laryngospasm and airway obstruction are reported, and though ketamine is a respiratory stimulant, a brief period of apnea around the time of injection is common. Reports of significant cardiorespiratory adverse events are rare, despite ketamine's frequent use in austere, poorly monitored settings. **Dysphoric emergence phenomena occur in 10% to 20% of cases; sedating medications are effective in preventing and managing these reactions.**

**CONCLUSION:** When ketamine is used for procedural sedation in adults, emergence phenomena occur in 10% to 20% of patients. Although providers must be prepared to recognize and manage airway obstruction, cardiorespiratory adverse events are rare and typically do not affect outcomes.

| AGENT         | ROUTE         | ONSET (min) | DURATION (min) | ADVANTAGES                                                                 | ADVERSE EFFECTS                                                      |
|---------------|---------------|-------------|----------------|----------------------------------------------------------------------------|----------------------------------------------------------------------|
| Midazolam     | Intravenous   | 1-2         | 30-60          | Rapid onset                                                                | Respiratory depression                                               |
|               | Intramuscular | 10-15       | 60-120         | Short duration                                                             |                                                                      |
|               | Oral          | 15-30       | 60-90          | Easy to titrate                                                            |                                                                      |
|               | Rectal        | 10-30       | 60-90          | Multiple routes                                                            |                                                                      |
|               | Intranasal    | 10-15       | 45-60          |                                                                            |                                                                      |
| Methohexital  | Intravenous   | <1          | 4-7            | Rapid onset                                                                | Respiratory depression<br>Apnea<br>Hypotension                       |
|               | Rectal        | 5-10        | 20-60          | Short duration<br>Airway reflexes maintained                               |                                                                      |
| Pentobarbital | Intravenous   | 1-2         | 30-60          | Rapid onset<br>Airway reflexes maintained                                  | Respiratory depression<br>Apnea<br>Hypotension<br>Prolonged recovery |
| Ketamine      | Intravenous   | 1           | 15             | Airway reflexes maintained                                                 | Emergence phenomena<br>Emesis<br>Laryngospasm<br>↑ICP and ↑IOP       |
|               | Intramuscular | 5           | 15-30          | No respiratory depression                                                  |                                                                      |
|               | Oral          | 30-45       | 120-240        | Predictable                                                                |                                                                      |
|               | Rectal        | 5-10        | 15-30          |                                                                            |                                                                      |
|               | Intranasal    | 5-10        | 30-120         |                                                                            |                                                                      |
| Etomidate     | Intravenous   | <1          | 5-10           | Rapid onset<br>Short duration<br>Minimal CV effects<br>Cerebral protective | Respiratory depression<br>Myoclonus<br>Adrenal suppression           |
| Propofol      | Intravenous   | <1          | 8-10           | Rapid onset<br>Short duration<br>Antiemetic<br>Cerebral protective         | Respiratory depression<br>Hypotension<br>Injection pain              |

- Dozu yetişkinlerde GS için;
  - **0.5 yada 1.0 mg/kg başlangıç dozunu** takiben
  - İstenen sedasyon düzeyine ulaşana kadar her 3-5 dakikada bir **0.5 mg/kg ek dozlar** şeklinde verilir.

## Prevention of pain on injection of propofol: systematic review and meta-analysis.

Jalota L<sup>1</sup>, Kalira V, George E, Shi YY, Hornuss C, Radke O, Pace NL, Apfel CC; Perioperative Clinical Research Core.

### ⊕ Author information

#### Abstract

**OBJECTIVE:** To systematically determine the most efficacious approach for preventing pain on injection of propofol.

**DESIGN:** Systematic review and meta-analysis.

**DATA SOURCES:** PubMed, Embase, Cochrane Library, www.clinicaltrials.gov, and hand searching from the reference lists of identified papers.

**STUDY SELECTION:** Randomised controlled trials comparing drug and non-drug interventions with placebo or another intervention to alleviate pain on injection of propofol in adults.

