THE COST OF DESFLURANE IN MINIMAL FLOW ANAESTHESIA VERSUS MEDIUM FLOW ANAESTHESIA

CHRISTOPHER TING KAH MING

FACULTY OF MEDICINE
UNIVERSITY OF MALAYA
KUALA LUMPUR

2018

THE COST OF DESFLURANE IN MINIMAL FLOW ANAESTHESIA VERSUS MEDIUM FLOW ANAESTHESIA

CHRISTOPHER TING KAH MING

DISSERTATION SUBMITTED IN PARTIAL FULFILMENT OF THE REQUIREMENTS FOR THE DEGREE OF MASTERS OF ANAESTHESIOLOGY

FACULTY OF MEDICINE
UNIVERSITY OF MALAYA
KUALA LUMPUR

2018

UNIVERSITY OF MALAYA
ORIGINAL LITERARY WORK DECLARATION

Name of Candidate: Christopher Ting Kah Ming

Matric No: MGE 150004

Name of Degree: Masters of Anaesthesiology

Title of Project Paper/Research Report/Dissertation/Thesis: The cost of Desflurane in minimal flow anaesthesia versus medium flow anaesthesia

Field of Study: Anaesthesiology and Intensive Care

I do solemnly and sincerely declare that:

(1) I am the sole author/writer of this Work;
(2) This Work is original;
(3) Any use of any work in which copyright exists was done by way of fair dealing and for permitted purposes and any excerpt or extract from, or reference to or reproduction of any copyright work has been disclosed expressly and sufficiently and the title of the Work and its authorship have been acknowledged in this Work;
(4) I do not have any actual knowledge nor do I ought reasonably to know that the making of this work constitutes an infringement of any copyright work;
(5) I hereby assign all and every rights in the copyright to this Work to the University of Malaya ("UM"), who henceforth shall be owner of the copyright in this Work and that any reproduction or use in any form or by any means whatsoever is prohibited without the written consent of UM having been first had and obtained;
(6) I am fully aware that if in the course of making this Work I have infringed any copyright whether intentionally or otherwise, I may be subject to legal action or any other action as may be determined by UM.

Candidate's Signature Date:

Subscribed and solemnly declared before,

Witness's Signature Date:

Name:

Designation:

THE COST OF DESFLURANE IN MINIMAL FLOW ANAESTHESIA VERSUS MEDIUM FLOW ANAESTHESIA

ABSTRACT

This was a prospective pilot study conducted at University Malaya Medical Centre (UMMC) in which 10 patients were recruited to undergo minimal flow anaesthesia and another 10 underwent medium flow anaesthesia. This study was conducted using a standardized general anesthesia delivery machine which is the Maquet FLOW-i anesthesia delivery system. Study population included subjects aged between 18 to 75 years old with American Society Of Anaesthesiologists (ASA) I to II status planned for elective surgery under general anaesthesia (with or without paralysis) with anaesthesia time more than 1 hour. The results showed mean volume of Desflurane used for minimum flow anaesthesia was 47.5 mL/hour which translates to RM 116.90/hour whereas the mean volume of Desflurane used for medium flow anaesthesia was 72.5 mL/hour which translates to RM 178.40/hour. Independent t test was applied showing no statistical significance in the difference of the mean volume and cost of Desflurane used per hour between minimum flow anaesthesia and medium flow anaesthesia. (p value = 0.140)

Keywords : minimal flow anaesthesia, desflurane, pharmacoeconomics

THE COST OF DESFLURANE IN MINIMAL FLOW ANAESTHESIA VERSUS MEDIUM FLOW ANAESTHESIA

ABSTRAK

Ini adalah satu kajian pilot prospektif yang dijalankan di Pusat Perubatan Universiti Malaya di mana 10 pesakit direkrutkan untuk menjalani “minimal flow anaesthesia” dan 10 lagi menjalani “medium flow anaesthesia”. Kajian ini dijalankan dengan menggunakan mesin bius Maquet FLOW-i. Subjek kajian menrangkumi pesakit – pesakit berumur 18 hingga 75 tahun berstatuskan American Society of Anaesthesiologists (ASA) I dan II yang dijadualkan untuk menjalani pembedahan elektif di bawah bius am (dengan atau tanpa paralisis) dengan tempoh bius melebihi satu jam. Keputusan menunjukkan bahawa isipadu Desflurane yang digunakan untuk “minimum flow anaesthesia” ialah 47.5 mL/jam bersamaan dengan RM 116.90 sejam manakala isipadu Desflurane yang digunakan untuk “medium flow anaesthesia” ialah 72.5 mL/jam bersamaan dengan RM 178.40 sejam. Analisis t test menunjukkan bahawa tiada perbezaan statistic signifikan di antara isipadu dan kos Desflurane yang digunakan untuk “minimum flow anaesthesia” dan “medium flow anaesthesia”. (p = 0.140)

