Desflurane Concentrations and Consumptions during Low Flow Anesthesia

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Background: *Desflurane is the least soluble and most expensive inhalation agent. Hence, low flow technique is suitable for anesthesia with desflurane. However, one of the disadvantages of low flow technique is the discrepancy among the end-tidal concentration, inspired concentration, and vaporizer setting.*

Objective: *To measure the concentrations of desflurane at different sites of the anesthesia circuit by varying fresh gas flow (FGF) rates but fixing expired concentration.*

Material and Method: *Thirty ASA PS I-II adult patients were enrolled in this crossover study. After induction of anesthesia and ten minutes of wash-in period, the flow meters of oxygen and air were then adjusted to maintain FiO_2 at 0.3 with the random sequences of FGF rates at 0.5, 1 and 2 L.min^{-1}. Desflurane vaporizer was adjusted to obtain 5% end-tidal desflurane concentration (FeDES) throughout the study period. After FeDES reached the target and was stable for 20 minutes, inspired concentration of desflurane (FiDES) and delivered desflurane concentration at fresh gas outlet (FdDES) were measured. Lastly, the consumption of desflurane was calculated.*

Results: *FdDES was higher than FiDES in every FGF rates. FdDES at FGF 0.5 L.min^{-1} (6.13±0.12) was significantly higher than FdDES at 1 and 2 L.min^{-1} (5.68±0.08, 5.54±0.07, respectively), but not significantly different between FGF 1 and 2 L.min^{-1}. FeDES/FdDES at FGF 0.5, 1 and 2 L.min^{-1} were 0.82±0.014, 0.88±0.012 and 0.87±0.011, respectively. There was no significant difference of FeDES/FdDES between FGF 1 and 2 L.min^{-1}, but there was significant difference between FGF 1 and 0.5 L.min^{-1} with the p-value <0.001. The calculated liquid desflurane consumption per hour at FGF rate of 0.5, 1 and 2 L.min^{-1} were 8.77±0.17, 16.28±0.24 and 31.73±0.41 mL.hr^{-1}.*

Conclusion: *Using FGF 2 L.min^{-1} has no advantage over FGF 1 L.min^{-1}, because they both have the similar FdDES. Regarding at FGF 0.5 and 1 L.min^{-1}, the delivered concentration has to be increased to obtain the desired expired concentration with more intense at FGF 0.5 L.min^{-1} because there are more discrepancies between FdDES and FeDES.*

Keywords: *Low flow anesthesia, Desflurane, Concentration, Consumption*

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Low flow anesthesia is the anesthesia conducted by the use of low fresh gas flow (FGF) rate. The term low flow can be defined as a) FGF rate is lower than alveolar ventilation but higher than basal requirement[1,2] or lower than 25 x body weight in kg$^{-3/4}$ x 2.5 mL.min^{-1}[3] or lower than 1.0 L.min^{-1}[4], b) the rebreathed fraction is more than 50% in the absorber system[5]. FGF rate of 0.5 L.min^{-1} is sometimes classified as minimal flow anesthesia[6]. When such a low FGF rate is used, the anesthetic gases must be delivered to the patient via semi-closed or closed rebreathing systems[1,7].

The advantages of low flow technique are increasing in rebreathing fraction and consequently reduction of excess gas volume and anesthetic pollution[8,9], improving warming and humidification of anesthetic gases[10-12], gradual changes of anesthetic depth[13], economic benefit by improving the efficiency of inhalation anesthesia[14-16]. However, the major disadvantage of low flow anesthesia is the difference between inspired concentration of anesthetic agent and vaporizer setting[17-19]. Other disadvantages are accumulation of undesired gases and vapor in the system (e.g. carbon monoxide, acetone, methane, hydrogen, nitrogen, toxic metabolites of anesthetic agents)[20-24], risk to hypercarbia due to inactive absorbent, inability to quickly alter inspired concentration. In addition, the essential components to provide safe low flow anesthesia are greater knowledge and attention of the anesthesiologist and the availability of appropriate equipment such as leak-free anesthesia circuit, active carbon dioxide absorber and gas analyzer[13]. The increase in

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awareness towards health and ecological system together with modern monitoring equipment make low flow anesthesia an attractive technique.

