CASE REPORT

Anesthesia management using ROP-1680 AsisTIVA : a case report

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Abstract : AsisTIVA is total intravenous anesthesia support software for syringe pump control. It remains the only automated program to have achieved both practical and commercial viability. AsisTIVA has been certified for use at Tokushima University, Tohoku University, and at its developer institution, Fukui University. We conducted our initial anesthesia management with AsisTIVA at Tokushima University. This initial experience was successful, with no adverse effects. AsisTIVA controls propofol and remifentanil concentrations to maintain a Bispectral index of 45 and adjusts rocuronium concentrations to maintain a Train Of Four value of 1. By managing these anesthetics, AsisTIVA allows anesthesiologists to focus on other aspects of anesthesia management. Its use is expected to expand further. J. Med. Invest. 72 : 211-216, February, 2025

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INTRODUCTION

AsisTIVA is software that automatically calculates and administers propofol, remifentanil, and rocuronium doses during total intravenous anesthesia in adult patients. It was developed to assist with total intravenous anesthesia. AsisTIVA is the core software of a "Robot Anesthesia System" that automatically controls the administration of intravenous anesthetics and is the first medical device approved in Japan to simultaneously control sedatives, analgesics, and muscle relaxants. The number of general anesthesia surgeries in Japan is rising, but there is a nationwide shortage of anesthesiologists, resulting in long working hours. The resulting physical and mental stress has made reconsideration of the anesthesiologist's work style a potential challenge.

AsisTIVA was developed under the leadership of physicians at the University of Fukui, in collaboration with the National Center for Global Health and Medicine and Nihon Kohden Corporation, with support from the Japan Agency for Medical Research and Development (AMED). The clinical trial was completed, and the product has been available on the market since July 2023.

While automated anesthetic administration programs have been developed in Western countries (1-5), AsisTIVA remains the only automated program that has achieved practical and commercial viability. Johnson & Johnson developed an automated sedation device using propofol and once introduced it to the market, but it was discontinued due to poor sales in the United States. Mechanization and automation would not have progressed without advancements in engineering, medical technology, and the development of social acceptance (6).

AsisTIVA is currently the only commercially available automated anesthetic administration program. However, to ensure safety, the Japanese Society of Anesthesiologists has strictly specified facility criteria and physician requirements for its use. As of May 2024, AsisTIVA has been certified for use at Tokushima University and Tohoku University in Japan, in addition to the developer, Fukui University.

As of the writing of this paper, only five anesthesiologists—two at Tokushima University and three at Tohoku University—have been certified to use AsisTIVA, apart from the Fukui University staff involved in its development.

Since AsisTIVA was released to the market, there have been no reports of its use by individuals not involved in its development. Herein, we report our first experience of anesthesia management using AsisTIVA at Tokushima University.

About AsisTIVA

Various monitors have been used to assess anesthesia status (7-11). AsisTIVA acquires Bispectral index (BIS) and Train Of Four stimulation (TOF) data from the monitoring system. For anesthetics administered during total intravenous anesthesia, the amounts of sedative (propofol) and analgesic (remifentanil) are automatically calculated based on the BIS, and the syringe pump settings are controlled in a closed-loop manner. The amount of muscle relaxant (rocuronium) is also automatically calculated based on the TOF, and the syringe pump setting is controlled in a closed-loop control (Figure 1).

About the Automatic delivery control algorithm.

Propofol administration algorithm

AsisTIVA calculates the estimated effect-site concentration for each patient based on the propofol administration history and pharmacokinetic parameters. It collects paired data on BIS values and propofol effect-site concentrations from the start of propofol infusion and fits these data to a sigmoidal regression curve in real time. Using this curve, the estimated target effect-site concentration required to achieve a BIS value of 45 is calculated in real time, and the propofol administration rate is adjusted accordingly.

Remifentanil administration algorithm

AsisTIVA calculates the estimated effect-site concentration for each patient using the remifentanil administration history and pharmacokinetic parameters. Paired data on remifentanil and propofol effect-site concentrations required to achieve a BIS value of 45 are collected from the start of remifentanil infusion.

