Performance evaluation study of a commercially available smart patient-controlled analgesia pump with the microbalance method and an infusion analyzer

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Background: Patient-controlled analgesia (PCA) has been widely used as an effective medical treatment for pain and for postoperative analgesia. However, improper dose errors in intravenous (IV) administration of narcotic analgesics from a PCA infusion pump can cause patient harm. Furthermore, opioid overdose is considered one of the highest risk factors for patients receiving pain medications. Therefore, accurate delivery of opioid analgesics is a critical function of PCA infusion pumps.

Methods: We designed a microbalance method that consisted of a closed acrylic chamber containing a layer and an oil layer with an electronic balance. A commercially available infusion analyzer (IDA-5, Fluke Co., Everett, WA, USA) was used to measure the accuracy of the infusion flow rate from a commercially available smart PCA infusion pump (PS-1000, UNIMEDICS, Co., Ltd., Seoul, Korea) and compared with the results of the microbalance method. We evaluated the uncertainty of the flow rate measurement using the ISO guide (GUM:1995 part3). The battery life, delay time of the occlusion alarm, and bolus function of the PCA pump were also tested.

Results: The microbalance method was good in the short-term 2 h measurement, and IDA-5 was good in the long-term 24 h measurement. The two measurement systems can complement each other in the case of the measurement time. Regarding battery performance, PS-1000 lasted approximately 5 days in a 1 ml/hr flow rate condition without recharging the battery. The occlusion pressure alarm delays of PS-1000 satisfied the conventional alarm threshold of occlusion pressure (300-800 mmHg). Average accuracy bolus volume was measured as 63%, 95%, and 98.5% with 0.1 ml, 1 ml, and 2 ml bolus volume presets, respectively. A 1 ml/hr flow rate measurement was evaluated as 2.08% of expanded uncertainty, with a 95% confidence level.

Conclusion: PS-1000 showed a flow accuracy to be within the infusion pump standard, which is ± 5% of flow accuracy. Occlusion alarm of PS-1000 was quickly transmitted, resulting in better safety for patients receiving IV infusion of opioids. PS-1000 is sufficient for a portable smart PCA infusion pump.

Keywords: Flow Rate; Infusion Pumps; IV Smart Pump; Microbalance; Patient Controlled Analgesia.

INTRODUCTION

Infusion pumps have been commonplace in today's pain medicine care, as an estimated 90% of hospitalized patients receive intravenous (IV) medications via infusion pumps [1-3]. Infusion pumps are medical infusion devices that administer IV medications to patients [1]. It is vital that IV infusion pumps maintain the prescribed medication levels in patients without dangerous levels [1]. For

example, after orthognathic surgery, an IV patient-controlled analgesia (PCA) infusion pump is an important method for managing postoperative pain intensity and frequency [4]. IV sedation in dentistry to reduce pain-related anxiety and phobia can help keep patients calm during dental procedures using a smart syringe pump [5].

Traditional infusion pumps can be categorized into mobile, home, or long-term care settings. Traditional infusion pumps include syringe infusion pumps, disposable pumps, large volume pumps, elastomeric (balloon) pumps, and PCA pumps [1,6-8]. The pumping mechanism varies in infusion pumps, from a positive displacement type with a computer-controlled threaded bar (syringe type) to a peristaltic or rotary pumping type, by manipulating the fluid with a series of plungers at a set rate with invariable volume (volumetric type) [1]. These infusion pumps have advantages and dis-advantages. For example, volumetric pumps are equipped with motors that control the infusion flow rates. It is also possible to control the dose of medicine as an occasional demand. However, most volumetric pumps are expensive and too heavy to carry, owing to their size and weight. Conversely, disposable elastic devices are easy to carry and are low cost. However, the elasticity of disposable pumps can easily be changed, resulting in an inaccurate flow rate. In addition, it is impossible to control the flow rates of the disposable elastic infusion pumps. PCA infusion pumps have advantages, such as accuracy, controllability of flow rates, and portability. PCA infusion pumps can be portable and can administer a precise dose of pain medicine [7-13]. For pain management, patients can efficiently manage their pain with a predetermined bolus dose of medication on demand at their preferred dose using PCA infusion pumps. Therefore, with regard to acute postoperative pain management, postoperative PCA is a common practice. Hospital patient satisfaction can be improved by postoperative PCA with decreased pain intensity compared to non-PCA routes of medication administration [12-14].

However, there are many reports of the observed

adverse effects of narcotic analgesics using PCA infusion pumps [15-17]. Morphine, fentanyl, and hydromorphone have been mainly used as narcotic analgesics [18]. In the United States, more than 39% of reported cases involve overdose of narcotic analgesics by users. An overdose of narcotic analgesics causes many adverse effects such as dizziness, dysphoria, euphoria, sedation, respiratory depression, constipation, endocrine system suppression, cardiovascular disorders, convulsions, nausea, vomiting, and death [15,19,20]. Especially, long-term use of opioid analgesics can produce tolerance and physical depen-dence [18,21,22]. Therefore, controlling the safe dose of narcotic analgesics is a very important function of PCA infusion pumps [19]. One of the most important functions of PCA infusion pumps is to administer a precise dose of narcotic analgesics. The PCA infusion pump should satisfy the balance between patient safety and infusion accuracy of pain medications [14,19].

In this study, we designed a microbalance method that can measure low flow rates in real-time. We also compared the results of the flow rate measurements for the two measurement systems, the microbalance method and an infusion analyzer (IDA-5, Fluke Co., Everett, WA, USA) with a commercially available PCA infusion pump, PS-1000. We evaluated the uncertainty of the flow-rate measurement. Several functions of the PS-1000 PCA infusion pump (UNIMEDICS, Co., Ltd., Seoul, Korea) were also measured, including the accuracy of the infusion flow rates, occlusion pressure alarm function, battery performance, and bolus function.

