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ORIGINAL RESEARCH

Accuracy of Gravity-Based Automatic Infusion System for Chemoport Intravenous Infusion

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Background: An infusion pump designed to deliver a specific volume at a predetermined rate is unable to detect extravasation and may continue infusion despite increased tissue resistance caused by extravasation. Consequently, it is recommended that vesicant drugs, such as chemotherapeutic agents, be administered via gravity infusion to reduce the risk of tissue damage. However, intravenous flow regulators used for gravity infusion have limitations because the infusion rate is influenced by the height, venous pressure, and viscosity of the fluid, which can change with temperature. In this study, we measured the accuracy of Accudrip, a new gravity-based automatic infusion control device designed to correct fluctuating infusion rates.

Methods: In 59 cancer patients administered with anticancer drugs, the actual administration rate using Accudrip under various administration conditions and the theoretical administration rate were measured and analyzed 100 times.

Results: Comparing the theoretical and actual administration rates using Accudrip confirmed that it can be injected with an average error rate of 4.75%, which clinically demonstrated sufficient accuracy for fluid administration.

Conclusion: The gravity-based automatic infusion system showed high accuracy consistent with the theoretical rate of administration even under multiple infusion conditions of cancer patients with chemoport. This system (Accudrip) will greatly contribute to accurate drug administration and minimization of adverse events in real-world hospital settings.

Keywords: gravity based automatic infusion system, intravenous infusion, accuracy

Introduction

Administering fluids and medications at the correct rate is crucial for patient safety.[1,2] In particular, cancer patients need to have higher accuracy of infusion devices than other patient groups.[3] Infusion pumps have various models depending on the purpose and function of use, and their performance and functionality also differ. They are generally divided into Volumetric pump, Syringe pump, PCA pump, and Wearable pump. For chemotherapy, volume control and syringe pumps are mainly used for precise drug delivery and safety. An volume control infusion pump, commonly used in clinical settings, such as hospitals, nursing homes, and home care, works by producing mechanical pressure to move fluids through peristaltic action. This process involves synchronized compression and decompression of the IV tube to deliver a precise amount of liquid (Figure 1C). This system can deliver precise fluid infusion rates owing to its volume-controlled mechanism. However, this method carries the risk of pressure injury. Even when the pressure around the catheter increases owing to extravasation, infusion continues, potentially causing tissue damage. The pressure sensor of an infusion pump cannot reliably detect extravasation, because it can only measure the pressure outside the infusion tube, leading to insufficient sensitivity for clinical detection. It triggers an alarm only when the tube is completely blocked.[4] The extravasation of vesicant drugs, including chemotherapy, antibiotics, cardiovascular drugs, electrolytes, and total parenteral nutrition, can cause significant tissue damage.[5] These side effects occur more frequently in clinical practice than are commonly recognized.

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Several studies and guidelines recommend peripheral intravenous administration of vesicant drugs using gravity infusion rather than infusion pumps.[6–8] This is because gravity infusion maintains a constant pressure gradient based on fluid levels and automatically stops fluid infusion if the pressure around the catheter increases to a certain level, thereby mitigating the risk of tissue damage. Fluid administration via gravity infusion relies on the hydrostatic pressure determined by the height of the fluid. The IV roller clamp adjusts the flow rate by gradually clamping the small passage spacing of the IV tube to <0.1 mm, while the gravity infusion setup (IIFR) adjusts the flow rate by adjusting the length of the long and narrow passage to generally approximately 60 mm (Figure 1A and B). The physically extended flow passage within an IV infusion flow regulator enables a higher control resolution compared with an IV roller clamp, which has a very limited control distance. However, currently used flow regulators exhibit significant variations among products from different companies, often resulting in discrepancies between the indicated scale and actual flow rate, even when the controlled variables are appropriately managed.[9] Furthermore, a gravity infusion setup, including an intravenous infusion flow regulator, inherently fails to maintain a consistent flow rate owing to variables, such as the height of the fluid, the patient's venous pressure, temperature, and even filters attached to the IV line. Additionally, as the fluid is infused and the fluid level in the IV bag decreases, a reduction in the hydrostatic pressure leads to a decrease in the infusion rate. This lack of accuracy is a primary limitation, particularly when administering critical medications, such as chemotherapy agents, that require precise rate control. Therefore, despite the risk of pressure damage, injection pumps are widely used for accurate drug administration.

