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PROPOFOL-FENTANYL VERSUS PROPOFOL ALONE FOR LUMBAR PUNCTURE SEDATION IN CHILDREN WITH ACUTE HEMATOLOGIC MALIGNANCIES: PROPOFOL DOSING AND ADVERSE EVENTS

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Abstract

Objective—We sought to determine whether the combination of propofol and fentanyl results in lower propofol doses and fewer adverse cardiopulmonary events than propofol and placebo for lumbar puncture (LP) in children with acute hematologic malignancies.

Design—Randomized, controlled, double blind, crossover study.

Setting—Pediatric Sedation Program

Patients—Children with acute leukemia or lymphoma receiving sedation for LP.

Interventions—Each patient received two sedations in random order, one with propofol/placebo and one with propofol/fentanyl. The study investigator and patient/parent were blinded to placebo or fentanyl. Data collected included patient age and diagnosis, propofol dose and adverse events. Adverse events included oxygen saturation < 94%, airway obstruction, apnea, hypotension and bradycardia (< 5% mean for age). Logistic regression analysis was utilized to assess probability of adverse events and the Wilcoxon Signed Rank and McNemar's tests were used for paired comparisons.

Measurements and Main Results—Twenty-two patients were enrolled. Fourteen patients were male and 8 were female. Each patient was studied twice for a total of 44 sedations. The median age was 5.0 years (range 2.2–17.2 years). All procedures were successfully completed. The median total dose of propofol was 5.05 mg/kg (range 2.4–10.2 mg/kg) for propofol/placebo versus 3.00 mg/kg (range 1.4–10.5 mg/kg) for propofol/fentanyl ($p < 0.001$). Twelve adverse events occurred in 11 of 22 patients (50.0%) propofol/placebo compared to 6 of 22 (18.2%) propofol/fentanyl ($p = 0.02$). The most common adverse event was hypotension.

Conclusions—The combination of propofol and fentanyl versus propofol alone for LP sedation in children with acute hematologic malignancies resulted in lower propofol doses and fewer adverse events.

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propofol; fentanyl; pediatric oncology; procedural sedation

In a standard protocol to treat acute lymphoblastic leukemia (ALL), the most common malignancy of childhood, a child receives 10 to 15 lumbar punctures (LP) and bone marrow procedures during their first year of treatment.¹ Invasive procedures continue to be one of the most stressful parts of cancer treatment for children and their families.^{2–6} Poorly controlled procedural discomfort in children with cancer is accompanied by the development of anxiety related symptoms, depression and reduced analgesic effects in subsequent procedures.^{4,5,7} In 1990 the American Academy of Pediatrics (AAP) published guidelines for the management of procedural pain control in children with cancer.⁸ In their report the AAP proposed that procedural pain control be part of the “frontline treatment” in children with cancer. Yet, significant variation in sedation practice continues to exist between institutions.^{9,10}

Since the AAP report, a number of different sedative regimens for invasive oncology procedures in children have been studied, each with their own advantages and disadvantages. Several studies have recently evaluated the use of propofol, a sedative/anesthetic drug with rapid onset and recovery, as the sole agent for procedural sedation in children with cancer^{11,12}. Propofol is easy to titrate, induction is rapid and recovery is smooth. However, when used as a single agent the majority of patients will experience an adverse event.^{11,12}

Propofol-opioid combinations are commonly used in anesthetic practice.¹³ Advantages include increased speed of anesthetic induction, faster recovery and lower total propofol dose requirements. Few studies have examined the benefits of combining propofol with an opioid in pediatric procedural sedation. Compared to propofol alone, the combination of propofol-fentanyl reduces adverse events and enhances ease of endoscopy in children undergoing oesophagogastroduodenoscopy.¹⁴ Similarly, in a retrospective study comparing propofol alone to propofol with fentanyl in children receiving invasive oncology procedures, patients receiving the drug combination had a faster time to recovery.¹⁵ Regardless of the setting, a propofol-opioid combination consistently results in lower total propofol doses compared to propofol alone. To date, there have been no randomized controlled prospective studies comparing propofol alone to propofol in combination with fentanyl for procedural sedation in children with cancer.