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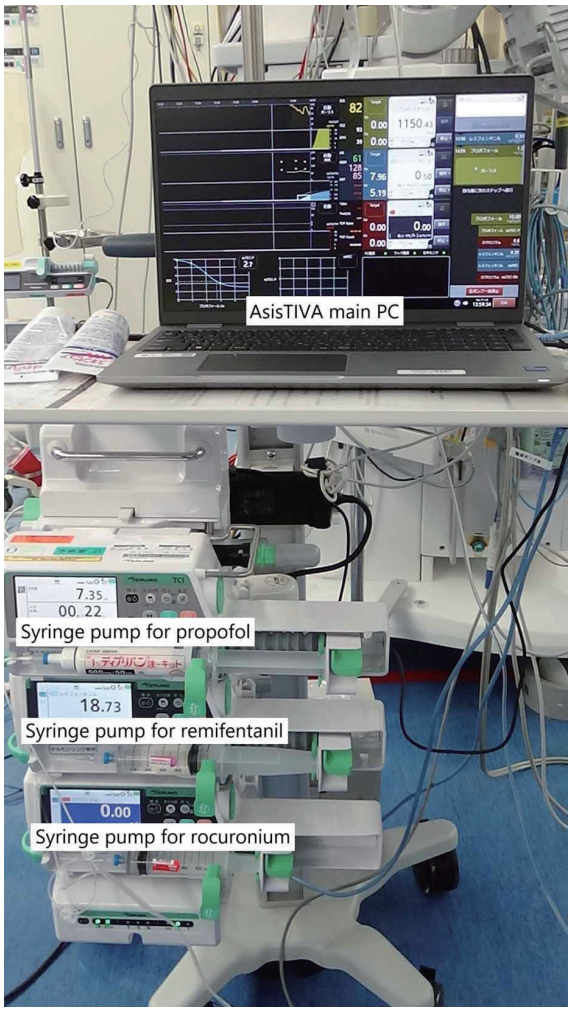

Figure 1. General view of the Automated Syringe Infusion System for Total Intravenous Anesthesia system (AsisTIVA)

These data are used to derive an equipotential curve for analgesia (x-axis) and sedation (y-axis) through regression analysis with a rectangular hyperbolic function ($y = c/(x - a) + b$). Using this curve, AsisTIVA determines the remifentanil concentration required to maintain a BIS value of 45 and adjusts the dose accordingly.

Rocuronium administration algorithm

AsisTIVA calculates the estimated effect-site concentration for each patient based on the rocuronium administration history and pharmacokinetic parameters. Continuous administration of rocuronium is maintained at the effect-site concentration corresponding to the time when %T1 recovers to 3% on the TOF monitor. The dose is subsequently adjusted in real time based on feedback from actual TOF values.

The actual method of administration

Remifentanil is administered based on the patient's ideal body weight. It is initially started at 0.5 μg/kg/min. When the effect-site concentration of remifentanil reached 5 ng/ml, 1 mg/kg of propofol was administered, and continuous auto-administration of propofol (dosed by actual body weight) was started. As the BIS values decrease after propofol administration, AsisTIVA learns the patient's responsiveness to propofol from the variations in BIS values and estimates the propofol effect-site concentration required to maintain a BIS value of 45. It continuously learns the responsiveness to both remifentanil and propofol and adjusts their concentrations to target a BIS of 45.

As for muscle relaxants, rocuronium is administered based on the patient's ideal body weight. Rocuronium 0.6 mg/kg is administered if the BIS value falls below 55 after induction of anesthesia or at least 3 minutes after starting propofol administration. If the TOF value does not reach 0 within 1 minute, an additional 0.3 mg/kg of rocuronium is administered. The TOF value is then continuously measured, and AsisTIVA calculates the rocuronium effect-site concentration throughout this period. When muscle relaxation wanes and the TOF value continuously shows 1, AsisTIVA automatically administers rocuronium to maintain that effect-site concentration, receiving continuous TOF feedback to keep the TOF value at 1.

After intubation is completed, entering the command to complete intubation on AsisTIVA reduces the remifentanil dose to 0.25 μg/kg/min. When the command to begin the surgical procedure is entered at time-out, the remifentanil dose increases to 0.5 μg/kg/min. Thereafter, propofol and remifentanil doses are continuously adjusted according to the patient's responsiveness.

After the surgery is completed, all drug infusions are stopped on AsisTIVA. The anesthesiologist then awakens and extubates the patient.

To ensure the safety of AsisTIVA, conditions for the facilities and physicians performing the procedure are strictly specified. To be certified as a practitioner, an anesthesiologist with at least 300 cases of experience in total intravenous anesthesia must attend a training course, pass a written examination, and undergo practical training at Fukui University.

AsisTIVA can automatically administer anesthetics based on BIS and TOF values, but it cannot assess conditions in the operative field. It is also unable to perform circulatory or respiratory management. Therefore, the certified anesthesiologist must be present to monitor and operate the AsisTIVA, as well as to manage other aspects of anesthesia.