A new injection control device called Accudrip uses a drip sensor to measure the current flow rate and sends this information to the main unit, which continuously maintains the desired injection rate through a feedback system by controlling a dedicated flow regulator.

This study aimed to evaluate the accuracy of Accudrip, which can correct the inherent inaccuracy of the flow controller in an actual clinical setting.

Method

Patient Characteristics

Various patients with cancer who underwent chemotherapy using a chemoport between October 2023 and January 2024 were enrolled in this study. Patient data on age, sex, TNM stage, pathology, ECOG status, and chemotherapy were collected. Informed consent was obtained from all enrolled patients. Patients received chemotherapy by accurately setting the dose and timing of the anticancer drug according to each regimen. All chemotherapy side effects, including extravasation, were recorded. This study was approved by the Institutional Review Board of the Konyang University Hospital and complied with the guidelines for good clinical practice.

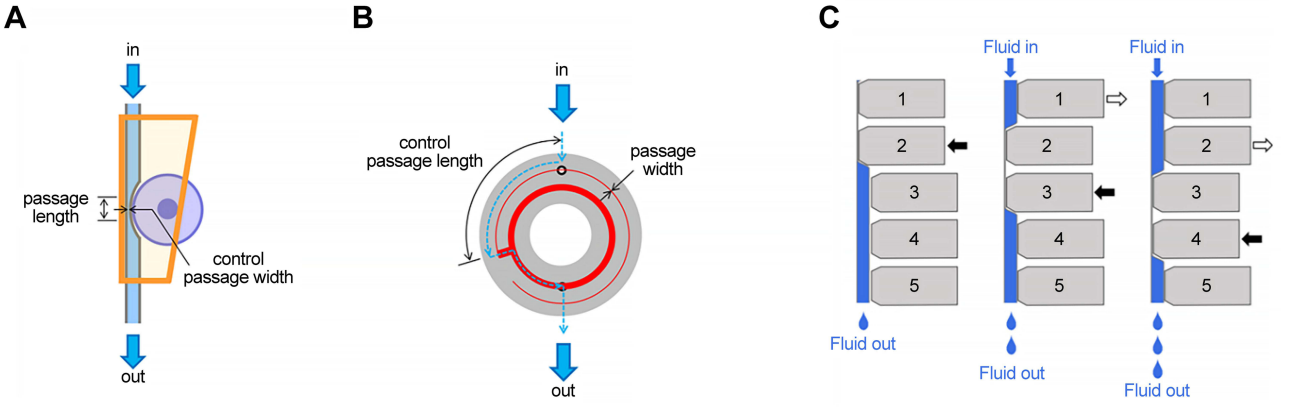

Figure 1 Mechanism of flow rate control (**A**) IV Roller Clamp (**B**) Intravenous Infusion Flow Regulators (IIFRs) (**C**) Infusion Pump.

Fluid Mechanical Back Grounds

A flow regulator is a fluid-mechanical device that controls the infusion flow rate by adjusting the length of the flow passage. Thus, its performance is governed by the fluid mechanical theory and can be described by several equations from fluid mechanics.

For the flow inside the tube, the flow rate increased with an increase in the pressure difference applied between both ends of the tube and decreased with an increase in the resistance of the tube. The pressure difference during the infusion process is derived from gravity. The basic relationship between the flows inside a tube is described as follows:[1]

$$V^2 = \frac{2}{\rho f}\frac{D}{L}\Delta P \tag{1}$$

where V is the velocity of the flow inside the tube, P is the applied pressure difference, D is the tube diameter, L is the tube length, and f is the friction or resistance of the tube. The pressure difference is proportional to the square root of the pressure difference, as shown in eq.(1) for a turbulent flow. The flow around us is generally turbulent. But the width of flow passage of the flow regulator is around 0.15 mm, and this small cross-sectional area increase possibility of flow pattern to become laminar not turbulent. The criterion for the flow pattern is a Reynolds Number Re of less than 2300 means the flow pattern is laminar.[2]