The purpose of this study was to compare sedation with propofol alone to propofol plus fentanyl for lumbar puncture in children with acute hematologic malignancies. To enhance procedure homogeneity we chose to solely study LP sedations. In addition, LPs were studied because they are the most common invasive procedure performed on children with acute hematologic malignancies and require minimal patient motion for successful completion.¹⁶ Our primary hypothesis was that a propofol/fentanyl combination would result in lower total doses of propofol and consequently fewer adverse cardiopulmonary events compared to propofol alone. We have previously reported overall fewer adverse events with the combination of propofol and fentanyl.¹⁷

MATERIALS AND METHODS

Study Design

This study was a prospective, randomized, controlled, double blind, crossover design. The University of Wisconsin (UW) Institutional Review Board and the General Clinical

Research Center (GCRC) approved the study. Written parental consent for all study patients and patient assent for children seven years of age or older was obtained.

Study Population

Patients eligible for the study were children 2 to 18 years of age with the diagnosis of acute leukemia or lymphoma undergoing sedation for LP. We chose to study children with an acute hematologic malignancy because they comprise the majority of pediatric oncology patients receiving multiple LPs and benefit from well-controlled sedation and analgesia. Members of the Division of Pediatric Hematology/Oncology in the UW Department of Pediatrics cared for all patients. Patients were scheduled to receive sedation for LP in the University of Wisconsin Children's Hospital (UWCH) Pediatric Sedation Program. At our institution faculty members of the Division of Pediatric Critical Care Medicine provide sedation for all children with cancer that are sedated for invasive oncology procedures. Sedations were managed in accordance with the American Academy of Pediatrics (AAP) guidelines for pediatric sedation.¹⁸ Exclusion criteria included an American Society of Anesthesiology (ASA) physical status $\geq$ III, cardiorespiratory instability, allergy to propofol or its components, age < 2 years, patients receiving concomitant sedatives and analgesics and patients with an oxygen requirement.

Pediatric oncology nursing and/or physician staff first identified children eligible for the study during the induction phase of chemotherapy. A study investigator, GCRC research nurse or the principle investigator, enrolled patients during the consolidation or maintenance phase of chemotherapy, typically greater than one month following diagnosis when the scheduled frequency of LPs was every 1 to 12 weeks. Patients were enrolled following induction of chemotherapy, at a time when patients and families had had more time to emotionally adjust to the diagnosis and the contribution of pain from the underlying disease process was less.³

Prior to consent, parents were provided a detailed description of the research protocol by the study investigator, which included the risks and benefits of enrollment. Patients older than seven years of age were provided an assent form and a one page simplified description of the study. Once enrolled patients were assigned a study number to ensure patient confidentiality. The patient study number and weight was sent to the UW Children's Hospital pharmacy where each patient was randomized to receive either propofol and placebo or propofol and fentanyl for their first study period. All eligible patients were randomly allocated to receive propofol or fentanyl and propofol sedation at the first study period using a permuted block randomization with a block size of four. The randomization list was generated using a random number generator. Pharmacy assigned subjects to the treatment groups by opening a sealed envelope, which included the treatment assignment. On the day of study pharmacy was notified by phone by the study investigator of the patient's arrival. Randomization numbers were assigned in sequential order immediately prior to treatment. The study drug, fentanyl or placebo was delivered by the pharmacist in a concealed paper bag to the sedation area.

Patients were studied on two separate occasions, once with propofol and placebo (normal saline) and once with propofol and fentanyl. The study investigator, parents, patient and oncologist performing the LP were blinded to fentanyl and placebo administration. The sedation nurse and physician administering the drug were knowledgeable of the study drug. The ASA physical status and baseline modified Yale Preoperative Anxiety Scale (m-YPAS)¹⁹ was recorded by the study investigator. The m-YPAS is a score developed as a pre-operative tool to assess anxiety in children prior to anesthetic induction. In our study m-YPAS was measured at baseline and just before propofol induction to assess the sedative/anxiolytic effects of fentanyl or placebo.

Oxygen saturation was used as a primary adverse event endpoint to determine the sample size of this crossover study. Specifically, a total sample size of 40 patients was proposed to detect an anticipated difference of 3% in oxygen saturation between the two treatment assignments (propofol and fentanyl versus propofol alone) with >90% power and two-sided significance level of 5%. In order to account for patient exclusion, the total accrual goal was 44 patients. One interim analysis was planned after 22 patients had been enrolled, with the decision to terminate the study early if there was a significant difference in the adverse event rate between the two treatment assignments. The Pocock stopping rule²⁰ with a fixed nominal level ($\alpha=0.031$) was employed to determine whether to stop the study early due to efficacy or futility.

Study Protocol

Initial evaluation—Patients were admitted to the UWCH Pediatric Sedation Program sixty minutes prior to the scheduled LP sedation. Shortly after arrival the sedation nurse and/or physician, in the presence of the study investigator, conducted a brief history and physical examination and obtained baseline vital signs and oxygen saturation.