METHODS

1. Microbalance method to measure the micro-droplet mass

To calculate the precise flow rates of the PS-1000 smart PCA infusion pump (UNIMEDICS, Co., Ltd., Seoul, Korea), a balance XPE-205 (Mettler-Toledo, Columbus, OH, USA) that can measure the change of 0.01 mg with five decimal places was used (Fig. 1). The maximum
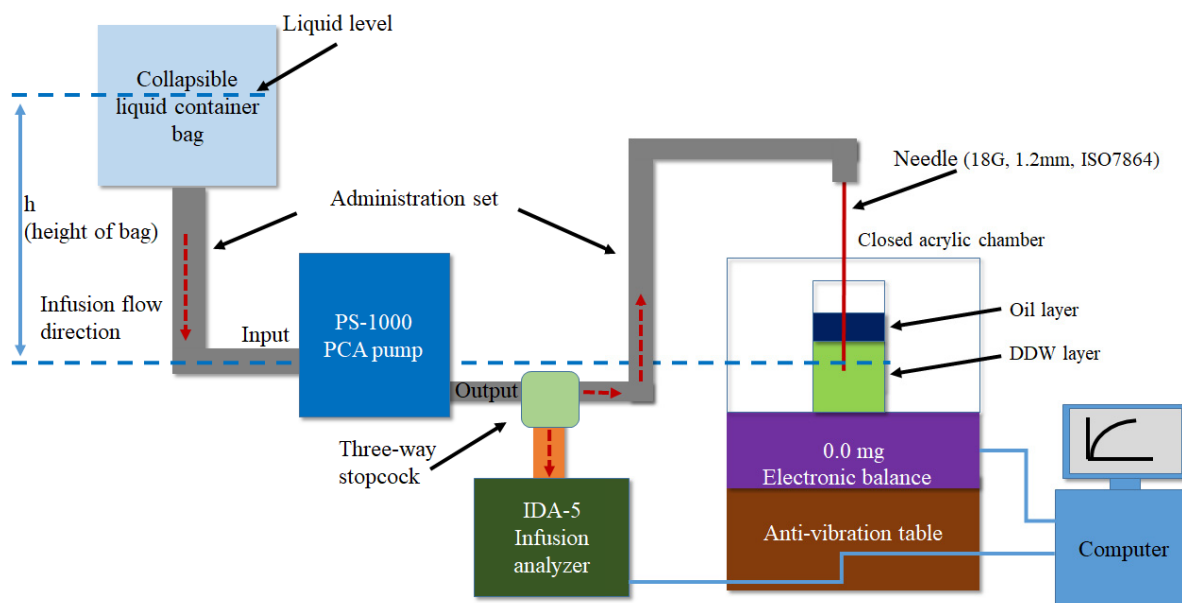
Fig. 1. Diagram of the infusion pump testing system with the microbalance method and IDA-5. PCA, patient-controlled analgesia.

capacity, the readability, and the minimum weight (lowest possible) of the balance was 220 g, 0.01 mg, and 14 mg, respectively. A 0.9% normal saline (N/S) (JW Pharmaceutical Co., Korea) was used. The experimental environment was designed according to International Electrotechnical Commission (IEC) International Standard 60601-2-24. IV tubes were connected to the PS-1000, and the IV bag was placed 30 cm (h = 30 cm) above the PCA pump (Fig. 2). The injection needle (18G 1.2 mm ISO 7864) was immersed in the water layer. This large-bore needle is effective in preventing resistance (back pressure) in the system at high infusion flow rates [23]. The height of the input IV tube was the same as the tip of the needle; the center of the IV tube diameter was placed at the same height as the tip of the needle [24] (Fig. 1).

To measure the precise amount of infusion, it is important to prevent the evaporation of the fluid during the test while minimizing the influence of uncertainties, such as evaporation and vibration [25,26]. Therefore, moisture exchange with the outside air should be prevented, and the balance should be on an anti-vibration table.

We designed a closed acrylic chamber that contained deionized distilled water layer and oil layer. To maintain the same moisture content, distilled water was placed in the plate, and the oil layer was placed on top of the water to prevent evaporation. The acrylic chamber blocked the moisture exchange with the outside air (Fig. 2a). The tip of the needle was placed at the same height as the IV tube of the PS-1000 PCA pump, as shown in Fig. 1. The needle was immersed in the water layer to prevent droplet formation from infusion flow. When the infusion of PS-1000 started, the mass of the falling droplet, which was on the microgram scale, was measured every 30 s for 2 h using the XPE-205 balance on an anti-vibration table (Fig. 2a and 2b). The flow rate was calculated using fluid density. In this paper, we call this measurement system the microbalance method system.

2. Measurement with IDA-5 infusion pump analyzer

A commercially available infusion device analyzer-5 (IDA 5, Fluke Co., Everett, WA, USA) was used to measure the infusion flow rate of PS-1000. IDA-5 is typically used in hospitals and testing institutions to measure the performance of medical infusion pumps in accordance with the international standard IEC 60601-2-24 [24]. The results from the IDA-5 and microbalance methods were compared and analyzed. The flow rate test was set in a continuous infusion mode,
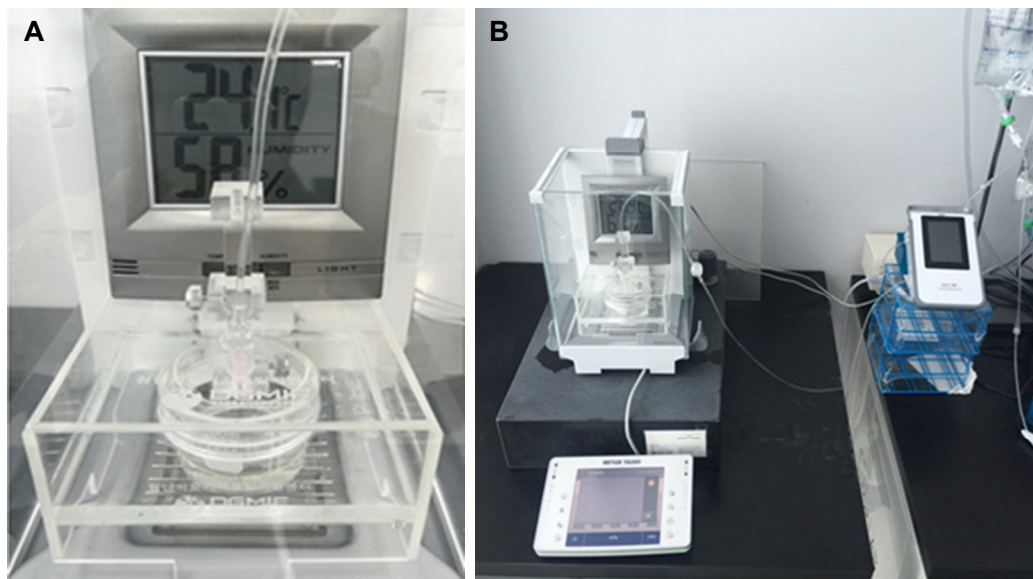
Fig. 2. (A) A closed acrylic chamber of the microbalance method, (B) the microbalance method with PS-1000.

which is the basic mode of the PCA pump. To minimize measurement error, the sample test was repeated four times, and the average and standard deviation were calculated. At a flow rate of 1 mL/h, PS-1000 was tested for 2 h as the short-term period and for 24 h as the long-term period.

