

EVALUATION OF A GRAPHICAL ANESTHESIA DRUG DISPLAY FOR SPACE TRAVEL.

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Abstract

As the frequency and duration of space travel increase, the potential need for emergency medical care in space grows, and with it the need for patient monitoring devices supporting therapeutic treatment. Providing emergency care to an injured astronaut may necessitate immediate surgery. During such events, the timely administration of anesthetic agents will need to be performed by someone who is not a formally trained anesthesiologist. The availability of usable real-time displays of intravenous anesthetic concentrations and effects could significantly enhance intraoperative clinical decision-making both in space and on earth. The effectiveness of the real-time anesthesia display on the management of total intravenous anesthesia was determined by 31 anesthesiologists participating in a simulation study. In the presence of the anesthesia drug display, clinicians maintained physiologic indicators such as blood pressure and heart rate closer to baseline levels. Participants also reported an increase in perceived performance when using the drug display. The results indicate that surgeries on earth and in orbit would benefit from the implementation of this display.

Introduction

Monitoring devices that show intravenous (IV) drug concentrations and effects currently do not exist in space or in the modern operating room. However, the pharmacokinetic and pharmacodynamic models are available to estimate past, present and future effect site drug concentrations and associated physiological effects. An interdisciplinary research team (bioengineering, architecture, clinical anesthesia, and cognitive psychology) developed a graphic display that shows the predicted concentrations of intravenous drugs in real-time.

During surgery, levels of sedation, analgesia and neuromuscular blockade are controlled by the timely administration of anesthetic drugs. Drugs are titrated while vital signs are monitored. The patient's response is observed until the desired effects are achieved. Compared with the administration of volatile anesthetics, this task is more demanding for increasingly popular IV anesthesia since drug plasma or effect site concentrations cannot be easily measured in real-time. Accurate administration of anesthetic agents could also be further complicated in a zero gravity environment.

Figure 1. The new and improved drug display

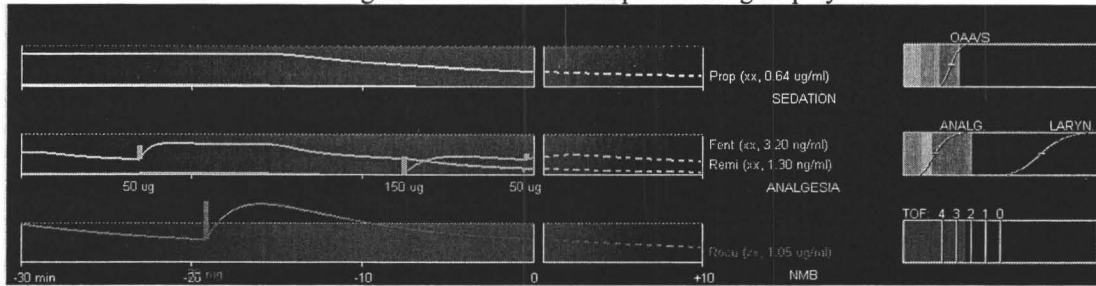


Figure 1: The drug display showing drug doses, predicted effect site concentrations and predicted effects on sedation, analgesia and neuromuscular blockade. The three plots show trends (solid lines) and predictions (dashed lines) for the modeled effect site concentrations for the three classes of drugs. The current effect site concentrations are seen at time zero (just to the right of the middle of the display). Past history moves to the left of time zero (to -30 min) and the predicted future levels move to the right (to +10 min). The bar graphs on the far right show the combined effects of all drugs administered on sedation, analgesia, and neuromuscular blockade.

Multi-compartment pharmacokinetic models and their pharmacodynamic relationships have been developed that predict the arterial plasma and effect site concentrations for many intravenous anesthetics, analgesics, and neuromuscular blocking agents. These models permit the calculation of effect-site concentration for each agent, using iterative difference equations.^{1,2} When a bolus of drug is administered, the pharmacokinetic model can provide a prediction of the resulting effect site concentration. The model-based predictions should provide a guide to drug administration resulting in better control of plasma drug concentrations.