Desflurane is the least soluble inhalation anesthetic with the lowest blood-gas partition coefficient of 0.42 that allows rapid change in alveolar concentration. The low tissue-gas partition coefficient of desflurane promotes faster elimination and rapid emergence from anesthesia[25,26]. In addition, desflurane is more stable in sodalime and less biodegradable by the liver than most agents[27-29]. These described properties and high cost make desflurane promising for low flow anesthesia[30].

The objective of the present study was to investigate desflurane concentrations at fresh gas outlet (FdDES) and inspired concentrations (FiDES) with various FGF rates: 2, 1, and 0.5 $L.min^{-1}$. The present study was conducted in the same patient and fixed 5% end-tidal or expired desflurane concentration (FeDES). Then, the authors can conclude the most appropriate FGF rate for low flow anesthesia with desflurane. Desflurane consumption was also calculated.

Material and Method

After the Institutional Review Board approval and informed consent, 30 patients were enrolled in this crossover study. The patients with ASA physical status I or II were scheduled for elective neurological surgery under desflurane for anesthesia with anticipated anesthetic time of at least three hours. Patients with significant hepatic, renal, cardiovascular, or pulmonary diseases, susceptible to malignant hyperthermia were excluded. If the patients had unstable hemodynamics or their operation took less than three hours, the studies were terminated and not included for analysis. All patients were randomly assigned into six groups by random table numbers. Each group was conducted at different sequence of flow rate during anesthesia.

Group A: FGF rate 2 → 1 → 0.5 $L.min^{-1}$
Group B: FGF rate 2 → 0.5 → 1 $L.min^{-1}$
Group C: FGF rate 1 → 2 → 0.5 $L.min^{-1}$
Group D: FGF rate 1 → 0.5 → 2 $L.min^{-1}$
Group E: FGF rate 0.5 → 2 → 1 $L.min^{-1}$
Group F: FGF rate 0.5 → 1 → 2 $L.min^{-1}$

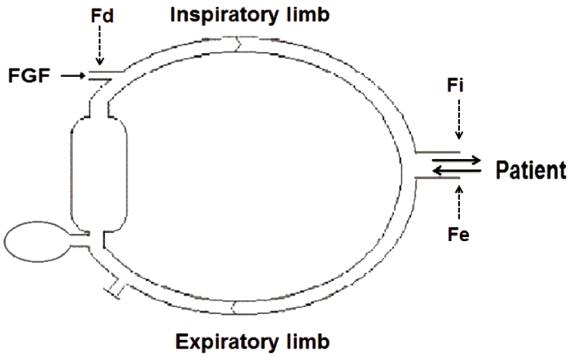
The equipment in the present study was Datex-Ohmeda 7100 S/5 anesthesia machine with Drager D-vapor VAD-8 vaporizer. Datex-Ohmeda S/5 anesthesia monitor was calibrated and used for analyzing anesthetic gases.

Anesthetic protocol

No premedication was given to any patient. After preoxygenation with 6 $L.min^{-1}$ of 100% oxygen for three minutes via circle breathing system, anesthesia was induced by thiopentone 5 $mg.kg^{-1}$ and fentanyl 1 $mcg.kg^{-1}$ pancuronium 0.1 $mg.kg^{-1}$ was administered to facilitate tracheal intubation. The lungs were ventilated manually with 5% dial setting of desflurane in 100% oxygen and the trachea was intubated. The position of the tracheal tube was verified by equal breath sounds on both sides and the presence of exhaled CO_2. The lungs were ventilated mechanically keeping the end-tidal CO_2 at 30 to 35 mmHg. Anesthesia was maintained by oxygen/air mixture with the FGF of 4 $L.min^{-1}$ and desflurane. The flow meters of oxygen and air were adjusted to maintain the FiO_2 of 0.3 to 0.4. The desflurane vaporizer was adjusted to obtain the FeDES of 5%. This target concentration of desflurane was appropriate to maintain depth of anesthesia during neurosurgery in our institute. FiDES, FeDES were sampled at the tracheal tube connector and FdDES were measured at the fresh gas outlet of the anesthesia machine (Fig. 1).