3. Trumpet curve calculation

The trumpet curve is a graph showing both the maximum ± error value of the flow rate from the pre-fixed infusion rate over time. The equation for the trumpet curve, which is identified by IEC 60601-2-24 (2012-10) [24], can then be written as

$$Q_i = \frac{60(W_i - W_{i-1})}{Sd} ml/hr$$
$$i = 1, 2, \ldots, T_0/S \qquad \text{Equation (1)}$$

, where

W_i: $T_0(g)$ The first sample during the test

T_0: Analysis period (min)

S: Sample interval (min)

d: Density of water (0.998 g/ml, 20°C), N/S (1.005 g/ml)

E_p(max.) and E_p(min.) calculation using the trumpet algorithm is as follows:

Observation interval is P = 2 min, 5 min, 11 min, and 31 min and during the analysis period 'Tx', observed

maximum value 'm' is as follows:

$$m = \frac{(T_x - P)}{S} + 1 \qquad \text{Equation (2)}$$

, where

m: Maximum value in the observation range

P: Observation period

S: Sample interval (min)

T_x: Analysis Period (min)

During the observation period 'P', the percentage of maximum E_p(max.) and minimum E_p(min.) is as follows:

$$E_p(max.) = \underset{j=1}{\overset{m}{MAX}} \left[\frac{S}{P} \times \sum_{i=j}^{j+\frac{P}{s}-1} 100 \times \left(\frac{Q_i - r}{r} \right) \right] (\%)$$
$$\text{Equation (3)}$$

$$E_p(min.) = \underset{j=1}{\overset{m}{MIN}} \left[\frac{S}{P} \times \sum_{i=j}^{j+\frac{P}{s}-1} 100 \times \left(\frac{Q_i - r}{r} \right) \right] (\%)$$
$$\text{Equation (4)}$$

, where

$$Q_i = \frac{60(W_i - W_{i-1})}{Sd} ml/hr$$

W_i: The first test sample during the analysis period $T_x(g)$

r: Speed (ml/hr)

S: Sample interval (min)

P: Observation site duration time (min)

d: Density of water (0.998 g/ml, 20°C), N/S (1.005 g/ml)

Calculate the overall average percentage error 'A' by using 'A' value measure during period 'T'.

$$A = \frac{100(Q-r)}{r} (\%)$$

Equation (5)

Hereinafter,

$$Q = \frac{60(W_i - W_k)}{Td} ml/hr$$

Equation (6)

r: Speed (ml/hr)

W_j: Collected test sample after analysis period T_1(g)(j=240)

W_k: Collected test sample after analysis period T_1(g) (k=120)

T: Analysis Period (min)

d: Density of water (0.998 g/ml, 20°C), N/S (1.005 g/ml)

We used MATLAB$^®$ to calculate the trumpet curve, which was set as the maximum and minimum values of the trumpet curve at 15 and −15, respectively.

4. Uncertainty of measurement

A general overview of the uncertainty and errors associated with the gravimetric measurement method is presented in other studies [23,25-28]. Briefly, these errors are from the balance resolution, balance stability setting, time delay, balance measurement repeatability, buoyancy effect of the immersed needle, evaporation rate, etc. We briefly evaluated the uncertainty of the flow-rate measurement at 1 ml/h. To obtain an expanded uncertainty in the flow rate measurement, the mathematical model for the flow rate 'F' (mL/h) calculation of the microbalance method can be calculated using Equation (7)[29].

$$F = \frac{\varepsilon \times m}{t \times d_{water}} + \delta_{evap} \; (mL/h)$$

Equation (7)

where ε is the buoyancy correction factor due to the immersed needle as 1.00106 [30], "m" is the difference in delivered mass and measured mass, "t" is the measurement time, "d_{water}" is water density. The evaporation rate (δ_{evap}) was required as a correction factor for the volume flow rate. To minimize the evaporation effect, we used a closed acrylic chamber and low-volatility oil layer.

According to the ISO/IEC guide (Guide to the Expression of Uncertainty in Measurement, GUM), the combined standard uncertainty of flow measurement, $u_c(F)$, can be defined as follows [29,31]:

$$u_c(F) = \sqrt{\sum_i c_i{}^2 \times u^2(x_i)} = \sqrt{\sum_i \left(\frac{\partial F}{\partial x_i}\right)^2 \times u^2(x_i)}$$

$$= \sqrt{\left(\frac{\partial y}{\partial m}\right)^2 u^2(m) + \left(\frac{\partial y}{\partial \varepsilon}\right)^2 u^2(\varepsilon) + \left(\frac{\partial y}{\partial t}\right)^2 u^2(t) + \left(\frac{\partial y}{\partial d}\right)^2 u^2(d) + u^2(q_t) + u^2(q_{resol}) + u^2(q_{repeat}) + u^2(q_{evap})}$$

Equation (8)

where $c_i^{\,2}$ is the sensitivity coefficient giving the weight of each individual standard uncertainty, $\frac{\partial F}{\partial x_i}$ is the partial derivative of equation (7), $u^2(x_i)$ is the standard uncertainty referring to the measurement of each quantity contributing to the final result, $u(q_t)$ is the uncertainty of the elapsed time, $u(q_{resot})$ is the uncertainty of the resolution of the balance, $u(q_{repeat})$ is the standard deviation of the measurements, and $u(q_{evap})$ is the uncertainty of evaporation in the microbalance method system.