Our research group at the University of Utah developed and tested a prototype of a continuous display design containing predicted effect site concentrations and drug effects based on state-of-

the-art pharmacokinetic and pharmacodynamic models. The value of the prototype display to clinicians was assessed favorably as they delivered bolus doses of remifentanyl and propofol using a software based patient simulator.³ Results from this study led our development group to alter the prototype design in an effort to further improve performance.

The new display (see Figure 1) can predict values for drugs administered in isolation and also when multiple drugs of the same class are used. Some drugs combined synergistic effects. Multiple drug effects and their interactions within a class and also between classes are also displayed. The information presented to the anesthesiologists is mapped to clinically relevant information rather than an arbitrary scale from zero to 100%.

Figure 2. Sedative effect window.
Eyes Open ← → Eyes Closed

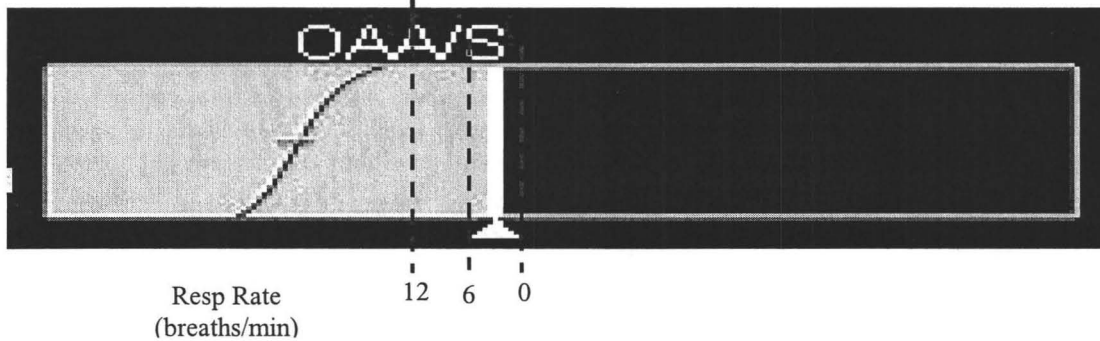


Figure 2: Consciousness levels change with the predicted level of sedation. The OAA/S curve is drawn from the 5th to the 95th percentile. Below the 95th percentile, the patient's eyelids are open and the respiratory rate is 12 breaths/min. As the sedation level continues to increase above the 95th percentile, the patient's eyelids close and the respiratory rate falls to 6 and then to 0 breaths/min.

Figure 3. Analgesic effect window.

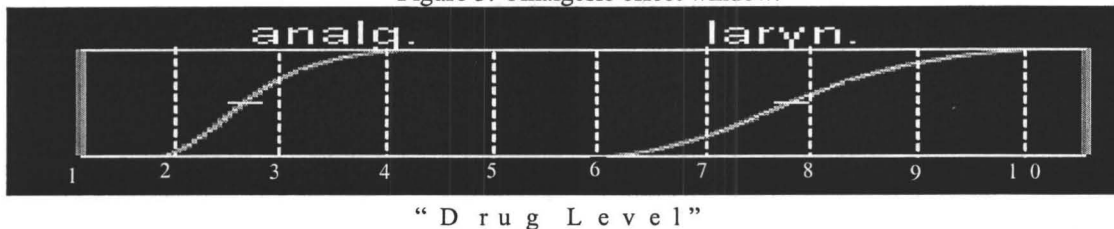


Figure 3: The drug level (effect-site concentration) for Analgesia. The first curve corresponds to mild surgical stimuli and the second curve applies to laryngoscopy. When analgesia levels exceed the area under the curve the patient has sufficient analgesia for the type of stimulus.

Examples of other changes made to the display are shown in Figures 2 and 3. Figure 2 shows the effect site concentration window for the sedative class of drugs as produced in the current iteration of the display. Within the effect site concentration window for sedatives the Observer's Assessment of Awake or Asleep Scale (OAA/S) sigmoidal function has been added to indicate the range of drug level to necessary to anesthetize 95% of the population.