**RESULTS:** Data were analysed from 177 randomised controlled trials totalling 25,260 adults. The overall risk of pain from propofol injection alone was about 60%. Using an antecubital vein instead of a hand vein was the most effective single intervention (relative risk 0.14, 95% confidence interval 0.07 to 0.30). Pretreatment using lidocaine (lignocaine) in conjunction with venous occlusion was similarly effective (0.29, 0.22 to 0.38). Other effective interventions were a lidocaine-propofol admixture (0.40, 0.33 to 0.48); pretreatment with lidocaine (0.47, 0.40 to 0.56), opioids (0.49, 0.41 to 0.59), ketamine (0.52, 0.46 to 0.57), or non-steroidal anti-inflammatory drugs (0.67, 0.49 to 0.91); and propofol emulsions containing medium and long chain triglycerides (0.75, 0.67 to 0.84). Statistical testing of indirect comparisons showed that use of the antecubital vein and pretreatment using lidocaine along with venous occlusion to be more efficacious than the other interventions.

**CONCLUSIONS:** The two most efficacious interventions to reduce pain on injection of propofol were use of the antecubital vein, or pretreatment using lidocaine in conjunction with venous occlusion when the hand vein was chosen. Under the assumption of independent efficacy a third practical alternative could be pretreatment of the hand vein with lidocaine or ketamine and use of a propofol emulsion containing medium and long chain triglycerides. Although not the most effective intervention on its own, a small dose of opioids before induction halved the risk of pain from the injection and thus can generally be recommended unless contraindicated.

## KETOFOL (ketamin + propofol)

| Ketamin                  | Propofol                 |
|--------------------------|--------------------------|
| Uzun etki                | Kısa etki                |
| Hipertansif              | Hipotansif               |
| Kafa içi basıncı artırır | Kafa içi basıncı düşürür |
| Analjezi sağlar          | Analjezi özelliği yok    |
| Kusma                    | Anti emetik              |
| Halüsinasyon             | hipnotik                 |

## **Ketamine-Propofol Versus Propofol Alone for Procedural Sedation in the Emergency Department: A Systematic Review and Meta-analysis.**

Yan JW<sup>1,2</sup>, McLeod SL<sup>1,2</sup>, Iansavitchene A<sup>2</sup>.

### **⊕ Author information**

#### **Abstract**

**OBJECTIVES:** Propofol is an agent commonly used for procedural sedation and analgesia (PSA) in the emergency department (ED), but it can cause respiratory depression and hypotension. The combination of ketamine-propofol (K-P) is an alternative that theoretically provides a reduction in adverse events compared to propofol. The primary objective of this review was to determine if K-P has a lower frequency of adverse respiratory events in patients undergoing PSA in the ED than propofol alone. Secondary objectives were to compare the proportion of overall adverse events, sedation time, procedure time, and recovery time between K-P and propofol.

**METHODS:** Electronic searches of Medline, EMBASE, Cochrane Central Register of Controlled Trials, and CINAHL were conducted and reference lists were hand-searched. Randomized controlled trials (RCTs) published in English comparing the use of K-P to propofol alone for PSA in the ED were included.

**RESULTS:** Six RCTs were included with a combined total of 932 patients (K-P = 520, propofol = 412). Five RCTs reported the proportion of adverse respiratory events; the pooled estimate revealed fewer adverse respiratory events with K-P compared to propofol (29.0% vs. 35.4%; risk ratio [RR] = 0.82; 95% confidence interval [CI] = 0.68 to 0.99). There was no significant difference with respect to the proportion of overall adverse events (38.8% vs. 42.5%; RR = 0.88; 95% CI = 0.75 to 1.04). Procedure time was similar when the groups were compared.

**CONCLUSIONS:** The premise of combining ketamine with propofol is based on the many synergies that theoretically exist between these two agents. In this study, K-P had a lower frequency of adverse respiratory events in patients undergoing PSA in the ED compared to propofol alone.

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## **Ketamine-propofol combination (ketofol) vs propofol for procedural sedation and analgesia: systematic review and meta-analysis.**

Jalili M<sup>1</sup>, Bahreini M<sup>1</sup>, Doosti-Irani A<sup>2</sup>, Masoomi R<sup>3</sup>, Arbab M<sup>1</sup>, Mirfazaelian H<sup>4</sup>.

### **⊕ Author information**

#### **Abstract**

**OBJECTIVE:** This meta-analysis of trials was conducted to evaluate the analgesic and side effects of ketamine-propofol combination (ketofol) in comparison to propofol in procedural sedation and analgesia (PSA).

**METHODS:** Medline, EMBASE, Scopus, CINAHL, and Cochrane Central Register of Controlled Trials were searched for clinical trial. The administration complications were the key outcomes of interest.