Various mechanisms are programmed into AsisTIVA to ensure the safe operation of automatic anesthetic administration. During surgery, the use of electrocautery, for example, can affect BIS values. If BIS readings temporarily become poor, AsisTIVA is designed to keep propofol and remifentanil concentrations constant to prevent intraoperative awakening due to insufficient intraoperative anesthesia. If poor BIS readings continue, the propofol effect-site concentration is increased by 0.1 μg/ml to prevent inadequate sedation (i.e., intraoperative arousal) (6). However, if the BIS value remains poorly measured for an extended period, cannot be measured intraoperatively, or fluctuates beyond AsisTIVA predictions, automatic administration of propofol and remifentanil cannot continue. In such cases, the anesthesiologist must manually adjust the doses based on experience.

Similarly, intraoperative measurement errors can occur with respect to TOF values. If abnormal TOF values persist beyond AsisTIVA's learning curve, or if measurement is not possible, automated administration is discontinued, and the anesthesiologist must manually administer muscle relaxants based on clinical judgement.

CASE REPORT

A 75-year-old woman with a height of 150 cm and weight of 43 kg was scheduled for thyroid carcinoma resection. The patient had a history of hypertension managed with amlodipine besylate and was classified as American Society of Anesthesiologists Physical Status 2. Following departmental conference approval, AsisTIVA was selected for anesthesia management.

In accordance with recommendations of the Japanese Society of Anesthesiologists, eligible patients were provided written information about AsisTIVA, and informed consent was obtained.

Standard monitors have been established before anesthesia induction, including blood pressure, electrocardiogram, peripheral oxygen saturation, and end-tidal carbon dioxide. General anesthesia was induced after BIS and TOF monitoring were established. At our institution, the BIS module (QE-910P, Nihon Kohden®, Tokyo, Japan) was used for BIS measurements. To ensure accurate and stable BIS values, impedance was minimized. The electromyography TOF module (AF-201P, Nihon Kohden®, Tokyo, Japan) was used for TOF measurements (Figure 2).

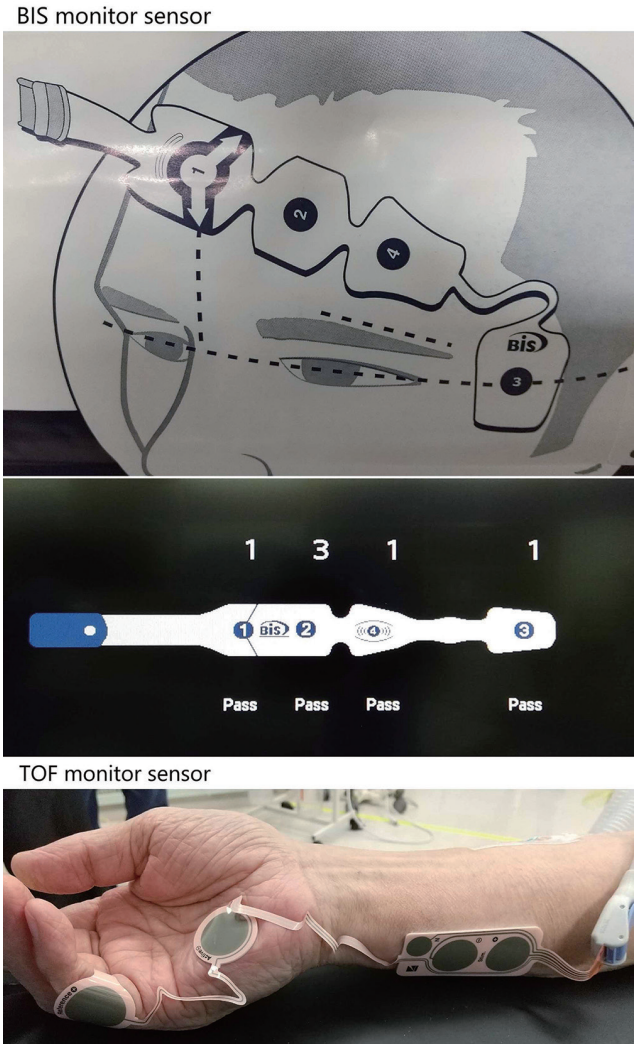

Figure 2. Images of the Bispectral index (BIS) and Train Of Four (TOF) sensors.
Impedance value of BIS, which was maintained at <5 for accuracy.

AsisTIVA automatically adjusts the rocuronium dose to maintain a TOF count of 1 (12). In this case, we used a 20 G indwelling IV cannula (Nexiva, Becton Dickinson, Franklin Lakes, NJ, USA). Each drug syringe was attached to the patient via a triple-lumen extension tube connected to one of the drug infusion ports of the indwelling IV cannula (Figure 3).