For the standard uncertainty calculation, each standard uncertainty can be arranged as $u(q_t) = \frac{time}{2\sqrt{3}}$ (s), $u(q_{resol}) = \frac{resolution}{2\sqrt{3}} = $ (mg), $u(q_{repeat}) = \frac{SD\_repeat}{\sqrt{N}} = (\mu L/s)$ (N = sampling number, SD_repeatability = standard deviation of balance repeatability), $u(q_{evap}) = \frac{\Delta evap}{\sqrt{3}} (\mu L/s)$. The expanded uncertainty U is defined as follows [31].

$$U = k \times u_c(F)$$

Equation (9)

where k is the coverage factor of $k = 2$ (95% level of confidence) [29].

5. Battery performance evaluation

To test the performance of the lithium polymer battery of PS-1000, the battery was fully charged and tested. After inserting the fully charged battery into PS-1000, we measured the operating time of the battery after running PS-1000 at flow rates of 1, 25, and 120 ml/hr, respectively. The battery performance tests were repeated four times to obtain the average and standard deviation of the battery operation time.
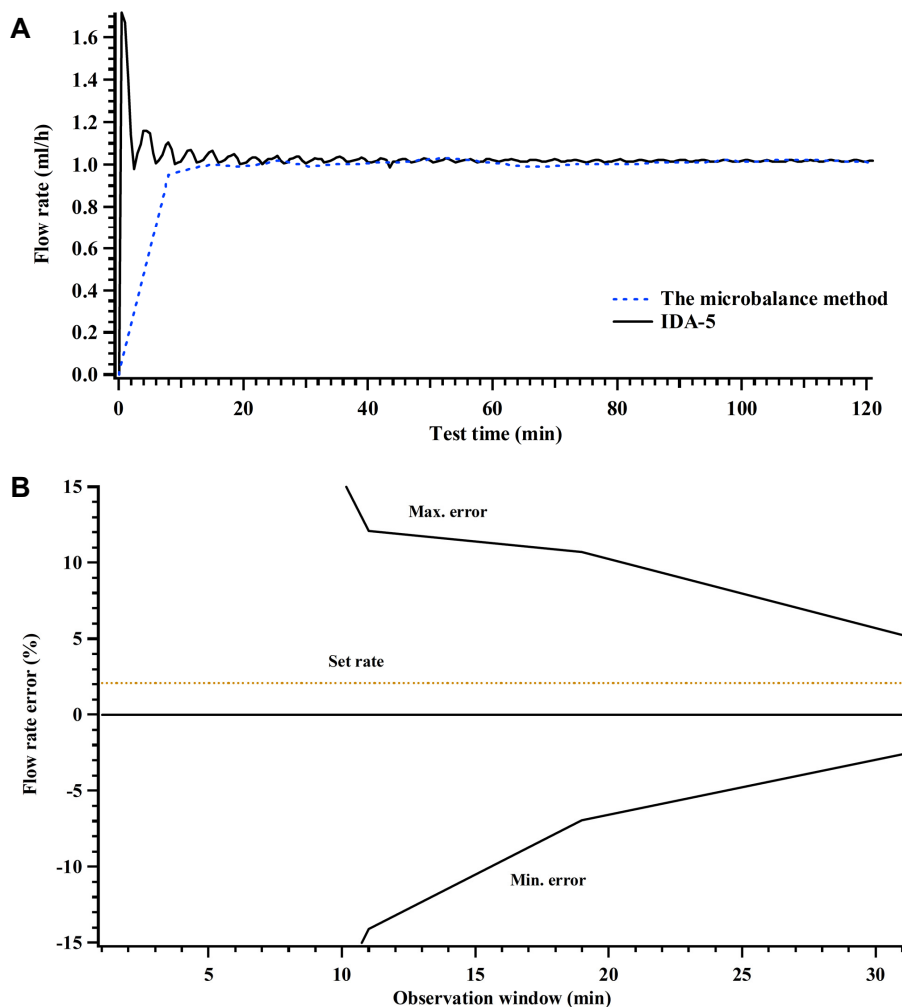
Fig. 3. (A) Comparison of accuracy in 1 ml/hr flow rate of PS-1000 between the microbalance method and IDA 5 for 2-h (B) trumpet curve from the microbalance method. The dashed line (set rate) is the mean flow error equal to $+$ 2.09%.

6. Occlusion pressure alarm function test

We measured the occlusion pressure threshold and the occlusion pressure sensor alarm time of the PS-1000 PCA infusion pump. We tested the occlusion pressure alarm function using the occlusion pressure checking function of the IDA-5. To evaluate the occlusion pressure alarm function of PS-1000, we measured the time of the occlusion activation sound for each flow speed (1, 25, 100, and 120 ml/hr). We also measured occlusion pressure values at the occlusion alarm points.

7. Accuracy of bolus volume

Regarding the PS-1000 bolus function measurement,

the accuracy of 1 ml bolus injection volume was measured at a 1 ml/hr flow rate of PS-1000 with a 15-min lockout interval time. The accuracy of the bolus injection dose was tested thrice every 15 min for 1 h.