In Figure 3, the analgesic effect site concentration is shown. Within this display window sigmoidal curves indicate the level of analgesia relative to mildly painful surgical stimuli such as skin incision and severe surgical stimuli such as laryngoscopy. When the level of analgesia exceeds the area under the curve, the amount of analgesic is sufficient to block pain for 95% of the population. Other changes include the mapping of the neuromuscular blockade effect site concentration to the train of four stimulus. The amount of neuromuscular blockade on board as shown in the display predicts accurately the amount of paralysis for 95% of the population. After these and other changes in the arrangement of information in the display, we tested the new iteration of the display design on a sample of anesthesiologists.

In this study we test the hypothesis that pharmacodynamic models which predict levels of sedation, analgesia and neuromuscular blockade, help the clinician to choose the optimum combinations of drugs; thus maximizing the desired therapeutic effects while minimizing adverse side effects. The new display should be able to help the anesthesiologist maintain levels of sedative, analgesic and neuromuscular blocking agents at levels appropriate for the changing demands of the surgical procedure relative to a control condition performing without the display. Pain response,

wake up time and duration of anesthetic should all be reduced in the display condition. A further hypothesis predicts that NASA-TLX workload assessments⁴ would also indicate an overall reduction in perceived workload associated with improved performance. Additionally subjects should continue to subjectively rate the display favorably.

The experimental task was made challenging by changing the needs of the surgeon, and thus the demands of anesthesia, midway through the simulated surgical procedure. As levels of painful stimulus change, anesthesiologists using the drug display should be better able to manage the changing needs of the patient relative to the control group. Additionally anesthesiologists were asked to care for their patient in a METI high fidelity simulator environment

Methods

Subjects

Thirty-one anesthesiologists and anesthesiologists with a range of clinical experience (CRNA, CA-2 and CA-3, and faculty) participated in this study. All participants were paid \$50.00 for their participation in the study. All participants were affiliated with the University of Utah School of Medicine.

Procedure

Upon arriving at the Center for Patient Simulation, subjects completed a questionnaire to elicit their experience level, length of time working prior to the study, caffeine consumption, sleep history, color-vision, and whether they required vision correction. Subjects were instructed to provide anesthesia to a simulated patient during surgery using the total intravenous anesthesia method (TIVA). A standardized training (see below) followed where all participants were trained in the use of the drug display, instructed in the use

Figure 4. Outline of painful surgical stimulus

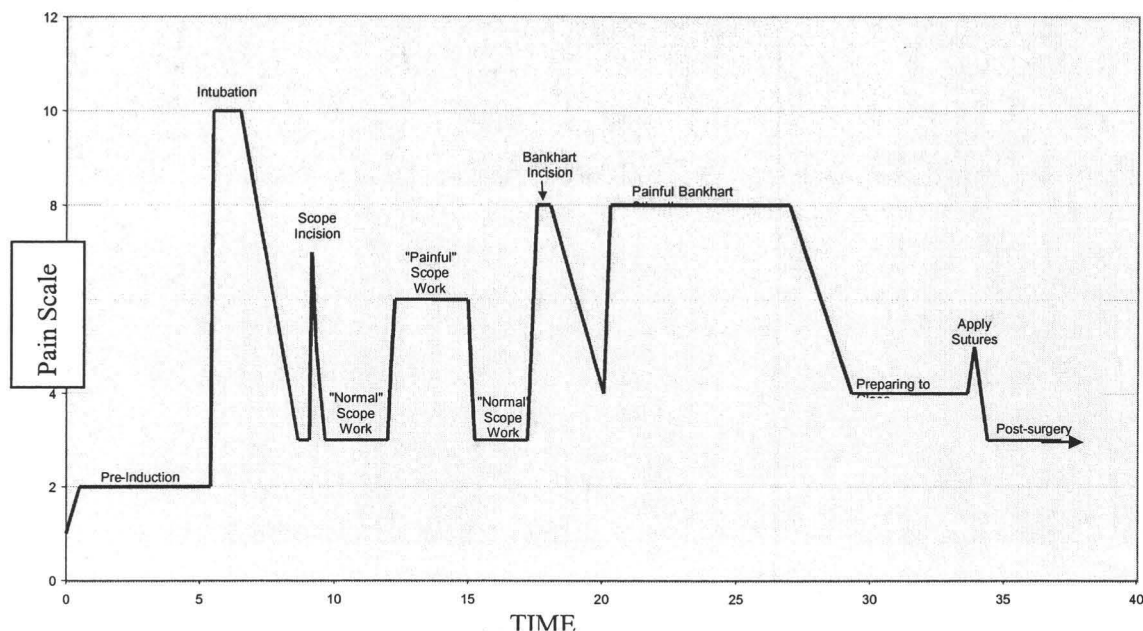


Figure 4: Diagram of the surgical procedure as a function of painful stimuli and time. Participants were required to administer appropriate analgesic and sedative for the changing dynamics of the surgical procedure.

of the METI simulator, and the equipment used for the delivery of the drugs.