AsisTIVA started auto-administration of remifentanil at 0.5 μg/kg/min while we fully oxygenated the patient at a flow of 6 L/min. When the remifentanil effect-site concentration exceeded 5 ng/ml, 43 mg of propofol was administered, and thereafter, propofol was automatically administered. Rocuronium 38.1 mg was administered when the BIS value fell below 55, and tracheal intubation was performed once the TOF value reached 0. A 7.0-mm Neuro Intensive Monitor tube was used for intubation to assess vocal cord response to recurrent nerve stimulation. To monitor the recurrent nerve stimulation, rocuronium was not administered automatically ; only the initial 38.1 mg dose was administered. After intubation, the remifentanil infusion was reduced to 0.25 μg/kg/min, and from the start of the surgery, remifentanil was shifted to auto-administration by AsisTIVA. Ephedrine and phenylephrine were administered when the systolic blood pressure dropped below 90 mmHg before tracheal intubation.

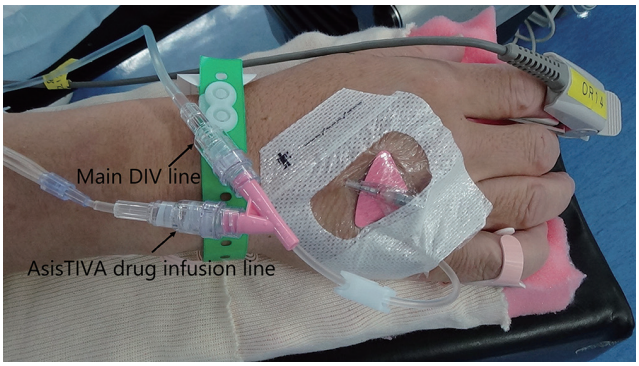

Figure 3. Close-up view of the patient receiving anesthetic drugs through a cannula with an integrated drug administration port (Nexiva).

Intermittent doses of ephedrine and phenylephrine were administered once before tracheal intubation (ephedrine 2 mg and phenylephrine 0.05 mg), once after intubation (ephedrine 4 mg and phenylephrine 0.1 mg), and twice during the procedure when the systolic blood pressure fell below 90 mmHg (ephedrine 4 mg and phenylephrine 0.1 mg, and ephedrine 2 mg and phenylephrine 0.05 mg). For postoperative analgesia, a total of 200 μg of fentanyl and 640 mg of acetaminophen were administered intraoperatively, and metoclopramide and dexamethasone were administered to prevent postoperative nausea and vomiting. Automatic drug administration was terminated at the end of the surgery, with final effect-site concentrations of 4.3 μg/mL for propofol and 34 ng/mL for remifentanil. Since the TOF ratio had recovered to over 90%, sugammadex was not administered. Extubation occurred 20 minutes after stopping the drug administration. The patient awoke clearly and without intraoperative recall. Operation time was 90 minutes and anesthesia time was 147 minutes. The total dose of propofol was 627 mg, and the total remifentanil was 3.16 mg. The infusion volume was 800 ml, the blood loss was 10 g, and the urine output was 500 ml (Figure 4).

No adverse events occurred during anesthesia, such as BIS spikes or bucking. Intraoperative BIS values often became unstable due to noise from the electrocautery. At that time, AsisTIVA was designed to maintain the propofol and remifentanil doses unchanged. The various settings were very user-friendly, including that anesthetics were sustained even when BIS could not be measured. The patient recovered well and was discharged on postoperative day 5.

Figure 4a. The anesthesia progress chart

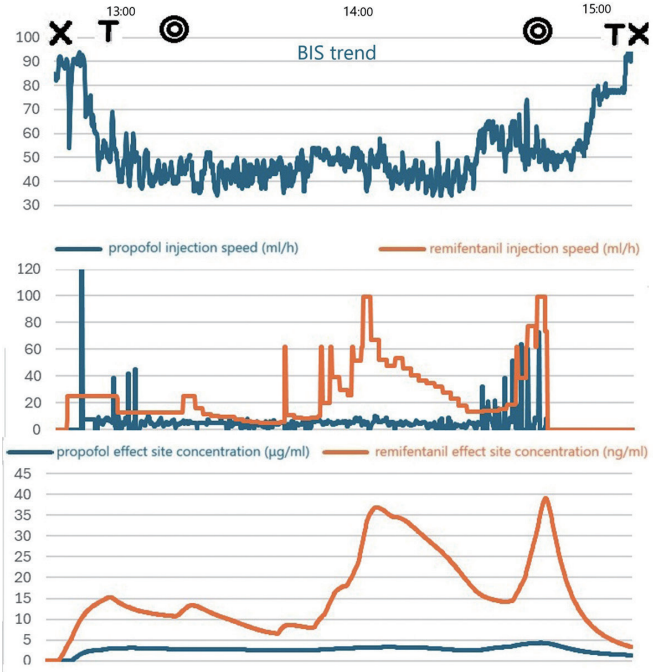

Figure 4b. The propofol/remifentanil dosage and effect-site concentration trends
High concentrations of remifentanil were used throughout, with a particularly rapid increase in remifentanil concentration toward wound closure.