ACKNOWLEDGEMENTS

First of all, I would like to express my deepest gratitude to my supervisor, Professor Dr Lucy Chan, Consultant Anaesthesiologist, Department of Anaesthesiology and Intensive Care, University Malaya for her invaluable guidance and assistance in the completion of this dissertation.

I would also like to acknowledge Col Dato’ Dr Jaseemuddeen bin Abu Bakar, Dr. Jeyaganesh Veerakumaran, Dr Chaw Sook Hui and of course Professor Marzida Mansor who is the Head of Department of Anaesthesiology and Intensive Care, University Malaya for their advice and insight throughout the entire study. I would also like to take this opportunity to thank Ms Siti Nur Faliza Zaharuddin for her contributions in data analysis.

Finally, I would like to thank both my parents for their continuous support and encouragement without which I would not have been able to complete this dissertation.

TABLE OF CONTENTS

LIST OF TABLES

LIST OF SYMBOLS AND ABBREVIATIONS

ASA : American Society of Anaesthesiologists

FGF : Fresh Gas Flow

MAC : Mean Alveolar Concentration

MAP : Mean Arterial Pressure

LIST OF APPENDICES

CHAPTER 1 : INTRODUCTION

Anaesthesia represents a fraction of the expense of a given surgical operation. Reducing the cost of anaesthesia therefore is not negligible because the large number of patients passing through a department of anaesthesia accounts for a huge annual budget.

Volatile anaesthetics contribute 20% of the drug expenses in anaesthesia, coming just behind the myorelaxants (26%).[1,2] However, the cost of inhaled agents has potential for savings because a significant part of the delivered amount is wasted when a non- or partial-rebreathing system is used. The cost of inhaled agents is related to more than the amount taken up. It also depends on their market prices, their relative potencies, the amount of vapour released per millilitre of liquid, and last but not least the fresh gas flow rate (FGF) delivered to the vaporizer—the most important factor determining the cost of anaesthesia.

Low flow anaesthesia has been gaining more and more popularity lately in view of its benefits. The benefits of low flow anesthesia include decreased use of inhaled agents, improved body temperature and humidity homeostasis, and reduced environmental pollution.[3] The disadvantages include a potential for ‘‘physiologic gas contamination’’ with the theoretical risk for a hypoxic gas mixture. Furthermore, there is a potential risk for inadequate anesthetic gas concentration due to a dilution effect and / or the risk of misunderstanding the much slower response of anesthetic depth to changes in the vaporizer dial setting.

Nevertheless, with new and advanced monitoring facilities, low-flow anaesthesia nowadays offers a high level of security and does not require special skills other than the knowledge of the pharmacokinetics of the volatile agents.

In this study, we aim to compare the cost of volatile anaesthetics (desflurane) using minimal flow (0.3L/min) anaesthesia vs medium flow anaesthesia (1 – 2L/min) which is the current common practice in University Malaya Medical Centre (UMMC)

CHAPTER 2 : LITERATURE REVIEW

Many anaesthetists have received little training in low flow anaesthesia during their residency and use medium to high flow anaesthesia without considering the waste and environmental pollution. [4]

The classification of fresh gas flow (FGF) rates into anesthetic circuits, as suggested by Baxter, [4] is generally well accepted:

Table 2.1 : Classification of fresh gas flow rates

Metabolic flow	< 250 mL/min
Minimal flow	250 - 500 mL/min
Low flow	500 – 1000 mL/min
Medium flow	1 – 2 L/min
High flow	2 – 4 L/min
Very high flow	> 4 L/min