Prior to beginning the simulation, participants reviewed the anesthesia record and patient information sheet providing them with medical information about the patient, including allergies and experienced past problems, and the planned procedure. Subjects then began to induce anesthesia, intubate the patient's trachea, and provide care for the simulated patient throughout a shoulder endoscopy procedure. Seventeen minutes into the endoscopy the surgeon announced that the originally planned scope procedure was not sufficient to repair the damaged shoulder, and that a more invasive Bankart procedure would need to be performed. The change in surgical procedure significantly altered the requirements for the delivery of anesthetics and the projected time requirements for the surgery (See Figure 4). After providing care for the duration of the surgical procedure the anesthesiologist extubated the patient and waited until the patient regained consciousness.

After completing the simulation, the subjects answered a NASA-TLX questionnaire and a questionnaire about the drug display and the realism of the simulation. The experimental session lasted approximately ninety minutes, and the subjects were debriefed and compensated \$50 for their participation.

Aparati

The METI anesthesia simulator (METI, Sarasota, FL.) at the University of Utah Center for Patient Simulation was used to conduct the simulation. An AS/3 anesthesia monitor (Datex, Helsinki, Finland) displayed the traditional electrocardiogram (ECG), arterial blood pressure (BP), pulse oximeter (SpO₂), and capnogram (CO₂) waveforms. Digital values for heart rate (HR), blood pressure (BP), oxygen saturation (SpO₂), end-tidal carbon dioxide (F_{et}CO₂), and fraction of inspired oxygen (F_iO₂) were displayed in addition. The pulse oximeter tone was also provided. Alarms were set to default mode. The drug display (Figure 1) was shown on a 17-inch monitor placed beside the AS/3 monitor.

Training

A computerized tutorial was presented to each subject in order to provide standardized training in use of the drug display for all subjects. Subjects viewed static screen shots of the drug display monitor depicting the effect site concentrations and current effects of propofol, remifentanyl, fentanyl, and rocuronium on sedation, analgesia and neuromuscular blockade. The display was explained in detail including: axes, labels, drug classifications, effect site concentrations according to clinically relevant variables, the effect bars,

effect site concentration and its relation to drug effect, predicted, past, and present concentrations. The participants were told the display shows estimated effect site concentrations and drug effects generated from pharmacodynamic models.

A minimum amount of training was required for the METI high fidelity simulator because most subjects were familiar with the simulator from previous exposure as part of their anesthesia training. All subjects were instructed in the use of the drug delivery systems. To demonstrate proficiency in use of the drug delivery system, each subject administered a fixed infusion rate and a specified bolus dose as practice. Training for the simulator was completed when the subject reported feeling comfortable with administration of the anesthetic agents in the simulated patient. On average, the training took 20 minutes. Half of the subjects were then assigned randomly to the drug display condition and the remaining half were assigned to the control condition.

Surgical Scenario

Prior to starting the simulation, the subjects were given the patient's preanesthetic evaluation form including: the patient's medical and surgical history, labs, baseline vital signs, planned surgical procedure, and the expected duration of the surgery. The patient was presented as having arrived in the operating room without prior sedation or pre-oxygenation; however, ECG electrodes, an IV, an arterial line, and a non-invasive blood pressure cuff were already in place. The anesthesiologist was told the patient was scheduled to receive a routine shoulder endoscopy to repair minor damage, a procedure usually lasting about 25 minutes. The subject was reminded that he or she may administer boluses or continuous infusions of propofol and remifentanyl, as well as bolus doses of fentanyl and rocuronium. Antagonist drugs and other cardiovascular agents were not available for use. The subject was given a new anesthetic record and was reminded to keep the record during the course of the simulation