Sedation period—(Figure 1) The sedation period was divided into 3 stages, the *Pre-Procedure stage*, *Procedure stage* and *Post procedure (Recovery) stage*.

1. *Pre-Procedure stage*: The sedation nurse administered equal volumes of fentanyl (1.0 mcg/kg IV) or placebo (normal saline) five minutes prior to propofol induction over a 1 to 2 minute period. Fentanyl was administered five minutes before propofol induction such that the full analgesic and sedative effects from fentanyl were present during the induction and procedure.²¹ Just prior to propofol administration, heart rate, respiratory rate, blood pressure, oxygen saturation and the m-YPAS were recorded by the study investigator.
2. *Procedure stage*: During induction, propofol was infused at a rate 1 to 2 mg/kg/min until the patient was asleep and able to be positioned for the procedure. (Induction time) Supplemental oxygen was administered during induction and throughout the procedure at 6 liters per minute via “blow by” facemask through a flow inflating anesthesia bag. The stridor score, a 4 point tool used to assess airway patency, was recorded during the sedation; 1-normal breath sounds by auscultation over trachea, 2-stridor over the trachea detected by stethoscope, 3-stridor detected without auscultation and 4-no airway sound detectable over trachea.²² Following induction, subcutaneous lidocaine (1%) was infiltrated at the anticipated LP site by the pediatric oncologist. During the procedure propofol was bolused in doses of 0.5 to 1 mg/kg to maintain a Children’s Hospital of Eastern Ontario Pain Score (CHEOPS) of ≤ 7 during the LP.²³ The CHEOPS score is an observational instrument of behavior during needle insertion. A comfortable appearing child with minimal movement characterizes a CHEOPS score of ≤ 7 . Once the CHEOPS score of ≤ 7 was achieved and maintained the pediatric oncologist conducted the lumbar puncture, collected cerebral spinal fluid and administered intrathecal chemotherapy.
3. *Post procedure stage*: Patient recovery was monitored and recorded by the sedation nurse and study investigator following the procedure. Supplemental oxygen was continued through the recovery period until the patient was awake. The recovery period started immediately following LP needle removal and was based on pediatric discharge criteria from the Connecticut Children’s Medical Center Scoring System.²⁴ Discharge readiness was characterized by stable vital signs and return of cardiorespiratory function and mental status to baseline. Patients were discharged from the sedation program once the above parameters were achieved.

Study Measurements

Respiratory rate, heart rate, oxygen saturation by pulse oximeter, and blood pressure were recorded at baseline, before propofol induction and at minimum every three minutes during the procedure and recovery phases by the study investigator. Heart rate and oxygen saturation was monitored continuously during the sedation period. M-YPAS was recorded at baseline and 5 minutes following fentanyl administration, just before propofol induction. The highest stridor score was recorded during each phase of the procedure.

Adverse events—Adverse events were defined as oxygen saturation < 94%, airway obstruction (stridor score of 4 or 3 requiring intervention), apnea, hypotension (< 5th percentile mean for age) and bradycardia, (< 5th percentile mean for age). Oxygen desaturation was further defined as, mild: 93-88%, moderate: 87-76% and severe < 76%. All interventions performed to treat adverse events were at the discretion of the sedating physician and recorded at that time.

Propofol doses and time periods—The total propofol dose administered for the sedation was recorded. In addition, propofol doses administered for induction and during the LP were documented. The total number of propofol boluses administered during the procedure was also determined.

Statistical Analysis

Categorical variables were summarized using frequencies and percentages. Comparisons of paired categorical variables between the propofol alone and propofol plus fentanyl treatment assignments were performed using a paired McNemar's test. All continuous variables were summarized and reported in terms of medians and ranges. Due to the small sample size comparisons of continuous variables between the two treatment assignments were performed using the Wilcoxon Signed Rank test, which is a non-parametric test for paired comparisons. All statistical tests were two-sided, and $P < 0.05$ was used to indicate statistical significance. Due to small sample sizes, exact p values were calculated in all analyses. Statistical analyses were performed using SAS software version 8.2. (SAS Institute, Cary, NC, USA).