RESULT

1. Short-term accuracy comparison test between the microbalance method and IDA-5 for PS-1000

At a 1 ml/hr flow rate setting for PS-1000, the average flow rate results from the microbalance method and IDA-5 were 1.028 ml/hr and 1.01 ml/hr, respectively, for 2 h. In the microbalance method, drop mass was
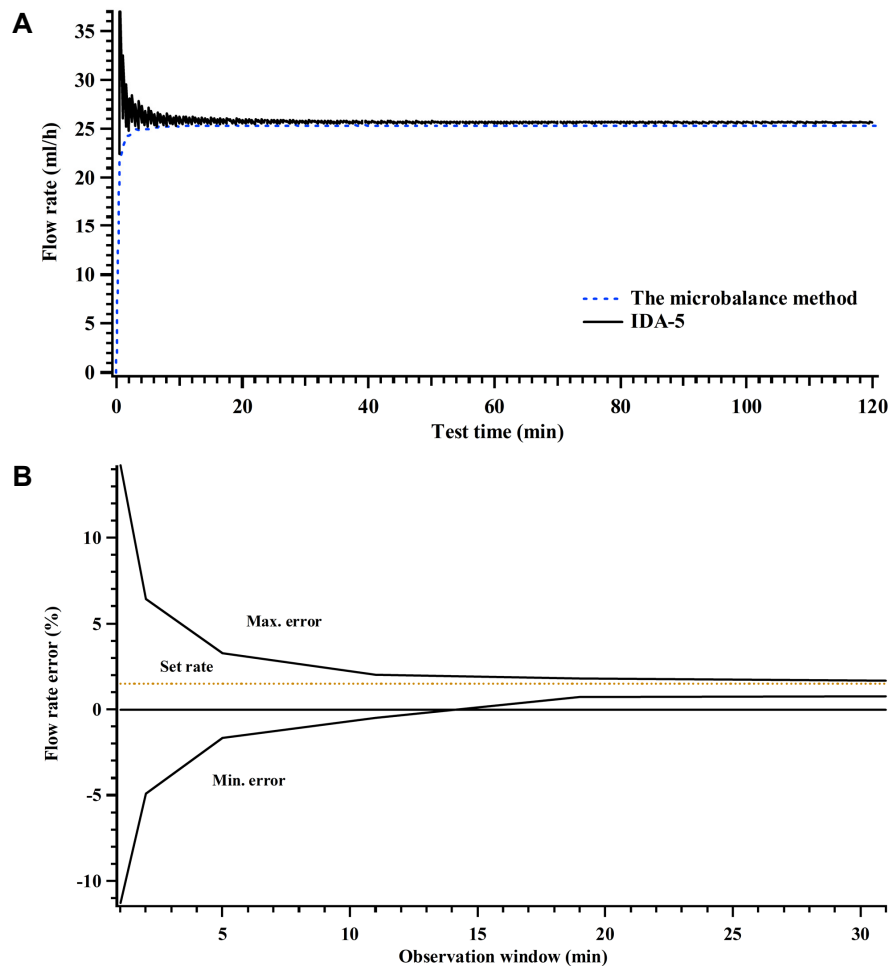
Fig. 4. (A) Comparison of accuracy in the 25 ml/hr flow rate of PS-1000 between the microbalance method and IDA 5 for 2-h (B) trumpet curve from the microbalance method. The dashed line (set rate) is the mean flow error equal to + 1.48%.

measured 240 times every 30 s for 2 h. In the IDA-5 method, the injection flow rate was measured 30 times, with a total injection volume of 2 ml condition. When we tested the infusion flow rate of PS-1000 with IDA-5, the flow rate was initially increased to 1.75 ml/hr and showed a zigzag pattern for approximately 17 min. The zigzag pattern gradually diminishes and reaches a flow rate of 1 mL/h. The final average flow rate was measured as 1.01 ml/hr (Fig. 3a).

The trumpet curve shows a minimum (min. error) and maximum (max. error) relative flow rate compared to the set rate on the vertical axis within the 2-h observation window. The mean flow error with respect to the set rate was equal to + 2.09% at 1 ml/hr flow rate (Fig. 3b). However, the error value of the trumpet curve decreases when the flow rate increases (Fig. 4b and Fig. 5b).

At 25 ml/hr flow rate setting of PS-1000, the average flow rate was measured as 25.27 ml/hr and 25.61 ml/hr by the microbalance method and IDA-5, respectively. The total flow volume of the IDA-5 was 54.22 ml for 2 h. The data were measured 483 times in IDA-5. The data from the microbalance method was also taken every 30 s until 7200 s (240 times) at 25 ml/hr condition. At the beginning of the running PS-1000 at 25 ml/hr, the data from the flow rate of IDA-5 increased up to 37 ml/hr showing the zigzag pattern of the flow rate and was stabilized at 25 ml/hr at after approximately 33 min (Fig. 4a). The error rate of the trumpet curve for PS-1000 at 25 ml/hr was approximately 5% in 2 min, which was decreased compared with the trumpet curve at 1 ml/hr
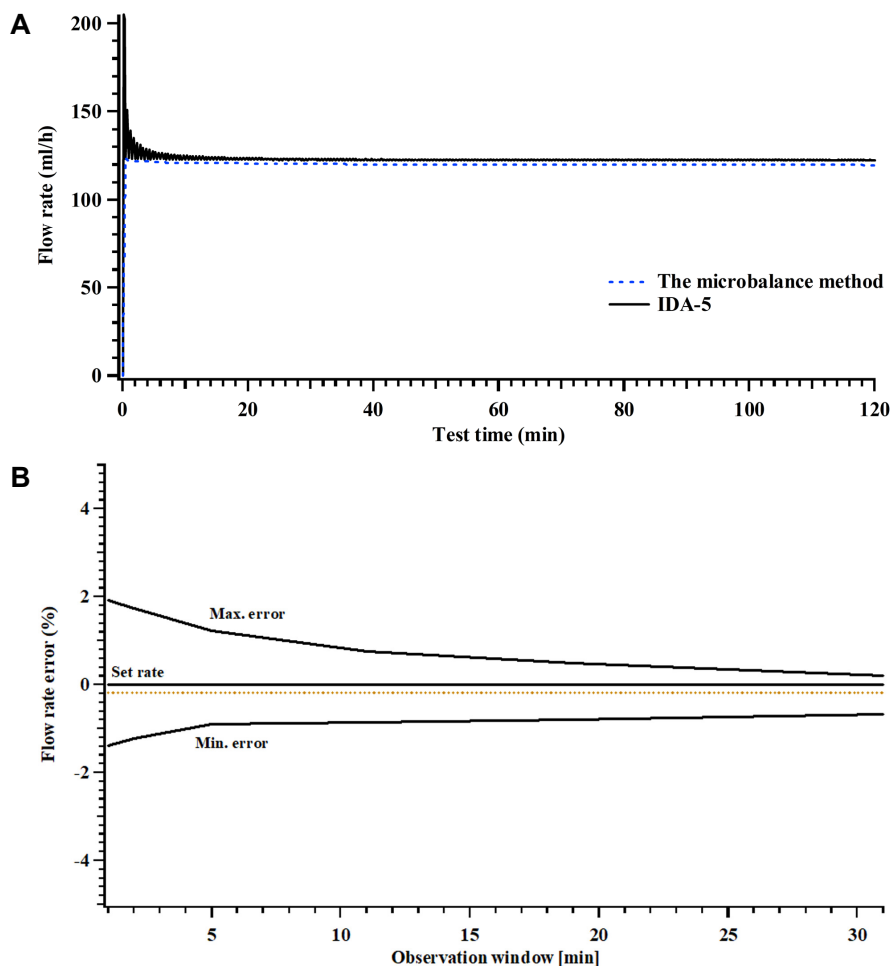
Fig. 5. (A) Comparison of accuracy in 120 ml/hr flow rate of PS-1000 between the microbalance method and IDA 5 for the 2-h (B) trumpet curve from the microbalance method. The dashed line (set rate) is the mean flow error equal to - 0.2%.