Data Collection

During the simulated surgery, predicted effect site concentrations of all administered drugs and model predicted levels of sedation, analgesia, and NMB were recorded. Patient vital signs were also recorded during the surgery. Minimum, maximum, mean, and percent deviations from baseline were calculated for heart rate, systolic, diastolic and mean blood pressure. The values of the vital signs were recorded at four-second intervals and the

effect site concentrations of all administered drugs were recorded at two-second intervals. The time duration from completion of skin closure to awakening (spontaneous respiration and eyes opening) and extubation were recorded.

Data Analysis

Pain Response

The goal during the surgery is to keep the vital signs as stable as possible, reducing patient risk. Thus the dependent measures for the difficult to manage Bankhart procedure were analyzed. Performance in analgesia management was measured by comparing the pharmacodynamic predicted level of analgesia with the level of surgical stimulation (Figure 4). Since the simulator was calibrated such that cardiovascular responses matched the pharmacodynamic predictions, subjects with and without the drug display had the same cardiovascular information available. Heart rate (HR) and mean arterial blood pressure (MAB) were used to measure periods when the patient responded adversely to pain.

Wake Up Time

To determine the time it took to wake the patient up, we measured the time between skin closure and the time when the patients eyes opened and had a respiratory rate of 6 breath per minute.

Total Time

The time for patient emergence was measured by determining the time between induction of anesthesia (the time of eye closure and respiratory rate of zero) and the patients eye-opening and return of the respiratory rate to 6 breath per minute.

Questionnaires

The mean and standard deviations of the scores were computed for the participants' answers to the NASA-TLX workload survey and the first question of the evaluation questionnaire regarding display usefulness. Ratings pertaining to the realism of the simulated surgery were also solicited.

Results

Pain Response

Overall analyses of pain response during the Bankhart procedure (unexpected and requiring changes in the anesthesia plan) indicate performance differences observed were due to the presence of the drug display. When anesthesiologists were using the drug display, their level of performance was higher indicated by

Table 1: Pain Response

	Drug display	Control
HR	65.4 (12.4)	57.4 (14.1)
MAB	90.1 (19.8)	79.6 (17.8)
Pain score	.67 (1.1)	1.2 (1.4)

Table 1. Means (standard deviations) for heart rate, mean arterial blood pressure, pain scores during the Bankhart procedure.

higher mean arterial blood pressure, higher heart rate, and lower pain levels than the performance of the control group (See Table 1).

As painful stimuli occur, the associated pain score (0-10) is compared with the predicted analgesic level (0-10). If the level of analgesia is below the pain score, the cardiovascular variables increase above baseline simulating a cardiovascular response. If the level of analgesia is higher than the pain score, the cardiovascular variables are lower than baseline.

Analyzing the patient's heart rate during the Bankhart procedure revealed a main effect of display condition ($F(1,25)=4.87$; $p=.037$), with average heart rate closer to baseline when subjects were using the drug display.

Analyzing the mean arterial blood pressure during the Bankhart procedure showed that subjects in the drug display condition were able to keep the blood pressure of the patient closer to baseline levels than anesthesiologists who were in the control group ($F(1,25)=4.379$; $p=.047$).

Analyzing the level of control for pain showed a similar picture as the analyses of heart rate and mean arterial blood pressure. Again, there is a reliable difference between the display condition and the control condition ($F(1,25)=5.507$; $p=.027$), with lower levels of pain in the group where anesthesiologists were using the drug display.

Wake Up Time

The same design as described above was used to analyze the time for emergence from anesthesia (see Table 2). Analyzing the time until eye opening showed a significant main effect of condition ($F(1,29)=4.26$; $p=.05$). Patients who were treated in the drug display condition woke up more than two minutes earlier than patients treated without using the drug display.