RESULTS

Patient Population

Thirty-one patients were eligible for the study. Nine patients/families declined to participate in the study due to satisfaction with their current sedative regimen and reluctance to consider other options. An interim analysis was conducted following enrollment of 22 patients over a 24 month period (July 2004 to June 2006). Forty-four LP sedations were performed, 22 propofol and placebo and 22 propofol and fentanyl. Fourteen (64%) of the study patients were male and 8 (36%) were female. All patients had an indwelling central venous catheter and were ASA physical status II. The median age was 5.0 years with a range of 2.2 to 17.2 years. Twenty (91%) patients had a diagnosis of acute lymphoblastic leukemia, one (4.5%) with acute myelogenous leukemia and one (4.5%) with T-cell lymphoma. Ten (45%) patients received propofol and placebo on visit number one whereas 12 (55%) patients received propofol and fentanyl on visit number one. Study periods were within 4 weeks of each other in 11 patients (50%) and within 12 weeks in 19 patients (86%). All procedures were successfully completed. There was no statistically significant difference between groups in the m-YPAS score either before or after fentanyl and placebo.

Propofol Dosage (Figure 2)

Median total propofol doses for LP sedation when patients received propofol and fentanyl were 3.00 mg/kg (range 1.4–10.5 mg/kg) versus 5.05 mg/kg (range 2.4–10.2 mg/kg) with propofol and placebo ($P < 0.001$). For induction, patients receiving propofol/fentanyl required a median dosage of 2.30 mg/kg (range 1.3–9.9 mg/kg) compared to 3.65 mg/kg (range 1.6–6.4 mg/kg) for propofol/placebo ($P = 0.011$). Median propofol doses during the procedure were 0.45 mg/kg (range 0.0–1.9 mg/kg) for propofol plus fentanyl in contrast to 1.35 mg/kg (range 0.5–6.1 mg/kg) for propofol alone ($P = 0.001$). The median number of propofol titrations required to maintain a CHEOPS score of ≤ 7 during the LP was 1 (range 0–4) for propofol and fentanyl and 2 (range 1–8) for propofol alone ($P = 0.005$).

Adverse events and interventions

Adverse Events—Adverse events occurred in 11 of the 22 patients (50%) receiving propofol and placebo compared to 4 of the 22 patients (18.2%) receiving propofol with fentanyl¹⁷ ($P = 0.02$). (Table 1). Three of the four patients having an adverse event with propofol and fentanyl also had an adverse event with propofol alone. There were a total of 12 adverse events in the 11 patients receiving propofol/placebo and six in the four patients receiving propofol/fentanyl. The breakdown of the adverse events occurring in each of the groups is outlined in Table 2. Hypotension was the most common adverse event in both groups occurring on six occasions with propofol/placebo and four with propofol/fentanyl. Oxygen desaturations occurred two times (one mild, one moderate) in propofol and placebo and two times (two mild) in the propofol and fentanyl group. No episodes of airway obstruction occurred in the propofol/fentanyl group while three patients receiving propofol/placebo experienced pharyngeal airway obstruction. Airway obstruction uniformly occurred during the procedure stage of the sedation. All adverse respiratory events in both groups occurred during the procedure phase of the sedation. One patient in the propofol placebo group had an emesis during the recovery stage. No occurrences of laryngospasm occurred in either group.

Interventions (Table 2)—An intervention was required in eight of the eleven propofol/placebo patients experiencing an adverse event. Four of the four patients experiencing an adverse event in the propofol/fentanyl arm received an intervention. The most common intervention in both groups was a fluid bolus. All three patients experiencing airway obstruction in the propofol/placebo group required airway maneuvers (e.g. chin lift, jaw thrust), two of whom also required positive end expiratory pressure. One patient with oxygen desaturation required positive end expiratory pressure via a flow inflating anesthesia bag. One patient in the propofol/fentanyl group received positive end expiratory pressure for oxygen desaturation. No patient required endotracheal intubation or hospitalization.

DISCUSSION

Propofol is a common and effective sedative/anesthetic for invasive procedures in children with cancer.^{11,12} Pharmacologic features of propofol include a rapid onset of action, easy titratability, and a smooth and quick recovery. Despite these desirable qualities, adverse cardiopulmonary events are common when propofol is used as a single agent.^{11,12} Our study demonstrates a distinct advantage of combining propofol with fentanyl to propofol alone for LP sedation in children with acute hematologic malignancies. We have previously described the lower overall incidence of adverse events, faster recovery and family preference with this combination.¹⁷ In terms of total propofol requirements and incidence of adverse events, the combination of propofol and fentanyl proved superior to propofol alone. To our knowledge this is the first randomized, controlled study to relate propofol dosing to adverse events in pediatric oncology patients receiving procedural sedation.