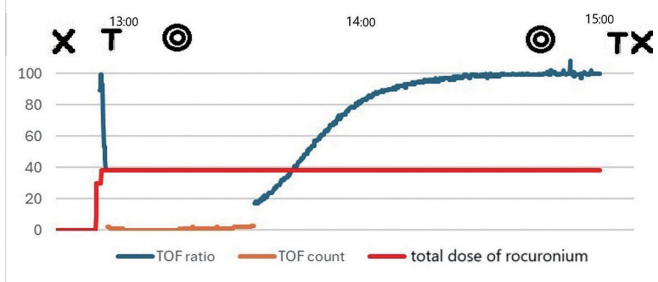

Figure 4c. The TOF progress

DISCUSSION

We performed the first anesthesia using AsisTIVA at Tokushima University. Currently, AsisTIVA is the only commercially available automated anesthetic administration program in the world (6). Aside from Fukui University Hospital, which was primarily involved in its development, it is clinically in operation only at our hospital and Tohoku University Hospital. Additionally, only two physicians at our hospital and three at Tohoku University are licensed to use AsisTIVA, apart from the staff at Fukui University. From this perspective, the anesthetic experience in this case—our first as a non-developer user—is extremely pertinent for the future dissemination of AsisTIVA.

Randomized controlled trials comparing anesthesia management using AsisTIVA to that by anesthesiologists have already been conducted by the developers (13). These studies showed that AsisTIVA was not inferior in maintaining anesthetic parameters, including BIS and TOF values. Similarly, in the present case, the intraoperative BIS value was well controlled at around 45 while BIS values were being measured.

AsisTIVA is a program that begins remifentanil at 0.5 μg/kg/min, whereas more than 75% of anesthesiologists at our hospital start at 0.3 μg/kg/min to avoid hypotension. Under conventional management, the remifentanil effect-site concentration at intubation is usually less than 10 ng/ml, but the anesthesia record for AsisTIVA shows that a higher concentration (≥10 ng/ml) was used at intubation. The patient developed hypotension with systolic blood pressure below 90 mmHg prior to intubation.

During our on-the-job training at Fukui University, we were advised that BIS values often increase more toward the end of surgery (e.g., near wound closure) than during the main operative period, leading to increased doses of both propofol and remifentanil (13). A similar trend was observed in the present case. Consequently, the remifentanil effect-site concentration at the end of surgery was 34 ng/ml, which is quite high for that stage. However, due to the pharmacological characteristics of remifentanil, the half-life of its effect-site concentration is extremely short (within 5 minutes) (14), resulting in no respiratory depression and good arousal at the time of extubation 20 minutes later. From these observations, the high remifentanil concentrations at the end of surgery attributed to AsisTIVA's automatic anesthetic control did not appear to be a major problem.

AsisTIVA does not have the capability to regulate blood pressure. If hypotension occurs after induction of anesthesia, the anesthesiologist must manually administer a vasopressor. Moreover, due to the high remifentanil concentration at induction, hypotension may occur soon after anesthesia induction. It is therefore considered necessary to have a vasopressor prepared prior to induction.

It was also clear that AsisTIVA cannot observe the operative field or manage aspects of anesthesia other than administering anesthetics, making the presence of an anesthesiologist essential. However, because it automatically controls the depth of anesthesia and muscle relaxation, the anesthesiologist can focus on observing the operative field and managing other anesthesia-related tasks, which is highly beneficial. The use of AsisTIVA is expected to remarkably reduce the workload of anesthesiologists and continue operating safely, with its application likely to expand in the future.

In conclusion, this case represents the first use of the commercially available total intravenous anesthesia support software, ROP-1680 AsisTIVA, for anesthesia management at Tokushima University. The automated anesthetic administration program was successfully implemented without adverse events. Its use is beneficial because it allows the anesthesiologist to concentrate on the operative field and overall anesthesia management, thereby reducing their workload. The use of AsisTIVA is expected to increase in the future.

CONFLICT OF INTEREST

The authors declare no competing interests.

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