**RESULT:** Eighteen clinical trials that met our criteria were included in the analysis. Pooling of data showed that ketofol is significantly effective for reduction of respiratory complication and with relative risk (RR) of 0.31 in 14 trials (95% confidence interval [CI], 0.47-0.7;  $P = .001$ ). Ketofol was also effective in reducing cardiovascular complications with hypotension RR of 0.11 in 9 trials (95% CI, 0.17-0.97;  $P = .04$ ) and bradycardia RR of 0.47 in 8 trials (95% CI, 0.28-0.72;  $P = .008$ ). The present study also showed that the summary of RR for psychomimetic complications was 1.95 in 13 trials were (95% CI, 0.79-4.81;  $P = .15$ ) and for muscle rigidity was 0.52 for 2 trials (95% CI, 0.06-4.67;  $P = .56$ ), and both were insignificant. In regard to nausea and vomiting, the RR was 1.23 in 12 trials (95% CI, 0.39-3.88;  $P = .72$ ) and insignificant.

**CONCLUSION:** This meta-analysis demonstrates good safety profile in cardiorespiratory problems and comparable rate of other complications with propofol in adult procedural sedation and analgesia.

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| AGENT         | ROUTE                                                        | ONSET (min)                             | DURATION (min)                             | ADVANTAGES                                                                 | ADVERSE EFFECTS                                                      |
|---------------|--------------------------------------------------------------|-----------------------------------------|--------------------------------------------|----------------------------------------------------------------------------|----------------------------------------------------------------------|
| Midazolam     | Intravenous<br>Intramuscular<br>Oral<br>Rectal<br>Intranasal | 1-2<br>10-15<br>15-30<br>10-30<br>10-15 | 30-60<br>60-120<br>60-90<br>60-90<br>45-60 | Rapid onset<br>Short duration<br>Easy to titrate<br>Multiple routes        | Respiratory depression                                               |
| Methohexital  | Intravenous<br>Rectal                                        | <1<br>5-10                              | 4-7<br>20-60                               | Rapid onset<br>Short duration<br>Airway reflexes maintained                | Respiratory depression<br>Apnea<br>Hypotension                       |
| Pentobarbital | Intravenous                                                  | 1-2                                     | 30-60                                      | Rapid onset<br>Airway reflexes maintained                                  | Respiratory depression<br>Apnea<br>Hypotension<br>Prolonged recovery |
| Ketamine      | Intravenous<br>Intramuscular<br>Oral<br>Rectal<br>Intranasal | 1<br>5<br>30-45<br>5-10<br>5-10         | 15<br>15-30<br>120-240<br>15-30<br>30-120  | Airway reflexes maintained<br>No respiratory depression<br>Predictable     | Emergence phenomena<br>Emesis<br>Laryngospasm<br>↑ICP and ↑IOP       |
| Etomidate     | Intravenous                                                  | <1                                      | 5-10                                       | Rapid onset<br>Short duration<br>Minimal CV effects<br>Cerebral protective | Respiratory depression<br>Myoclonus<br>Adrenal suppression           |
| Propofol      | Intravenous                                                  | <1                                      | 8-10                                       | Rapid onset<br>Short duration<br>Antiemetic<br>Cerebral protective         | Respiratory depression<br>Hypotension<br>Injection pain              |

- ⦿ IV 30-60 saniyede.
- ⦿ 0.1-0.15 mg/kg başlangıç dozunda.
- ⦿ Yaşlılarda, KC ve böbrek disfonksiyonunda derin ve uzamış etkileri olur.

# GS için yeni ilaçlar

- ◎ Fospropofol
- ◎ Dexmedetomidine
  - > Alfa-2 agonist
  - > Sedatif , hipnotik ve analjezik etkinliği var.

# GS- ilaç stratejisi

- ⦿ Hastanın risk durumu nedir?
- ⦿ İhtiyacımız olan sedasyon mu, analjezi mi?
- ⦿ Hedeflenen sedasyon derinliği?
- ⦿ Özellikle ilaç-hasta durumu var mı?

# GS- hangi durumda hangi ilaç?

## ◎ ACEP önerisi; (**Öneri düzeyi A**)

- › **Ketamine** çocuklarda güvenle kullanılabilir.
- › **Propofol** çocuklarda ve yetişkinlerde güvenle kullanılabilir.