$$Re = \frac{\rho DV}{\mu} = \frac{DV}{V} \tag{2}$$

For 25°C water in passage depth of 0.5 mm and flow rate of 200 mL/h, the Re is 62 which is far below 2000 and this means the flow is perfectly laminar. In laminar flow, the velocity V is linearly proportional to the applied pressure difference.[3] So, by introducing a constant C, the final relation for the flow inside the tube becomes:

$$V = C\frac{D}{L}\Delta P \tag{3}$$

The depth is not constant along the flow regulator passage; therefore, Eq.(3) is applicable for each discrete length. The meaning of Eq. (3), the flow rate is linearly proportional to flow passage diameter D and inversely proportional to passage length L.

For the clamp-type flow controller shown in Figure 1, the flow rate is controlled by adjusting the passage gap, which represents the diameter in Eq.(3). However, the gap is very small and should even be smaller than several tens of millimeters because the passage length involved in the flow rate control is very short. We could not obtain high control resolution within this small control distance range. Thus, the infusion flow rate cannot be accurately controlled by a clamp-type controller.

However, the flow regulator uses a narrow and long control passage, as shown in Figure 1, with a passage length of approximately 60 mm. This long control distance enables high-resolution flow rate control compared to the tenths of mm control distance of the clamp (Table 1).

Table 1 Difference Between an Infusion Pump and Accudrip

Parameter	Infusion Pump	Accudrip
Driving force	Mechanical pressure by peristaltic pump motor	Hydrostatic pressure by gravity
Flow rate control	The rotational speed of the motor controlling the rollers via a cam-follower system	Micro-channel length control of the rotary valve via a high-resolution servomotor
Motor driving	Continuous	Intermittent
Infusion type	Volumetric	Barometric
Extravasation injury	High risk	Low risk
Accidental bolus (Free flow)	O	X
Feedback	X	O
Monitoring	X	O

Hardware Components

An infusion pump administers drugs intravenously by sequentially compressing a tube via a peristaltic mechanism. The infusion rate was determined by the operating speed of the peristaltic mechanism, making it an open-loop system that did not require feedback. Therefore, measuring the infusion rate is unnecessary, and the motor continues to run throughout drug administration. By contrast, the gravity volumetric infusion controller adjusts the infusion rate by changing the flow resistance using a valve. The motor connected to the valve operated only when the error between the actual infusion rate measured by the drip sensor and the prescribed rate exceeded the allowable range. Because of the structural differences between the two systems, infusion pumps have a higher risk of adverse effects from forced infusion (Figure 1C), whereas gravity volumetric infusion controllers have a relatively lower risk of forced infusion, making them safer for administering drugs that pose a risk of tissue necrosis if extravasation occurs (Figure 2). The infusion pump (Accudrip) used in this study received GMP certification from the Ministry of Health and Welfare of the Republic of Korea in 2015, demonstrating the consistency of the product.

Circuit Diagram

The installation diagram of the gravity volumetric infusion controller is shown in Figure 3. The valve that controls the flow rate is connected to the motor of the gravity volumetric infusion controller, which uses the actual infusion flow rate measured by the drip sensor attached to the drip chamber to rotate the motor to correct the error between the prescribed and actual flow rates (Figure 3A). The drip sensor has an IR transmitter and receiver that are used to detect drips, and the detection signal is fed back to the MCU. Infusion through the volumetric infusion controller is driven by gravity, and the driving force is determined by the height difference between the fluid bag and the port connected to the patient's blood vessel. By reflecting the measured actual infusion flow rate in the control group, it was possible to maintain a constant infusion regardless of changes in the patient's venous pressure, movements, or temperature (Figure 3B).

Study Design An experimental method was outlined to evaluate the safety and accuracy of patients who underwent fluid treatment.

Setting Up the Infusion Pump: Check that the tubing is free of air bubbles by priming it with intravenous fluid. The tubing was loaded into the infusion pump correctly according to the manufacturer's instructions. The pump was programmed to deliver fluid at the intended rate (mL/hour).