After 10 minutes of wash-in period, FGF was reduced to the first FGF rate assigned for each group. The flow meters and desflurane vaporizer were adjusted to keep the FiO_2 and FeDES at target. After these values were stable for 20 minutes, FGF, FiDES, FeDES, FdDES, oxygen saturation (SpO_2), and hemodynamic parameters including systolic blood pressure, diastolic blood pressure, and heart rate were recorded.

After the first recording, total FGF was adjusted to the second setting of FGF rate. The procedure was repeated. The flow meters and



Fd = concentration of delivered anesthetic gas from fresh gas outlet; Fi = concentration of inspired anesthetic gas; Fe = concentration of expired anesthetic gas

Fig. 1 Diagram of breathing anesthetic circuit.

desflurane vaporizer settings were adjusted to keep the FiO_2 and FeDES at target. After 20 minutes of stable FiO_2 and FeDES, the above values were recorded. Finally, this procedure was repeated at the third setting of FGF rate and the records were collected.

Since the FeDES in the present protocol was 5%, the depth of anesthesia was then adjusted by additional doses of fentanyl 0.5 to 1 mcg.kg^{-1} if there was a more than 20% rising in blood pressure, and intravenous fluid or ephedrine 6 mg was administered if there was a more than 20% reduction in blood pressure. When the study was completed, the FGF was maintained at 1 L.min^{-1} for the rest of the operation. The FGF rate of 1 L.min^{-1} is the standard FGF rate used in our institute.

With respect to FdDes, liquid desflurane consumption in mL.hr^{-1} at each FGF rates (2, 1, 0.5 L.min^{-1}) was calculated according to the following formula:

Liquid desflurane consumption (mL.hr^{-1})
= Vapor desflurane consumption (mL.min^{-1} divided by 209.7 multiplied with 60

$$= \frac{\text{FdDes x FGF rate (mL.min}^{-1}\text{)} \times 60}{209.7}$$

209.7 is the unit volume of vapor desflurane vaporized from one unit volume of liquid desflurane[31,32]. This value is calculated from the formula as shown below[33].

$$\text{Vapor (ml) at 21°C/Liquid (ml)} = \frac{\text{Specific gravity x 22,400 x (273+°C)}}{\text{Molecular weight x 273}}$$

SPSS version 16.0 (SPSS Inc., Chicago, Illinois) was used for statistical analysis. All continuous data and variability were reported as mean and standard deviation (SD), respectively. Categorical data was expressed as number. Repeated-measure analysis of variance and pairwise comparisons (Bonferroni's test) were used to compare the values between the FGF rates. Paired t-test was used to compare the FiDES and FdDES of the same FGF rate. $P<0.05$ was considered significant.

Results

Demographic data is shown in Table 1. The hemodynamics in our study was stable and no patient was excluded during the study. When compared within the same FGF rate, FiDES and FdDES were significantly different (Table 2). Table 3 demonstrated FeDES/FiDES and FeDES/FdDES at various FGF rates. There was no significant difference in FeDES/FiDES among FGF rates 0.5, 1, and 2 L.min^{-1}. FeDES/FdDES between FGF rates 0.5 and 1, and between 0.5 and 2 L.min^{-1} were significantly different, but there was no difference between FGF rates 1 and 2 L.min^{-1}. The calculated liquid desflurane consumptions (mL.hour^{-1}) at fixed 5% FeDES for FGF rates 2, 1, and 0.5 L.min^{-1} were significantly different and shown in Table 4.

Discussion

Nowadays, the low flow anesthesia technique is more popular than in the past[34,35] because of economical and environmental reasons. However, when administering low-flow anesthesia, the anesthesiologists should concern about the discrepancies among the delivered concentration (Fd), inspired concentration

Table 1. Demographic data

Parameter	n	Mean ± SD (range)
Age (years)	30	46.0±13.6 (21-66)
Weight (kg)	30	58.7±9.4 (41-78)
Anesthetic time (min)	30	295.8±82.4 (180-510)
Sex male:female	15:15	
ASA I:II	10:20	

ASA = American society of anesthesiologists

Table 2. The mean of FiDES and FdDES of each FGF rate and comparison between the FiDES and FdDES at the same FGF rate