The synergy of a propofol-opioid combination has been clearly established in anesthetic practice. Studies consistently show that propofol requirements for anesthetic induction,^{25,26} airway placement,^{27,28} and surgical stimulus²⁹ are less when propofol is combined with an opioid than when propofol is used alone. Similar results have been found in both adults³⁰ and children^{14,15} undergoing sedation for invasive procedures. We observed the propofol sparing effect of fentanyl as well. Total propofol doses were 34.8% less when the two drugs were given together. Studies show that the magnitude of the propofol-opioid interaction is more pronounced the greater the stimulus.¹³ Consequently the propofol sparing effect of fentanyl would be expected to be greater for a painful stimulus than it would be for achieving unconsciousness. We found that propofol doses were reduced by 64.5% during the actual procedure, while only 20.3% for induction to loss of consciousness. We believe the lower incidence of adverse events in patients receiving propofol and fentanyl is the direct consequence of requiring lower doses of propofol to successfully complete the procedure.

Fifty percent of patients in our study experienced an adverse event when propofol was given alone in contrast to only 18.2% when given the two drugs together. While no one type of complication was statistically significant between groups, overall, patients were more likely to have some type of adverse occurrence when receiving only propofol. Our results are consistent with a similar study evaluating these two sedative regimens in children undergoing invasive gastrointestinal procedures.¹⁴ Disma, et. al.¹⁴ compared the combination of propofol and fentanyl to propofol alone in children undergoing oesophagogastroduodenoscopy. Fewer number of patients required supplemental doses of propofol during the procedure and complications were less when patients received the combination of propofol and fentanyl. Five percent of patients receiving propofol with fentanyl experienced an adverse event compared to 19% of patients receiving only propofol. Serious respiratory complications were particularly common in patients receiving propofol as a single agent, with one third of patients experiencing an adverse event requiring bag-and-mask ventilation. No patients receiving the combination of propofol and fentanyl required bag-mask ventilation.

The type and frequency of adverse occurrences in our patients receiving only propofol is comparable to other studies when propofol is used as a single agent for invasive oncology procedures in children.^{11,12} Hypotension is the most frequently observed adverse event during propofol sedation and may or may not be considered clinically significant enough to require intervention.^{11,12} Overall, systolic hypotension was the most common adverse event in our study, occurring in six propofol/placebo patients and four propofol/fentanyl patients.

Respiratory complications on the other hand, particularly airway obstruction and moderate oxygen desaturation, are clinically significant and typically require intervention. Our incidence of airway obstruction when propofol was used alone is similar to that found by Hertzog et. al. in children receiving only propofol for invasive oncology procedures.¹¹ In our study, no patients receiving fentanyl/propofol experienced airway complications or moderate oxygen desaturations. One patient receiving fentanyl/propofol was given positive end expiratory pressure for a mild oxygen desaturation during the procedural phase of the sedation. In patients receiving propofol/placebo, however, three children developed airway obstruction and one experienced moderate oxygen desaturation. All incidents of airway obstruction in patients receiving propofol alone occurred during the procedure phase of sedation. Propofol doses were nearly three-fold greater during the procedure when propofol was given alone, implying a relationship between total propofol dose and respiratory complications.

Our study was designed to achieve a common sedation endpoint between the two groups that we believed would be suitable for conducting the LP (CHEOPS score < 8). We chose a common sedation endpoint in order to compare safety at virtually identical sedation depths. To date, the mechanisms conferring an advantage of a propofol-fentanyl combination in terms of safety has not been clearly determined.¹³ One explanation is based on the findings of several studies showing a differential effect of various sedative drugs on upper airway tone, despite similar depths of sedation. For example, propofol is more prone to causing upper airway collapse than midazolam in spite of similar degrees of sedation.³¹ In addition, propofol reduces pharyngeal muscle tone and increases the propensity for upper airway collapse in a dose-dependent manner.³² We can only speculate that at similar levels of sedation fentanyl's effect on upper airway tone is proportionally less than propofol. Another explanation is the frequency in which propofol was bolused during the procedure to maintain a steady sedation state in patients receiving only propofol. Twice as many propofol boluses were required to maintain the desired sedation endpoint during the procedure when propofol was used alone. As a result, the risk of over-sedation and adverse respiratory events would undoubtedly be greater if the patient's level of sedation was more variable and more propofol boluses were required. We chose not to study propofol by continuous infusion because of how rapidly the LP was performed. In addition, while Klein et al. found that fewer propofol boluses were required when using a propofol infusion versus intermittent dosing for pediatric oncology procedures, the continuous infusion was associated with higher total propofol doses and a greater number of adverse events.³³