Low flow anaesthesia (reducing fresh gas flow to 1 L/min) was first described by Foldes et. al in 1952 [5] whereas minimal flow anaesthesia (reducing fresh gas flow to 0.5 L/min) was first described by Virtue in 1974.[6]

Low and minimal flow anaesthetics are characterised by the rate of fresh gas flow (L/min) which is fed into the breathing gas system of the unit. The deciding factor is for the fresh gas flow to be distinctly lower than the patient’s breathing minute volume. If a lower flow of fresh gas is set, the anaesthetic gases in the patient's exhalation air are returned to the patient via closed or semi closed rebreathing system after CO2 has been chemically bonded. This explains the name 'rebreathing system'. As a result of this process flow, the rebreathing volume consecutively increases with a reduction in fresh gas flow and the excess gas volume is continually reduced.

Hence, the basic requirement for conducting anaesthesia with a low fresh gas flow is the use of a rebreathing system. A characteristic of rebreathing system is a carbon dioxide absorber: it chemically removes and binds exhaled carbon dioxide from the breathing circulation system. During removal, heat (ΔT) and moisture (H2O) are also generated, helping condition the breathing gas in the circuit system. To absorb the CO2, soda lime is used.

The benefits and feasibility of low-flow anesthesia have been suggested for nearly two decades.[7] In 1995, Baum and Atikenhead presented the following summary:[8] ''Although there are potential risks associated with low-flow anesthesia, modern anesthesia machines meet all the technical requirements for the safe use of low-flow techniques if they are used in conjunction with equipment for monitoring inhaled and exhaled gas concentrations; these monitors are already increasingly available and, in the near future, are likely to become an obligatory safety standard in many countries. For both economic and ecological reasons, the use of new inhalational anesthetics, with low tissue solubility and low anesthetic potency, can be justified only if the efficiency of administration is optimized by using low flow anesthetic techniques.''

Furthermore, with the introduction of poorly soluble agents like desflurane and sevoflurane, the control of low flow anaesthesia can be facilitated as these poorly soluble agents can reduce the duration of temporary high-flow phases to rapidly wash in or adjust the circuit gas concentrations. [9]

Low flow anaesthesia had been shown to provide financial advantages over the year. Boulogne et al [10] showed that a decrease in FGF from about 7 to 0.5 L/minute reduced the first-hour consumption of liquid isoflurane by 146 mL (157 versus 11 mL) and reduced the cost by 14 times. Baum and Aitkenhead [8] estimated that a decrease in gas flow from 4.5 to 1 L/minute after an initial 30-minute period of high flow (4.5 L/minute) would save about 350 million litres of oxygen, 1000 million litres of nitrous oxide, 33000 L of liquid isoflurane and 46000 L of liquid enflurane per year in Germany and UK. This would represent a significant financial and ecological advantage. Cotter et al [11] compared the hourly consumption of liquid isoflurane in patients anaesthetized in anaesthetic rooms with a high FGF of 6.9 L/minute and during maintenance in the operating theatre with a flow of 2.7 L/minute. The consumption of isoflurane was reduced by 29.2 mL/hour and the hourly cost of isoflurane in low-flow patients was halved. Pedersen et al [12] compared three groups of patients who were anaesthetized for 2 hours with either a Mapleson A system and an FGF of 80 mL/kg or a circle system with a high flow of 3 L/minute or a low flow of 0.6–0.7L/minute preceded by 10minutes with 4.5L/minute. The consumption of liquid isoflurane decreased from 40.8 to 18.5 mL for median-flow and 7.9 mL for low-flow anaesthesia. The cost of isoflurane was five times higher with the non-rebreathing system compared to low flow.

Another factor that needs to be taken into account for the pharmocoeconomics of inhaled agents is the vast variation of the market price among different hospitals and over time. In 1993, Weiskopf and Eger,[13] comparing the costs of desflurane and isoflurane, indicated a price of $71 for a bottle of 100 mL of isoflurane ($0.71 per mL) and $70 for a bottle of 240 mL of desflurane ($0.29 per mL). In 2003, Odin and Feiss[9] stated that in France, the actual prices of liquid agents are 0.19 € for isoflurane, 0.34 € for desflurane and 0.67 € for sevoflurane.