condition (Fig. 4b). The mean flow error with respect to the set rate was equal to + 1.48% at 25 ml/hr flow rate. The difference between the two measurement systems was 0.34 ml/hr at a 25 ml/hr infusion condition for 2 h (Fig. 4a). This means that there is a dissidence of 0.34 ml for 1 h at 25 ml/hr of the flow rate condition, which is about 1.36% deviation of the two measurement systems. Therefore, the flow rate measurements of the two measurement systems correspond to each other, which has 98.64% in similarity and reliability in 25 ml/hr flow rate condition.

At 120 ml/hr flow rate setting of PS-1000 for 2 h, the average flow rate was measured as 119.66 ml/hr and 122.41 ml/hr by the microbalance method and IDA-5, respectively. The data from the microbalance method

were recorded every 30 s until 7200 s (240 times) at 120 ml/hr condition. The total flow volume of IDA-5 was 244.94 ml with 721 data measurements for 2 h. The number of data measurement points of IDA-5 was increased with increasing flow rate at a fixed measurement time. The average flow rate measured from IDA-5 was 122.41 ml/hr (Fig. 5a). This means that there is a dissidence of 2.75 ml for 1 h at 120 ml/hr of the flow rate condition, which is about 2.29% deviation of the two measurement systems. The error rate of the trumpet curve of PS-1000 at 120 ml/hr was approximately 2% in 1 min, which was decreased compared with the trumpet curves at 1 ml/hr and 25 ml/hr condition (Fig. 5b). The mean flow error with respect to the set rate was equal to - 0.2% at 120 ml/hr flow rate. The trumpet curves
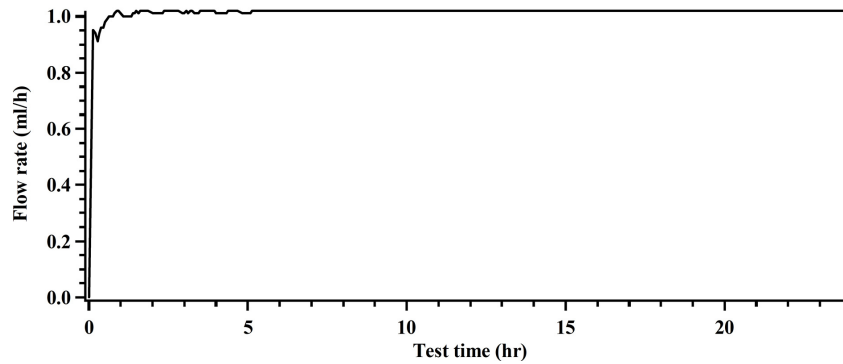
Fig. 6. Long-term accuracy measurement of 1 ml/hr flow rate of PS-1000 with IDA-5 for 24 h.

Table 1. Main uncertainty components for the microbalance method at 1 ml/hr flow rate. U_{comb} and U_{expand} indicatethe combined uncertainty and the expanded uncertainty of the microbalance method, respectively

Uncertainty components	Value of standard uncertainty, $u(x_i)$	Sensitivity coefficient, c_i	$(c_i \times u(z_i))^2$
Time (s)	7×10^{-4}	-3×10^{-4}	4.41×10^{-14}
Resolution (mg)	2.8867×10^{-3}	1	8.33×10^{-6}
Repeatability (µL/s)	1.5×10^{-4}	1	2.25×10^{-8}
Evaporation (µL/s)	1.4×10^{-8}	1	1.96×10^{-16}
U_{comb} (µL/s)	0.00289		
U_{expand} (mL/h)	0.0208		
U_{expand} (%)	2.079		

showed decreased values of the mean flow errors as + 2.09%, + 1.48%, - 0.2% with the increased flow rates of 1 ml/hr, 25 ml/hr, 120 ml/hr, respectively.

2. Long-term accuracy of the flow rate of PS-1000 in the continuous mode

Because IDA-5 was more appropriate for long-term measurement, we used IDA-5 to measure the long-term accuracy of the flow rate of PS-1000 at 1 ml/hr condition for 24 h (Fig. 6). The average flow rate was recorded as 1.1 ml/hr with a standard deviation ± 3.39% for 24 h with 24.43 total volume infusion.

3. Uncertainty measurement

We calculated the uncertainty of the microbalance method at a flow rate of 1 mL/h. We used the coverage factor $k = 2$, which for a normal distribution corresponds to a coverage probability of approximately 95%. For 1 ml/h flow rate measurement in the microbalance method for PS-1000, the average measurement result was 1.001

ml/h with an expanded uncertainty of 20.8 μl/h (2.08%). The calculated uncertainty results for the microbalance method are listed in Table 1.

4. Battery performance evaluation test

Battery life is an important factor in portable PCA infusion pumps. The test results of the battery of PS-1000 were as follows: average hours of battery use were 122 h and 38 min with a flow rate of 1 mL/h. With a flow rate of 25 mL/h, the average hours of battery use were 24 h and 30 min, which means that the user could use PS-1000 for 1 d without recharging the battery. At a flow rate of 120 mL/h, the average hours of battery use were 2 h and 24 min (Fig. 7).