FGF rate (L.min^{-1})	FiDES (%) (mean ± SD)	FdDES (%) (mean ± SD)	p-value
0.5	5.40±0.04	6.13±0.12	<0.001
1.0	5.33±0.03	5.68±0.08	<0.001
2.0	5.33±0.03	5.54±0.07	<0.001

FGF = fresh gas flow; FiDES = inspired concentration of desflurane; FdDES = desflurane concentration at fresh gas outlet

Table 3. The mean of FeDES/FiDES, FeDES/FdDES of each FGF rate and comparisons of FeDES/FiDES, FeDES/FdDES between FGF rates

FGF rate (L.min^{-1})	FeDES/FiDES (mean ± SD)	FeDES/FdDES (mean ± SD)
0.5	0.93±0.007	0.82±0.014*$^{+}$
1	0.94±0.004	0.88±0.012*
2	0.94±0.006	0.87±0.011^{+}

* Significant difference between FGF 0.5&1, p = 0.001
$^{+}$ Significant difference between FGF 0.5&2, p<0.001
FGF = fresh gas flow; FeDES = end-tidal concentration of desflurane; FiDES = inspired concentration of desflurane; FdDES = desflurane concentration at fresh gas outlet

Table 4. The mean of calculated liquid desflurane consumption ($mL.hr^{-1}$) at fixed FeDES of 5% in various FGF rates

FGF ($L.min^{-1}$)	Liquid desflurane consumption ($mL.hr^{-1}$) (mean ± SD)	p-value
0.5	8.77±0.17*+	<0.001*+#
1.0	16.28±0.24*#	
2.0	31.73±0.41+#	

* Significant difference between FGF 0.5&1
+ Significant difference between FGF 0.5&2
# Significant difference between FGF 1&2

(Fi) and expired concentration (Fe) of anesthetic gases in the anesthesia circuit that was previously mentioned. These discrepancies can be problematic, in particularly when anesthesia was conducted without gas monitoring and the anesthetic agent was set by dial setting only.

The purpose of the present study was to investigate the concentrations of desflurane in different sites in the anesthesia circuit during low flow anesthesia and estimated desflurane consumption. There are numbers of studies measuring desflurane consumption in low-flow anesthesia at fixed Fi or dial-setting. Coetzee and Stewart measured desflurane consumption at FGF rates of 3, 1, and 0.5 $L.min^{-1}$ with fixed vaporizer setting at 3.8 to 4% of desflurane. Desflurane consumption was calculated by dividing the total liquid volatile agent by total anesthetic time[36]. Stephan et al studied desflurane consumption at FGF of 1 $L.min^{-1}$ with dial setting at 4% desflurane. Desflurane consumption was also determined by weighing[37]. In 2001, Johansson et al described the kinetics of desflurane in low flow anesthesia, 2 and 1 $L.min^{-1}$, with the fixed dial setting at 5% of desflurane[19]. Elmacioglu et al investigated the desflurane consumptions in FGF of 0.5, 1.0, and 2.0 $L.min^{-1}$ within a range dial setting of 4 to 6%[38]. However, according to the principle of low flow anesthesia, Fi, Fd and dial setting are higher than Fe, depending on the FGF rate. This means that the doses of desflurane administered differed among patients to patients. Hence, the validities of all reported desflurane consumption were questioned because the Fe was not similar in every patient. For this reason, the authors chose the FeDES as the target during low flow anesthesia rather than vaporizer setting or FiDES. This concept is more appropriate because it represents the same dose of desflurane given in every patient. To our knowledge, there is no study on desflurane consumption during low flow anesthesia while Fe is fixed.

The present study is the crossover study that we investigated the characteristics of desflurane concentrations in three FGF rates in the same subject. The carrying-over effect when the FGF rate was altered is another concern. This was eliminated by randomization of all patients into six groups of sequential FGF rate. In addition, during the tuning period, 20 minutes of stable FeDES at 5% can represent the new equilibrium in the anesthesia circuit. This was shown as no difference in Fe/Fi of each FGF rate. Furthermore, the authors found that no significant differences of FiDES and FeDES at the same gas flow rate among six different sequential groups. FiDES and FdDES were recorded after FeDES had been stable for 20 minutes because 1) the tuning period must be more than three times of the time constant, 2) according to Yasuda's study, the ratio of inspired and alveolar concentration of desflurane was nearly constant after being administered for 20 minutes[25] and 3) from the pilot study conducted, the authors also found that Fi and Fd were steady after changing FGF for 20 minutes.