Analyzing the time for respiratory rate reaching the criterion of 50% of the baseline level shows a main effect of condition ($F(1,29)=11.39$; $p=.003$) with patients reaching this respiratory rate more than three minutes faster when they were

Table 2: Wake Up Time

	Drug display	Control
Opening eyes	736 (160)	862 (176)
Respiration 50%	577 (148)	774 (176)

Table 2. Time (standard deviations) in seconds during the wake up time interval and recovery of respiratory rate to 50% of baseline.

treated by an anesthesiologist in the drug display condition. These results indicate there was a strong effect of the display condition on performance. Shorter wake up latencies were observed and respiratory rate returned to normal more quickly when the patient was treated by an anesthesiologists using the drug display.

Total Time

Another way to analyze the performance in terms of the quality of delivering anesthesia is to look at the overall duration of the procedure. Since the surgical portion of the procedure was consistent between subjects, the differences in total time can be attributed to display condition. The data were analyzed by using the total time for the surgical procedure from the beginning of the preoperative phase to the point of extubation of the patient. The ANOVA revealed a main effect of condition ($F(1,30)=4.73$; $p=.039$), with anesthesia being delivered more efficiently when patients were treated by anesthesiologists using the drug display (see Table 3). The results again indicate there was a strong effect of the display condition on performance. Shorter procedure durations were observed when the anesthesiologists used the drug display.

Questionnaire data

The analyses of the NASA TLX revealed a reliable difference between conditions in terms of subjective performance ($F(1,30)=4.44$; $p=.045$). Subjects who were using the drug display rated

Table 3. Total Time

	Drug display	Control
Total time for procedure	2826 (542)	3215 (640)
	{47 minutes}	{54 minutes}

Table 3. Total procedure time in seconds (standard deviation) for the drug display and the control condition. Below is the total time in minutes.

their subjective performance higher (5.9 (1.6)) than subjects in the control group (4.5 (2.0)).

Analyzing subjects' impression about the fidelity of the simulation showed no difference between the two display conditions. All subjects thought the display should be added to their current monitoring capabilities.

Discussion

The results suggest that visualizing real-time drug pharmacokinetics and pharmacodynamics as drugs are administered results in better control of drug concentrations, more stable vital signs and an increase in perceived performance. Anesthesiologists more accurately controlled effect-site concentration of sedatives, analgesics and neuromuscular blockade when using the drug display, and this resulted in a more stable heart rate and fewer instances of hemodynamic response to pain.

This study supports the idea that observing the effect site concentrations of intravenous drugs helps clinicians to maintain drug levels within the "therapeutic window". As a result, there will be a decrease in intraoperative awareness, undesirable hemodynamic responses to pain and an improvement in the control of neuromuscular blockade with the use of such a display.

Results from the NASA-TLX indicate an increase in perceived performance associated with anesthesia administration while using the drug display. Participants also rated the display as a useful addition to the operating room.

In sum the results of this study indicate that anesthesiologists performance during surgery can be facilitated with the additional information provided in the drug display. This facilitation of performance will hopefully result in fewer critical events during surgery as well as post surgical injury associated with improper anesthetic administration. With the certain probability of the necessity for critical care in outer space, the means for displaying accurate and important information about a patient's status to an attending physician or astronaut is paramount. A display such as the design presented in this report may help to assist clinical decision making and critical care of patients in the modern day operating room and space travelers in orbit and beyond.

References

1.) Shafer SL, Gregg KM. Algorithms to Rapidly Achieve and Maintain Stable Drug Concentrations at the Site of Drug Effect with a Computer-Controlled Infusion Pump. Journal of Pharmacokinetics and Biopharmaceutics, 1992; 20(2)147-169.

2.) Schwilden H. A general method for calculating the dosage scheme in linear pharmacokinetics. Eur J Clin Pharmacol 1981; 20:379-386.

3.) Albert, R.W., Drews, F.A., Strayer, D.L., Syroid, N.D., Agutter, J.A., Westenskow, D.R., Bermudez, J.C., Prenzel, H., Loeb, R.G., Weinger, M.B., (2001). Development and evaluation of a graphical anesthesia drug display for astros on orbit. Proceedings of the NASA Fellowship Symposium. 7, 1-5.

4.) Hart SG and Staveland LE (1988). Development of NASA-TLX: Results of empirical and theoretical research in P.A. Hancock and N Meshkati (Eds.), Human mental workload (pp.139-183). Amsterdam: North-Holland.