Liquid Injection Rate Experiment: This accuracy of the injection speed was tested for four cases: 250 mL/30 min, -250 mL/60 min, 500 mL/90 min, and 500 mL/120 min. The goal was to analyze the difference between the actual injection speed and the injection speed set. This was performed 100 times by measuring each speed 25 times.

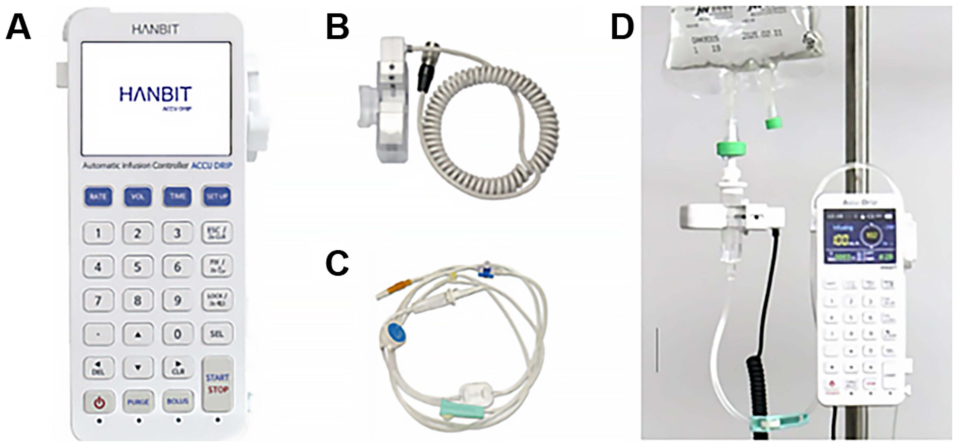

Figure 2 Infusion device configuration of Accudrip. (**A**) Main device (**B**) Drip sensor, which counts drop rate and gives feedback to main device. (**C**) Accuvalve IV set, which is dedicated IV sets for Accudrip (**D**) Example of Accudrip in Use.

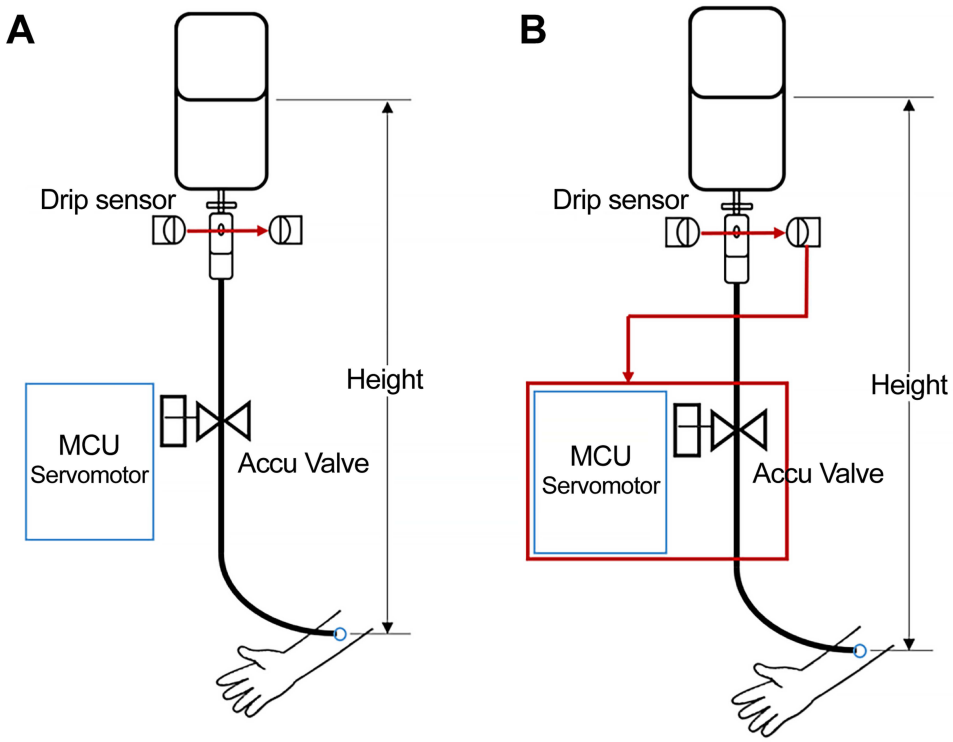

Figure 3 Mechanism of Accudrip. (**A**) The infrared drip sensor counts the number of drops and sends the signal to main body. (**B**) The main body performs Feedforward flow control by using the current flow rate measured from the drip sensor and the flow coefficient of the AccuValve angle. Real time monitoring enables the device to sound an alarm when detecting abnormal drip interval.