The major concern while administering low flow anesthesia was the Fe was not equal to the Fi and Fd. The present study showed that the figures of FiDES and FdDES did not differ at FGF of 1 and 2 $L.min^{-1}$ at 5% FeDES. In another way, administering FGF 2 $L.min^{-1}$ has no advantage over FGF 1 $L.min^{-1}$ in terms of discrepancies among Fe, Fi and vaporizer setting.

The FeDES/FdDES at FGF 0.5 $L.min^{-1}$ significantly differed from those at 1 and 2 $L.min^{-1}$. The anesthesiologists should consider that there are more discrepancies at such a low flow.

Direct measurement of liquid desflurane is not easily obtained. Weighing desflurane vaporizer was used in most studies[16,36-38]. However, this procedure needs periodically removing desflurane vaporizer from the anesthesia machine. Moreover, a specific scale is needed for measuring 7-kilogram desflurane vaporizer and the reading scale must be in gram. Another direct method is direct measurement of liquid desflurane. This method is not feasible because of the physical property of desflurane. The boiling point of desflurane is 22.8°celsius and approaches room temperature that can evaporate during drainage. Hence, the error of measurement can occur. For these reasons, desflurane consumption in the present study was quantified indirectly by measuring desflurane concentration at fresh gas outlet and then calculating liquid desflurane consumption in $mL.hr^{-1}$ according to the

formula. The calculated desflurane consumptions at FGF of 0.5 L.min^{-1} was 54% of 1.0 L.min^{-1} and 1 L.min^{-1} was 51% of 2.0 L.min^{-1}.

At present time, the desflurane consumption can be displayed by Zeus, the latest model of anesthesia machine (Dräger) with closed-loop end-expired feedback, or the new vaporizer, Sigma Alpha (Penlon). Nevertheless, they are not widespread used including in our institute. In 2008, Cooman et al reported that desflurane consumption was higher with Zeus than with the conventional anesthesia machine. The desflurane concentration delivered in Zeus was 4.6% expired concentration. On the contrary, the vaporizer in the conventional anesthesia machine was set at 6.5% desflurane during the first 15 minutes and 5.5% desflurane for the next 25 minutes. The reason was that the high initial wash-in period and intermittent flushing of the circuit by Zeus during the anesthetic period[39]. Further study should focus on comparison between Zeus and conventional anesthesia machine with Sigma Alpha vaporizer at equivalent expired concentration of desflurane.

In summary, FGF of 0.5 to 1 L.min^{-1} is the appropriate flow during low flow anesthesia. The higher Fd is needed for the lower flow with the ratio of 1.22 and 1.14 for 0.5 and 1 L.min^{-1}, respectively at 5% FeDES. Since there was no difference between FdDES at FGF 1 and 2 L.min^{-1}, using FGF 2 L.min^{-1} has no advantage over FGF 1 L.min^{-1}.

Potentials conflicts of interest

None.

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ความเข้มข้นและอัตราการใช้ desflurane เมื่อใช้อัตราการไหลของแก๊สต่ำระหว่างการระงับความรู้สึก

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ภูมิหลัง: Desflurane เป็นยาระงับความรู้สึกชนิดไอระเหยที่ละลายได้น้อยที่สุดแต่ราคาแพงที่สุด ดังนั้นเทคนิคที่เหมาะสมคือการใช้การไหลของแก๊สต่ำ แต่ข้อเสียของการใช้เทคนิคการไหลของแก๊สต่ำคือ ความแตกต่างระหว่างความเข้มข้น ณ ตำแหน่งที่หายใจออกสุดหายใจเข้า และค่าที่ตั้งของเครื่องควบคุมยาระงับความรู้สึกไอระเหย

วัตถุประสงค์: *เพื่อวัดความเข้มข้นของ desflurane ณ ตำแหน่งต่าง ๆ ของวงจรการระงับความรู้สึกเมื่อเปลี่ยนอัตราการไหลของแก๊สโดยให้ความเข้มข้นที่ลมหายใจออกคงที่*