# GS- hangi durumda hangi ilaç?

- ◎ ACEP önerisi; (**Öneri düzeyi B**)
  - > **Etomidat** yetişkinlerde güvenle kullanılabilir
  - > **Ketofol** (ketamin + propofol) çocuklarda ve yetişkinlerde güvenle kullanılabilir.

# GS- hangi durumda hangi ilaç?

## ◎ ACEP önerisi; (Öneri düzeyi C)

- › **Ketamine** yetişkinlerde güvenle kullanılabilir.
- › **Alfentanil** yetişkinlerde güvenle kullanılabilir.
- › **Etomidat** çocuklarda güvenle kullanılabilir.

# GS- ACEP ilaç önerileri

| Yetişkinlerde GS için öncelikli önerilen ilaçlar |                                        |                                                               |
|--------------------------------------------------|----------------------------------------|---------------------------------------------------------------|
| Öneri düzeyi                                     | İlaç                                   | Dozu                                                          |
| Düzyey A                                         | Propofol                               | 1 mg/kg (0.5 mg/kg ek dozlar)                                 |
| Düzyey B                                         | Ketofol (ketamin+propofol)<br>Etomidat | 0.5-0.75 + 0.5-0.75 mg/kg<br>0.15 mg/kg (0.1 mg/kg ek dozlar) |
| Düzyey C                                         | Ketamin                                | 1 mg/kg                                                       |

## GS- yetişkinler için ilaç seçiminde stratejiler

| Girişim tipi                  | Örnek                                                                                                            | Önerilen ilaç                                                                | Alternatif ilaç                                       | Yorum                                                                                                          |
|-------------------------------|------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|
| Ağrısız işlemler              | Radyolojik görüntüleme                                                                                           | Midazolam (IV)                                                               | Propofol (IV)                                         | İyi bilinen ve güvenli ilaçlar                                                                                 |
| Düşük ağrı, yüksek anksiyete  | Santral kateter, Lomber ponksiyon                                                                                | Midazolam (IV)                                                               | Propofol (IV)<br>Ketamin (IV)                         | Ağrı lokal anestezi veya topikal ilaçlarla giderilebilir                                                       |
| Yüksek ağrı, yüksek anksiyete | -Kırık veya eklem redüksiyonu<br>-abse drenajı<br>-yanık debritleme<br>-kardiyoversiyon<br>-Göğüs tüpü takılması | -Midazolam + fentanyl (IV)<br>-Propofol + fentanyl (IV)<br>- Ketamin (IV,IM) | Etomidate + fentanyl (IV)<br>Propofol + ketamine (IV) | Midazolam+fentanyl ikilisi daha çok olmak üzere diğer kombinasyonları da destekleyen çok sayıda literatür var. |

## GS- yetişkinler için ilaç seçiminde stratejiler

| Girişim tipi                  | Örnek                                                                                                            | Önerilen ilaç                                                                | Alternatif ilaç                                       | Yorum                                                                                                          |
|-------------------------------|------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|-------------------------------------------------------|----------------------------------------------------------------------------------------------------------------|
| Ağrısız işlemler              | Radyolojik görüntüleme                                                                                           | Midazolam (IV)                                                               | Propofol (IV)                                         | İyi bilinen ve güvenli ilaçlar                                                                                 |
| Düşük ağrı, yüksek anksiyete  | Santral kateter, Lomber ponksiyon                                                                                | Midazolam (IV)                                                               | Propofol (IV)<br>Ketamin (IV)                         | Ağrı lokal anestezi veya topikal ilaçlarla giderilebilir                                                       |
| Yüksek ağrı, yüksek anksiyete | -Kırık veya eklem redüksiyonu<br>-abse drenajı<br>-yanık debritleme<br>-kardiyoversiyon<br>-Göğüs tüpü takılması | -Midazolam + fentanyl (IV)<br>-Propofol + fentanyl (IV)<br>- Ketamin (IV,IM) | Etomidate + fentanyl (IV)<br>Propofol + ketamine (IV) | Midazolam+fentanyl ikilisi daha çok olmak üzere diğer kombinasyonları da destekleyen çok sayıda literatür var. |

# GS- sonuç olarak:)

- ◎ Minimal veya uzun sedasyon için
  - > **midazolam**,
- ◎ Riskli olmayan hasta grubunda
  - > **Propofol**
  - > **Ketofol**
- ◎ Riskli hasta grubunda
  - > Hipotansif hastada **etomidat** veya **ketamin**
  - > Potansiyel havayolu veya solunum probleminde **ketamin**

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