Type of Liquid Solution Experiment: Here Different types of fluids were tested: Normal Saline (N/S) and 5% Dextrose in Water (D/W). This was performed 100 times, with 50 measurements for each type. The objective of this study is to compare the effects of different solutions on the infusion process.

By conducting these experiments and collecting data as described, the researchers evaluated the safety and accuracy of patients undergoing fluid therapy under different scenarios by considering factors such as fluid height, injection rate, and type of liquid solution used.

Performance Evaluation

This study highlighted two main observations that ensure that the Accudrip pump operates within a 10% accuracy margin compared with the speed prescribed by the doctor and maintains accurate speed settings despite changes in fluid quantity and solute properties. % error calculation was used to evaluate the effectiveness of the treatment method, where % error was determined by the deviation between the actual treatment time and the set treatment time. Side effects were identified when the % error exceeded 10% of the set treatment duration. The evaluation criteria for effectiveness and safety were detailed, including accuracy assessments based on % error averages, safety evaluations related to the incidence of side effects, and confirmation of prescribed speed adherence in all patients. The reliability and consistency of treatment were guaranteed in the patient profiles for all treatment situations.

Data Analysis and Statistical Methods

The difference between the theoretical infusion time (converted into minutes) and actual infusion time was statistically verified. We tested whether the difference was zero using a paired *t*-test. The analysis of the relative error tested how different the input speeds were under the conclusion that there was a difference in the injection speed. In general, depending on the type of fluid, a relative speed error of up to 10% is allowed if it is sensitive, and up to 20% if it is not. We used a univariate *t*-test to determine whether there was a 10% difference in speed. Statistical analysis was performed using SPSS software (version 13.0; SPSS, Inc., Chicago, IL, USA). The data

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consisting of log2-transformed proportions followed a normal distribution, so Student's *t*-test was chosen to determine whether the difference between the two variables was statistically significant.

Ethical Statement

This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from Institutional Review Board of konyang University Hospital and all participants provided informed consent.

Result

Analysis of General Characteristics

The administration time of accudrips was measured 100 times in 59 patients. Patients with colorectal, gastric, pancreatic, and biliary tract cancers participated in the study, most of whom had stage IV cancer. Thirty-five men and 24 women participated in the study. Among the patients who received chemotherapy, 21 were under 60 years of age and 38 were over 60 years of age. According to the classification of the stages of the patients who participated in the study, 45 had metastatic cancer and 14 had early or locally advanced cancer. The accuracy of the administration rate was measured 68 times using normal saline and 32 times using 5% dextrose water containing a mixture of anticancer drugs. The number of times measured at an administration rate of 300 mL or more per hour was 34, the number of times measured at an administration rate of 200 mL or less per hour was 41, and the number of times administered at a rate between them was 25. Patients who participated in the study received various anticancer drugs, and the number of experiments with small molecule cancer drugs was 71 times, and the number of experiments with antibody anticancer drugs was 29 times (Table 2).

Table 2 Variable Factor Affecting Accudrip Infusion Time Error

Characteristic	Number (%)	Mean Accuracy (% error)	P-value
Sex			
Male	35 (59)	4.38	0.348
Female	24 (41)	3.95	
Age			
<60 years	21 (36)	3.74	0.01
≥60 years	38 (64)	6.12	
Disease stage			
Stage I–III	14 (24)	5.24	0.238
Stage IV	45 (76)	4.26	
Type of infusion fluids			
Normal saline: 100 mL	15 (25)	4.15	0.30
Normal saline: 250 mL	15 (25)	3.98	
5% dextrose water: 500 mL	15 (25)	6.18	
5% dextrose water: 1000 mL	15 (25)	5.12	
Administration rate			
<100 mL/h	7 (7)	2.17	0.04
100–200 mL/h	12 (12)	2.14	
200–300 mL/h	34 (34)	3.38	
300–400 mL/h	28 (28)	4.98	
>400 mL/h	19 (19)	6.12	
Chemotherapy regimen			
Gemcitabine + Cisplatin	23 (23)	3.26	0.19
FOLFOX	16 (16)	5.45	
FOLFIRI	17 (17)	4.12	
Immuneheck point inhibitor	24 (24)	2.56	
Trastzuamb/Pertuzumab	8 (8)	2.47	
Others	12 (12)	3.05	