วัสดุและวิธีการ: *ศึกษาในผู้ป่วยผู้ใหญ่ ASA PS I-II 30 ราย ภายหลังทำการนำสลบและระงับความรู้สึกเป็นเวลา 10 นาที เพื่อให้ถึงระยะเวลาที่ยาระงับความรู้สึกเข้าสู่ร่างกาย สุ่มปรับอัตราการไหลของแก๊สออกซิเจนและอากาศรวมเป็น 0.5, 1 และ 2 ลิตร/นาที โดยควบคุมความเข้มข้นของออกซิเจนที่ลมหายใจเข้าเป็นร้อยละ 0.3 และปรับความเข้มข้นของ desflurane ที่เครื่องควบคุมยาระงับความรู้สึกไอระเหยให้ความเข้มข้น ณ ตำแหน่งที่หายใจออกสุดเป็นร้อยละ 5 และคงที่เป็นเวลา 20 นาทีหลังจากนั้น วัดค่าความเข้มข้นของ desflurane ณ ตำแหน่งที่หายใจเข้า ตำแหน่งที่ออกจากเครื่องดมยาสลบ หลังจากนั้นนำค่าที่ได้มาคำนวณอัตราการใช้ desflurane ตามอัตราการไหลของแก๊ส*

ผลการศึกษา: *ความเข้มข้นของของ desflurane ณ ตำแหน่งที่ออกจากเครื่องดมยาสลบสูงกว่าความเข้มข้นที่ลมหายใจเข้าในทุกอัตราการไหลของแก๊ส ความเข้มข้นของของ desflurane ณ ตำแหน่งที่ออกจากเครื่องดมยาสลบขณะอัตราการไหลของแก๊สเป็น 0.5 ลิตร/นาที (ร้อยละ 6.13±0.12) จะสูงกว่าขณะอัตราการไหลของแก๊สเป็น 1 ลิตร/นาที (ร้อยละ 5.68±0.08) และ 2 ลิตร/นาที (ร้อยละ 5.54±0.07) อย่างมีนัยสำคัญ ($p<0.05$) แต่ไม่แตกต่างกัน ขณะอัตราการไหลของแก๊สเป็น 1 และ 2 ลิตร/นาที ($p<0.05$) อัตราส่วนระหว่างความเข้มข้นของ desflurane ณ ตำแหน่งที่ลมหายใจออกสุดกับความเข้มข้นตำแหน่งที่ออกจากเครื่องดมยาสลบขณะอัตราการไหลของแก๊สเป็น 0.5, 1 และ 2 ลิตร/นาที เป็น 0.82±0.014, 0.88±0.012 และ 0.87±0.011 ตามลำดับ ซึ่งไม่แตกต่างกันอย่างมีนัยสำคัญ ($p<0.05$) แต่ ขณะที่อัตราการไหลของแก๊สเป็น 1 และ 2 ลิตร/นาที แต่จะมีความแตกต่างอย่างมีนัยสำคัญ ($p<0.001$) เมื่ออัตราการไหลของแก๊สเป็น 0.5 และ 1 ลิตร/นาที ($p<0.001$) เมื่อคำนวณอัตราการใช้ desflurane เหลวจะเป็น 8.77±0.17, 16.28±0.24 และ 31.73±0.41 มล./ชม. ขณะอัตราการไหลของแก๊สเป็น 0.5, 1 และ 2 ลิตร/นาที ตามลำดับ*

สรุป: *เนื่องจากความเข้มข้น ณ ตำแหน่งที่ออกจากเครื่องดมยาสลบเท่ากัน ดังนั้นการใช้อัตราการไหลของแก๊ส 2 ลิตร/นาที ไม่มีประโยชน์มากกว่า 1 ลิตร/นาที ขณะอัตราการไหลของแก๊สเป็น 0.5 และ 1 ลิตร/นาที จะมีความแตกต่างระหว่างความเข้มข้น ณ ตำแหน่งที่ออกจากเครื่องดมยาสลบและลมหายใจออกสุด ดังนั้นจึงต้องปรับความเข้มข้นเพิ่มขึ้นเพื่อให้ความเข้มข้น ณ ตำแหน่งที่หายใจออกสุดเท่าเดิม โดยเฉพาะขณะอัตราการไหลของแก๊สเป็น 0.5 ลิตร/นาที*