5. Occlusion alarm test

To measure the occlusion pressure function, IDA-5 induced an occlusion pressure condition in PS-1000. The alarm sound was activated at 10.60 ± 0.31 psi (549.18 ± 16.03 mmHg) of the infusion tube of PS-1000. The
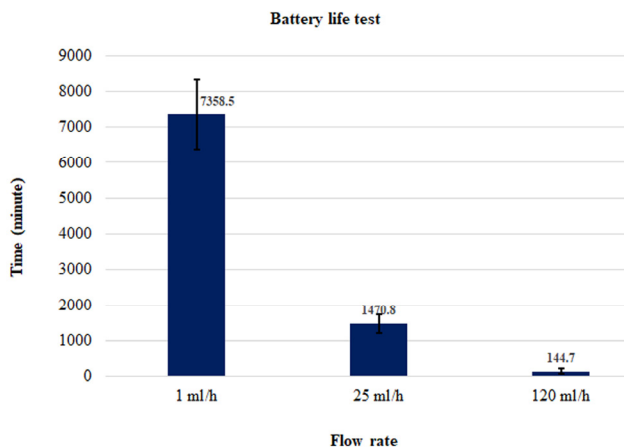
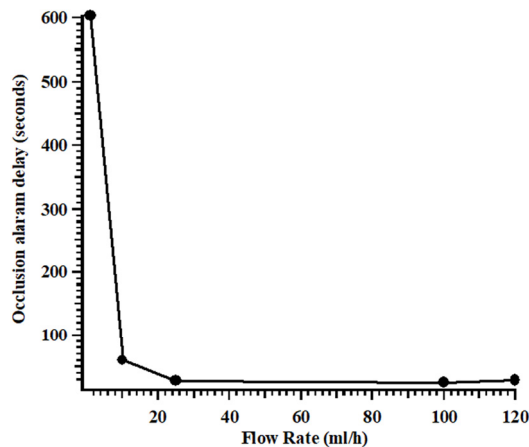Fig. 7. Battery life test with various flow rates of PS-1000.

Fig. 8. Occlusion alarm delay of PS-1000 at 1, 10, 25, 100, and 120 ml/hr flow rates.
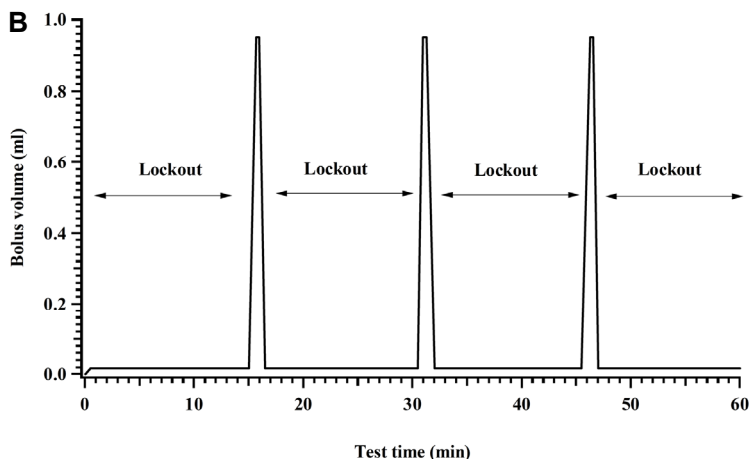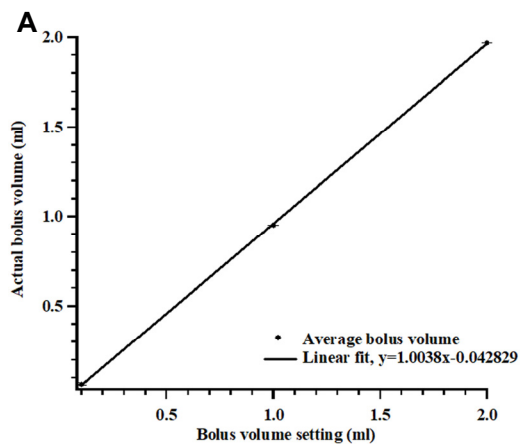

Fig. 9. (A) Average bolus volume graph for 0.1 ml, 1 ml, and 2 ml of bolus dose presets; (B) 1 ml bolus injection graph of PS-1000.

mean time to the occlusion alarm activation was also measured at various flow rates (Fig. 8). The occlusion alarm delay time was 10 min and 4 s in the 1 ml/hr condition, respectively. The mean time of occlusion alarm delay of PS-1000 was shortened to 60, 28, 26, and 29 s with increased flow rates of 10, 25, 100 and 120 ml/hr flowrates, respectively.

6. Accuracy of bolus dose

We tested the accuracy of the bolus dose function of PS-1000. For 0.1 ml, 1 ml and 2 ml of bolus dose presets and 0.063 ml, 0.95 ml, and 1.97 ml of bolus volume were measured, respectively. All bolus tests were repeated thrice. Average accuracy bolus volumes were 63%, 95%, and 98.5% with 0.1 ml, 1 ml and 2 ml bolus volume

presets, respectively. Overall, the infused bolus doses did not exceed the programmed bolus volumes. Fig. 9 shows the actual bolus flow graph and the 1 ml bolus setting of PS-1000.

DISCUSSION

In this study, we conducted a comparative analysis of the PS-1000 smart PCA infusion pump with two measurement systems: the microbalance method and a commercially available infusion analyzer, IDA-5. Whereas the microbalance method with a closed acrylic chamber system can measure the infusion flow rate of PS-1000 in real time, the mechanism of the IDA-5

Fig. 10. User interface and touch screen display of PS-1000.

operation to measure the infusion flow rate of PS-1000 is an averaging method that calculates the total flow volume over a given time period rather than a real-time measurement. Therefore, the flow rate calculated using IDA-5 is typically influenced by the sampling time. The zigzag pattern of the flow rate from IDA-5 in Fig. 3a during the initial stage is due to the mechanism of the peristaltic pump in IDA-5 and the initial air-water two-phase transition conflict phenomenon at a slow flow rate [32,33]. This phenomenon occurred when the liquid flowed slowly in the tube inside IDA-5, which was initially filled with air. These zigzag pattern periods gradually shortened as the flow rate increased in Fig. 3a-Fig. 5a. A comparison of the results from the microbalance method and IDA-5 showed no statistically significant differences at various flow rates.