Degree of Error of Infusion Injection Speed Control Devices

A comparison between the theoretical infusion time (converted to minutes) and the actual infusion time is shown as a box plot (Figure 4). The box plot shows that the actual infusion time was slightly shorter than the theoretical infusion prescription time. Whether the difference was 0 or not was tested using the paired *t*-test, but the difference between infusion times measured in minutes can be seen as a statistically significant difference because there is an average difference of 5.9782 min, and the difference is close to 0 in the P value (t = 9.286, df = 91, p-value = 7.959e-15). These results are presented in a two-dimensional plot (Figure 5). The infusion times were 30 min, 1 h, 1 h, and 2 h, and the actual infusion time was generally shorter than the theoretical infusion time. This difference tended to be greater in patients with longer prescription times. Based on the conclusion that there was a difference in the infusion rate, the extent to which there was a difference in the input rate was tested. (Actual infusion time-theoretical infusion time) The relative error value expressed as the absolute value of the theoretical infusion time was calculated and a histogram of this value was drawn (Figure 6). In general, depending on the type of infusion, a relative speed error of up to 10% is allowed if the infusion is sensitive, and up to 20% if it is not. A univariate *t*-test was used to determine whether there was a 10%

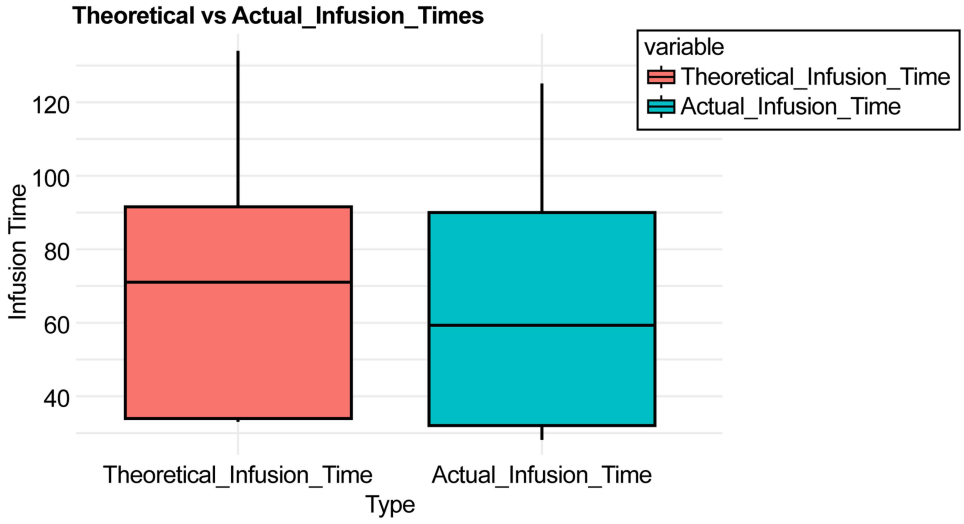

Figure 4 Box Plot. Box plot of the theoretical infusion time (converted in minutes) and the actual infusion time.