There were several limitations to our study. Our sample size was small and may not have adequately represented our patient population. In addition, we only studied children older than 2 years of age who were in the consolidation or maintenance phase of chemotherapy and in relatively good health. Consequently, our findings cannot be applied to children younger than 2 years of age or those children in the early stages of chemotherapy. Half way through the study a preliminary analysis was performed that demonstrated a lower incidence of adverse events in patients receiving propofol with fentanyl. Following closer examination, our data revealed a beneficial effect of the drug combination and the study was terminated. At that time the ability to maintain equipoise became increasingly difficult as well. We believe that the crossover nature of our study added power to our analysis and permitted us to reach statistical significance in our primary endpoints, propofol dosing and total adverse events. We chose the crossover design as well because of the lack of drug carry over effect between study periods and to eliminate inter-patient drug variability. Because of our small sample size, however, other endpoints such as comparison of individual adverse events like airway obstruction could not be adequately examined. A larger study would be required to further ascertain the benefits of a propofol/fentanyl regimen in terms of individual safety effects and efficacy.

Being truly blinded to fentanyl or placebo was initially identified as a potential drawback to our design. However, as identified by the m-YPAS score there were no significant differences in anxiety between the two groups. While the m-YPAS score is not meant as a sedation score the lack of any difference between fentanyl and placebo implies few effects on mental status. The probable reason for this is that all children had previously been sedated for procedures in our sedation program and consequently had little pre-procedure anxiety. An additional confounding variable was that the sedating physician was not blinded and may have consciously or unconsciously titrated propofol in an unbiased manner. Fortunately most sedating physicians were not intimately involved with the study and would not be expected to be biased one way or the other.

In 1990, the American Academy of Pediatrics (AAP) specifically addressed the importance of optimizing procedural sedation and pain control in children with cancer. Since that time a

number of different sedative regimens have been studied in this patient population. When administered by trained and skilled personnel, propofol is one of the most effective sedative/anesthetic agents for invasive oncology procedures in children with cancer. Our study builds upon the work of others who have studied sedation in this population. We showed that the combination of propofol and fentanyl resulted in fewer adverse sedation events in otherwise healthy children with hematologic malignancies undergoing LPs. We conclude that a fentanyl-propofol combination is a superior sedative regimen to propofol alone in children older than 2 years of age with hematologic malignancies and recommend its use for elective LP sedation.

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Abbreviations

LP	Lumbar Puncture
ALL	Acute Lymphoblastic Leukemia
m-YPAS	Modified Yale Preoperative Anxiety Scale
CHEOPS	Children's Hospital of Eastern Ontario Pain Scale

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FIGURE 1.

The sedation period was divided into 3 stages: pre-procedure stage, procedure stage and post procedure stage.

- (1) Pre-procedure stage: fentanyl or placebo administration.
- (2) Procedure stage: propofol induction, propofol titration during the procedure and performance of the LP.
- (3) Post procedure stage: recovery period and discharge.

FIGURE 2.

Propofol doses for each group, administered for induction, the procedure and for the entire sedation (total)

P/P: Propofol/Placebo group

P/F: Propofol/Fentanyl group

Box plot: Box = 75–25 percentile; bold line=median values; black dot=mean values; whiskers correspond to median $\pm$ 1.5 times the interquartile range; dot=values beyond median $\pm$ 1.5 times the interquartile range (outliers)

TABLE 1

Number of Patients Experiencing an Adverse Event Within Each Group and Individual Adverse Events

	PROPOFOL/PLACEBO n=22	PROPOFOL/FENTANYL n=22
Number of Patients with an adverse event ^a (%)	11 (50%)	4 (18.2%)
Total Adverse Events	12	6
- Hypotension	6	4
- Oxygen desaturation		
• Mild	1	2
• Moderate	1	0
• Severe	0	0
- Airway Obstruction	3	0
- Other	1 (emesis)	0

^aDifferences between groups were statistically significant at P=0.02.

TABLE 2

Interventions Within Each Group

	PROPOFOL/PLACEBO	PROPOFOL/FENTANYL
Number of patients requiring an intervention	8	4
Specific Interventions		
- Airway maneuver ($\pm$ positive end expiratory pressure)	3	0
- Positive end expiratory pressure	1	1
- Fluid bolus	4	3

^aPositive end expiratory pressure via a flow inflating anesthesia bag.