In 1998, Bach [14] calculated the cost of 1 MAC- hour sevoflurane as 3.70 € at 1 L/minute, 5.52 € at 2 L/minute and 9.93 € at 5 L/ minute for a unit price of 0.56 €/mL in Germany. In 1994, Hendrickx and De Wolf [15] calculated a cost of $6.36 for desflurane and $4.75 for isoflurane during the initial 9 minutes of high flow (5 L/minute with 1.6 MAC desflurane or 2 MAC isoflurane). When the circuit was closed and the alveolar concentration stabilized at 1.3 MAC, desflurane became less expensive than isoflurane after 49 minutes. For 169 minutes of anaesthesia, the costs of desflurane and isoflurane attained, respectively, $11.18 and $13.57, whereas with a high gas flow (5 L/minute) the costs would have been $30 for desflurane and $18 for isoflurane.

From the studies above, we can see variation of cost of inhaled agents based on administration technique and the ever evolving market prices in different regions. Therefore, it is practical to measure and to compare amounts of inhaled agents that are consumed with various fresh gas flow in our centre, University Malaya Medical Centre. This will enable us to compare our own data and practice with the previous published results, taking into account the local market prices of the inhaled agents.

CHAPTER 3 : METHODOLOGY

3.1 STUDY AIM & OBJECTIVE

Desflurane is the least soluble and most expensive inhalation agent. Hence, it is assumed to be especially suitable for application of low-flow anaesthetic techniques.

The aim of this study is to compare the cost of volatile anaesthetics (Desflurane) usage using minimal flow (0.3L/min) anaesthesia vs medium flow anaesthesia (1 – 2L/min). With the data and calculations obtained from this study, the usage of inhalational anaesthetics can be attuned accordingly for maximal economic benefit.

3.2 STUDY DESIGN

This was a prospective pilot study conducted at University Malaya Medical Centre (UMMC) in which 10 patients were recruited to undergo minimal flow anaesthesia and another 10 underwent medium flow anaesthesia. This study was conducted using a standardized general anesthesia delivery machine which is the Maquet FLOW-i anesthesia delivery system. Inclusion and exclusion criteria are as below:

3.3 STUDY POPULATION

There were 20 patients that were recruited for this study. The inclusion and exclusion criteria are as below:

<u>Inclusion criteria:</u>

1) Subjects aged between 18 to 75 years old
2) American Society Of Anaesthesiologists (ASA) I to II status

3) Elective surgery planned for general anaesthesia (with / without paralysis)
4) Anaesthesia time > 1 hour

Exclusion criteria:

1) Subjects with known case of central nervous system diseases e.g. Parkinson disease, cerebrovascular disease, dementia, etc.
2) Subjects with ongoing pregnancy
3) Subjects with significant cardiac, pulmonary and renal disease
4) Subjects who are on systemic active drugs or psychiatric medications
5) Difficult intubation
6) Subjects undergoing regional or total intravenous anaesthesia
7) Subjects with history of adverse response to inhalational agents
8) Surgeries with expected duration < 1 hour
9) Subjects with familial history or at risk of malignant hyperthermia

3.4 STUDY PROCEDURE

Subjects were divided into two groups. One group received minimal flow anaesthesia whereas the other group received medium flow anaesthesia.

Subjects of both groups received preoxygenation with 100% oxygen at flow of 6L/min for 1 – 3 minutes. Fentanyl 1-2 mcg/kg was administered intravenously to suppress the response to tracheal intubation. Induction of anaesthesia was done with Propofol 2-3 mg/kg followed by insertion of laryngeal mask airway or endotracheal intubation. For endotracheal intubation, paralysis was achieved by Rocuronium 1 mg/kg or Atracurium 0.5 mg/kg. Patient was then connected to the circuit system. Fresh soda lime was ensured to be available at all times to maintain $FiCO_2$ at zero. Bispectral index (BIS) monitoring was applied as well. BIS values between 40 and 60 were targeted as this range purportedly indicate adequate general anaesthesia for surgery. [17]

For the initial phase, fresh gas flow settings were set at Oxygen 2L/min and air 2L/min (50% oxygen and 4 L/min fresh gas flow) with Desflurane vaporizer set at 6%. Once the target MAC value of 1.0 to 1.3 has been reached:

For minimal flow group

Fresh gas flow for oxygen was reduced to 0.2 L/min, air to 0.1 L/min (70% oxygen and 0.3 L/min fresh gas flow) while vaporizer setting for Desflurane was increased to 8%

For medium flow group

Fresh gas flow for oxygen was reduced to 1 L/min, air to 1 L/min (50% oxygen and 2 L/min fresh gas flow) while vaporizer setting for Desflurane was maintained at 6%

If the depth of anaesthesia had to be changed, the following procedures were followed. If a rapid change was not required, only the vaporizer setting was adjusted while the flow remained constant. However, if a rapid change was required, the flow was increased to 3L/min in addition to adjusting the vaporizer setting. Additional muscle relaxant was administered as necessary.