Usually, the international standard IEC 60601-2-24 neglects the first 24 h of measurements in the trumpet curves, which is the stabilization period [24,34]. However, it is also important to determine the accuracy of IV medication (e.g., insulin) delivery over a shorter time, for example, 1−3 h [35-37]. Therefore, we focused on studying the short-period time (e.g., 2 h) observation window in the trumpet curve in this experiment. Unfortunately, IDA-5 cannot usually measure the trumpet curve because of insufficient data for calculating the trumpet curve in a short-period observation window. Therefore, we calculated the trumpet curve in the short-period observation window of PS-1000 with the microbalance method at 1 ml/hr using MATLAB$^{®}$ (Fig. 3b). The reason why the percentage error of the flow in the trumpet curve was up to 15% is due to low flow rate (1 ml/hr). Generally, the flow rate is inversely proportional to the friction factor [38,39]. The low flow rate could not overcome the air-water two-phase transition conflict phenomenon, air resistance, and friction factor from the tube surface, resulting in high percentage error values in the trumpet curve. The trumpet curves show decreased mean flow errors with increasing flow rates. Furthermore, it is important to note that only the extreme values (e.g., maximum and minimum errors) in the observation window of the trumpet curve are shown, and these values do not necessarily represent the accuracy of a PCA infusion pump [34,37]. Overall, the flow accuracy of PS-1000 showed a good agreement with the infusion pump standard, which is ± 5% of flow accuracy [39].

A PCA pump usually has four infusion modes for a patient: continuous, single bolus, periodic bolus, and complex. The continuous mode involves administering analgesic doses to a patient continuously for 24 h. The single-bolus mode is to administer an analgesic dose only once. If a bolus is required regularly, this becomes the periodic bolus mode. The complex mode is used to change the infusion time, interval, and dose rate as required. Regarding the long-term measurement conditions,

the acrylic chamber of the microbalance method was limited to containing a large volume of fluid for the 24 h long-term measurement. Therefore, the microbalance method was good for short-period (e.g., 2 h) measurements and IDA-5 was good for long-period (e.g., 24 h) measurements.

The flow rate measurement of PS-1000 by IDA-5 was unstable at the beginning of the first infusion during the total 24-h test (Fig. 6). This unstable flow rate was due to the air-water two-phase transition conflict and the change in the elasticity of the infusion tube. The elasticity of the tube might have been changed because the softened tube was induced by the peristaltic pump discs in the PCA pump during the infusion, resulting in a stable flow rate during the long-term measurement (Fig. 6). After approximately 5 h of infusion flow, the flow rate was stabilized to 1 ml/hr. Therefore, we can conclude that the two measurement systems can complement each other in the case of the measurement time.

Regarding the battery performance of PS-1000, users can use PS-1000 approximately for 5 days without recharging the battery under certain conditions. This battery performance is one of the advantages of the PS-1000 as a portable PCA infusion pump.

Occlusion is a blockage or closing of the infusion flow passage, usually referring to an interruption or impediment of an infusion tube due to a blockage, momentary closure, or obstruction of the passageway or blood vessel. Occlusion in the fluid tube of infusion pumps can prevent vital and time-critical medication from being delivered into the bloodstream of patients, resulting in patient harm caused by cessation of therapy [40,41]. Therefore, it is very important to immediately alert the patient and medical care providers to an occlusion event. The mean time to the occlusion alarm activation was also measured (Fig. 8). The measured alarm delay times were consistent with other studies, which showed that the mean time to trigger the occlusion alarm was significantly longer at low infusion rates [42]. The alarm delays of PS-1000 meet the overall time delay criteria of the conventional alarm threshold of the occlusion pressure (300–800 mmHg)

[41]. This is consistent with other reports [41,42].

Bolus function is an important function of a PCA pump to administer additional pre-fixed analgesic doses by the patient himself/herself. When a patient complains of pain, the programmed dose can be administered to the patient by himself/herself using the bolus button. In cases of severe pain, the additional opioid bolus dose may be several times higher than the usual protocol. Therefore, it is important to administer a bolus dose to patients safely and precisely. Fig. 9a shows the actual bolus flow graph and the 1 ml bolus infusion setting of PS-1000 (Fig. 9b). Fig. 9b shows the lockout interval, which is a safe guard to prevent patients from taking unnecessary additional doses. The deviation from the actual bolus volume was due to the peristaltic pump-disc mechanism of the PCA infusion pump. When the peristaltic pump discs were rotated to extract the fluid from the infusion tube, residual fluid remained in the tube.

PS-1000 has a 3.5-inch LCD (Liquid Crystal Display) touch screen which provides a good user interface similar to that of a smart mobile phone (Fig. 10). In addition, PS-1000 also has a wireless function to send patient information to medical care providers in real time, enabling remote monitoring of all infusions in hospital departments from a central computer or mobile device.

The balance resolution is the dominant contributor to the uncertainty components in the microbalance method at 1 ml/hr. The uncertainty in evaporation was negligible for this measurement because of the closed acrylic chamber and oil layer, which acted as an evaporation trap device. However, the uncertainty component contribution may change under different flow rate conditions. For example, buoyancy correction and evaporation rate become more important at very low flow rates (below 300 μl/h) [43]. The uncertainty for flow rate measurement of the microbalance method needs further research; however, 2.08% of the expanded uncertainty with a 95% of confidence level seems acceptable from the evaluation of currently available information. A wide range of exploration of the uncertainty components in the microbalance method measurement system is beyond the

scope of this study. Future research will be conducted to evaluate the uncertainty under various flow-rate conditions using the microbalance method.

In summary, the microbalance method and IDA-5 for the infusion flow rate measurement of PS-1000 were complementary in the case of measurement time. Overall, the flow accuracy of PS-1000 showed a good agreement with the infusion pump standard, which is ± 5% of flow accuracy. The expanded uncertainty of the microbalance method measurement was 2.08% with a 95% of confidence level at 1 ml/hr flow rate condition. PS-1000 has a good battery life, which is sufficient for portable PCA infusion pumps. PS-1000 also has good safety functions such as a sensitive occlusion alarm function, bolus accuracy, and lockout intervals. As a smart PCA infusion pump, PS-1000 has a good user interface and wireless communication function, enabling remote monitoring of all infusions in a department from a central computer.

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