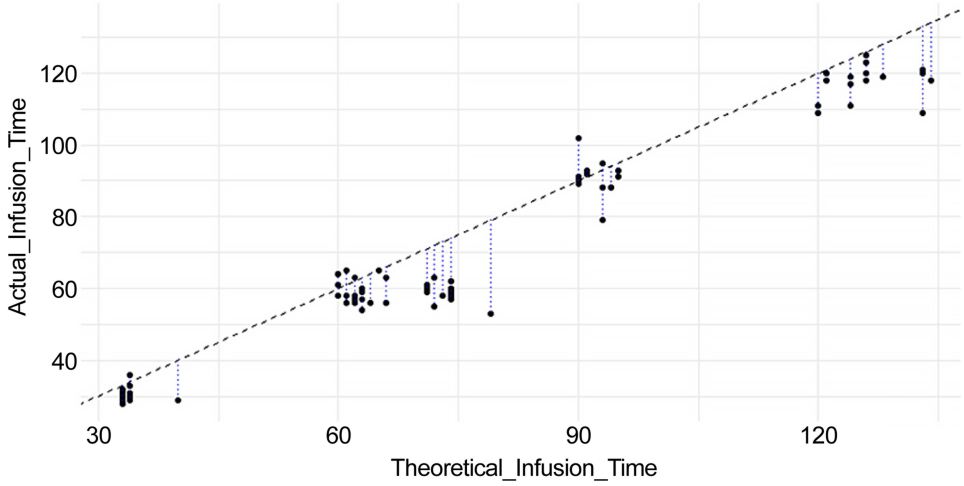

Figure 5 Mean Difference Plot. The large dotted line represents a straight equation with a slope of 1, indicating that if the theoretical value and the actual input value are the same, the points representing each patient should exist on this dotted line.

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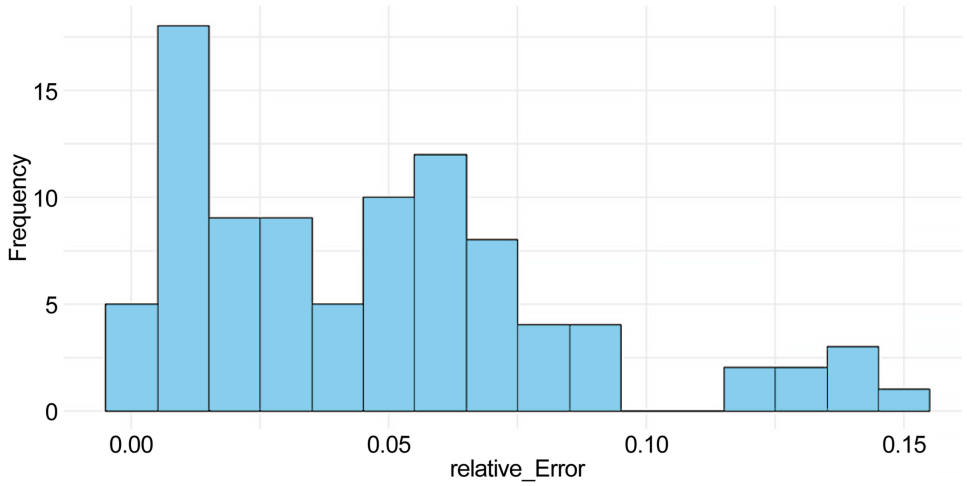

Figure 6 Histogram of Relative error values. The relative error value expressed as the absolute value of (Actual Input Speed-Theoretical Input Speed) / Theoretical input speed and drew a histogram of it.

difference in injection rate. It was concluded that the difference in the injection speed was not greater than 0.1. The relative difference in speed was found to be less than 5% on the 0.047 side (95% confidence interval: 0.04120649 sample estimates: mean × 0.04752557).

Factors Affecting Accudrip Error

The infusion time error was analyzed based on the key factors (Sex, Age, Disease status, Fluid type, Administration rate, Chemotherapy regimen) that can cause errors in an infusion pump. There was a statistically significant infusion time error according to the rate of fluid administration.When the rate of administration was set quickly, the error in injection time increased. Among the types of chemotherapy regimen, the injection time error tended to be smaller when administering drugs made of antibodies than when administering cytotoxic anticancer drugs. In addition, infusion time errors tended to be greater in elderly patients compared to younger patients. Although there was no statistical significance, there was an increased infusion time error in glucose fluid. Furthermore, there was a statistically significant infusion time error depending on the fluid administration speed. When the administration speed was set rapidly, the error in the infusion time showed an increasing pattern (Table 2).