The vaporizer was turned off after the last skin stitch and flow was switched to oxygen 6 L/min. Neuromuscular blockade was antagonized by Neostigmine 0.05 mg/kg plus Atropine 0.02 mg/kg or Glycopyrrolate 5 mcg/kg.

After completion of the surgery, the volume of volatile agent used which is accessible via data log on Maquet FLOW-i anesthetic machine was recorded.

3.5 SAFETY CONSIDERATIONS

Parameters monitored included ECG, pulse oximetry, non-invasive arterial pressure, capnography, inspired and expired gas partial pressure (oxygen and inhalational agents), airway pressure, tidal volume, ventilator frequency and minute volume. Neuromuscular transmission was monitored by train-of-four nerve stimulation.

The biggest concern when it comes to low flow anaesthesia is the risk of delivery of hypoxic mixture. Therefore, the inspiratory oxygen concentration must be monitored by an alarm system. The Maquet FLOW-i general anaesthesia machine has built-in safety features which preset the minimum permissible FiO2 with different levels of fresh gas flow (FGF). At FGF of 1 L/min, the minimum permissible FiO2 is 23% whereas at FGF of 0.3 L/min, the minimum permissible FiO2 is 67%. At any point of time, the FGF can be increased to prevent any delivery of hypoxic mixture.

Fresh soda lime is essential for low flow anaesthesia.[16] If the inspiratory CO2 concentration increases, this is an indication that the soda lime should be replaced.

CHAPTER 4 : RESULTS

4.1 DEMOGRAPHIC CHARACTERISTICS

A total of 20 patients were recruited for this study (10 for minimum flow anaesthesia and another 10 for medium flow anaesthesia). The demographics of the patients are summarized in Table 4.1.

Out of the 20 patients, 12 (60%) are females with 8 (40%) being male. Both groups have equal distribution of 4 males and 16 females. The mean age for the patients is 50.8 years old. The minimum flow group has a mean age of 50 years old whereas the medium flow group has a mean age of 51.5 years old. The overall mean BMI is 22.6 with the mean BMI for the minimum flow group being 23.1 and medium flow group being 22.1. The majority of the patients recruited are of Malay ethnicity which is 14 (70%) with 4 (20%) being Chinese, one Indian (5%) and one (5%) of other ethnicity.

Table 4.1: Patient demographics (n=20)

Variables	Mean (standard deviation)		
	All (n=20)	Minimum flow (n=10)	Medium flow (n=10)

Age (years)	50.8 (19.25)	50.0 (21.14)	51.5 (18.28)
BMI	22.6 (7.07)	23.1 (3.03)	22.1 (9.79)
Gender*			
Male	8 (40.0)	4 (40.0)	4 (40.0)
Female	12 (60.0)	6 (60.0)	6 (60.0)
Ethnicity*			
Malay	14 (70.0)	7 (70.0)	7 (70.0)
Chinese	4 (20.0)	2 (20.0)	2 (20.0)
Indian	1 (5.0)	1 (10.0)	0 (0.0)
Other	1 (5.0)	0 (0.0)	1 (10.0)
MAP	77.8 (10.08)	78.6 (8.14)	77.0 (12.17)
HR	77.9 (16.05)	78.6 (19.75)	72.7 (10.08)

*Frequency (%)

4.2 PRIMARY OUTCOME

The primary outcome is measured by the mean volume of Desflurane consumed per hour (measured in mL/hour) which is summarized in table 4.2. This volume will be converted into cost in Ringgit Malaysia (RM). The cost of one bottle of 240 mL of Desflurane (Baxter) is RM 590, hence every mL of Desflurane costs RM 2.46. The mean cost of Desflurane per hour (RM/hour) is summarized in table 4.3.