Discussion

In this study, we compared targeted flow rates with actual flow rates to demonstrate that the new gravity-based automatic infusion control device (Accudrip) is accurate even in cancer patients with chemoport. Considering that the typical error rate for standard infusion pumps is within 5%, the results of this study are significant. Recent studies comparing the accuracy of flow regulators and infusion pumps show that the average error rate for smart infusion pumps used as "standards" ranged from 0.8% to 4%, with maximum deviations ranging from −10% to 8%.[10] In this study, the average error rate was 4.75% with a maximum deviation of 14.7%. The high maximum deviation was likely due to frequent or excessive patient movements, which affected the feedback system of the device. In addition, infusion time errors according to the patient's condition or injection conditions showed statistical differences in age and administration rate, but did not show statistical significance in sex, disease progression status, type of infusion fluid, and chemotherapy regimen.

Another limitation of this study is that owing to the characteristics of cancer patients undergoing chemotherapy, we could only measure the accuracy in the high-flow range (>150 mL/h). However, considering the structure of the flow passage in the AccuValve, the flow rate variations due to external factors are more significant in the high-flow range. This may have enhanced the reliability of the results. Additionally, considering that conventional flow regulators cannot operate effectively in high-flow ranges (above 250 mL/h), the clinical usefulness of the AccuValve is significant.

Because gravity infusion is considered safer than infusion pumps, some companies have developed devices to improve the accuracy of gravity infusion and advocate its use during chemotherapy.[8] Although these devices use feedback systems to regulate the flow rates, they employ traditional clamp-type mechanisms for flow control, resulting in reduced accuracy. In contrast, the device used in this study provides precise control by regulating the flow through a long, narrow passage within the dedicated IV flow regulator, Accuvalve.

The drugs that can cause extravasation include chemotherapeutic agents, antibiotics, cardiovascular drugs, electrolytes, and parenteral nutrition. Although administering these medications with an infusion pump is inherently risky, precise control of infusion rates often necessitates the use of infusion pumps in clinical practice.[11] Therefore, a device that allows the safe and accurate administration of these medications using gravity-based infusion is essential in clinical settings.

In this context, acudrips provide several benefits (Table 1). First, its gravity-based infusion system features an intrinsic pressure-control mechanism that prevents excessive pressure by maintaining pressure limits based on the height of the fluid surface, typically approximately 1 m. This is clinically significant because it can reduce the risk of extravasation. Additionally, recent studies have shown that the squeezing mechanism of infusion pumps can generate subvisible particles, which pose a risk of immunogenicity when administering antibody agents (eg, human immunoglobulin). However, Accudrip does not use a squeezing mechanism, which prevents the formation of subvisible particles.[12] A 5-μm in-line filter integrated into the tubing of the gravity-based infusion set was effective in reducing particles, especially in the range of ≥10 μm.[13] The peristaltic pump was found to generate more subvisible particles than the gravity infusion set because of the constant peristaltic motion, which causes stress.[14] Subvisible particles generated during the preparation or administration of biopharmaceuticals can pose risks, such as immunogenicity, inflammation, or organ dysfunction.[15,16] The filter also maintained the particle level even after pre-exposure of the samples to silicone oil-lubricated syringes, drop shock, or agitation.[17] This study highlights the importance of selecting an appropriate infusion set with an inline filter based on the sensitivity of the product.

Given these benefits, we anticipate that this device can be safely utilized not only in chemotherapy, but also in nursing homes and home care settings.

Conclusion

In this study, we confirmed that the new gravity-based automatic infusion control device (AccuDrip/IC-A) manufactured by Hanvit MD achieves an accuracy comparable to that of infusion pumps when administering fluids to cancer patients with chemoport. Using this device, we proposed a novel approach for administering anti cancer drugs, overcoming the limitations previously associated with infusion pumps.

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Author Contributions

The authors confirm contribution to the paper as follows: study conception and design: Jong Gwon Choi; experiment and data collection: Dong Won Yang, Young Gyu Park; analysis and interpretation of results: Jong Yeup Kim, Poomin Park, Dong Won Yang. Author; draft manuscript preparation: Young Kyu Park, Seung Tack Lee; supervised and modified final version manuscript: Jong Gwon Choi. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare no conflicts of interest in this work.

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