The mean volume of Desflurane used for minimum flow anaesthesia was 47.5 mL/hour which translates to RM 116.90/hour whereas the mean volume of Desflurane used for medium flow anaesthesia was 72.5 mL/hour which translates to RM 178.40/hour.

Independent t test was applied with significant p value level at 0.05 and it showed no statistical significance in the difference of the mean volume and cost of Desflurane used per hour between minimum flow anaesthesia and medium flow anaesthesia. (p value = 0.140)

Table 4.2: Comparison of Mean Volume of Desflurane used per hour between minimum flow and medium flow Anaesthesia patients (n= 20)

	Mean (SD)		t statistic (df)	P-value[a]
	Minimum flow (n= 10)	Medium flow (n=10)		
Volume of Desflurane used (mL/hour)	47.5 (27.73)	72.5 (43.05)	-1.54 (18)	<0.140

[a]Independent t test was applied, Significant level at 0.05

Interpretation: There was no significant difference of mean Volume of Desflurane used per hour between minimum flow and medium flow anaesthesia (t statistics (df) = -1.54 (18), p-value=0.140).

Table 4.3: Comparison of Mean Cost of Desflurane per hour between Minimum flow and Medium flow Anaesthesia patients (n= 20)

	Mean (SD)		t statistic (df)	P-value[a]
	Minimum flow (n= 10)	Medium flow (n=10)		
Cost of Desflurane (RM/hour)	116.9 (68.21)	178.4 (105.90)	-1.54 (18)	<0.140

[a]Independent t test was applied, Significant level at 0.05

Interpretation: There was no significant difference of mean cost of Desflurane per hour between minimum flow and medium flow anaesthesia (t statistics (df) = -1.54 (18), p-value=0.140).

CHAPTER 5 : DISCUSSION

It is generally accepted that a low FGF is pharmacoeconomic due to the reduction in the consumption of volatile agents. Weiskopt and Eger calculated the Desflurane consumption with various FGFs through simulation under the assumption that 1 MAC was kept constantly and found that Desflurane consumption increased nearly twice — directly proportional to a twofold increase in FGF.

However, in our study, the Desflurane consumption per hour decreased less than a half (47.5ml vs 72.5ml) with a threefold decrease in FGF (0.3L/min vs 1L/min). Several hypotheses to explain the cause can be postulated. First, a constant MAC was not maintained during anaesthetic management in the present study. Proper anaesthetic depth varies depending on the situation, and such factors including preparation for the operation after the anaesthetic induction, a difference of surgical stimuli for the entire operation time, and individual variation can affect the depth. Second, relatively high concentrations of volatile anaesthetics in low FGFs are required to reach the same anaesthetic depth or MAC because the absolute amount of anaesthetics to be delivered to the respiratory circuit of the anaesthesia machine is decreased when FGF is decreased. In our study, a higher concentration of Desflurane should be required in the minimum flow group compared to the medium flow group, when the increase of MAC was needed during the surgery.

There are some limitations to our study. Our study was conducted during anaesthetic management for surgical stimuli, so it was difficult to maintain an equal anaesthetic depth simultaneously in both groups. Secondly, it’s important to note that when the FGF is low, the rebreathing fraction through the carbon dioxide absorbent is increased so that carbon monoxide production is increased by the degradation of anaesthetics with the absorbent. Therefore the cost of carbon dioxide absorbent should also be considered. Thirdly, a larger sample size is perhaps needed to be able to demonstrate any significant statistical difference in the consumption of Desflurane between minimum and medium flow groups.

CHAPTER 6: CONCLUSION

From our study, the Desflurane consumption per hour was less in the minimum flow group compared to the medium flow group and the amount of Desflurane saved was less than half during anaesthetic management in surgery. Although there is no statistical significance demonstrated, there is still a huge potential in cost saving especially if minimum flow anaesthesia is used on a broader scale.

REFERENCES

1. Torsher L, Martineau RJ, Tierney Metal. A survey of anaesthetic drug expenditures. Can.J.Anaesth.1992; 39: A113.
2. Feiss P, Coût de l’anesthésie. In: Conferences d’Actualisation de la SFAR. Elsevier, Paris, 1996, pp. 151– 159.
3. Brattwall M, Warren-Stomberg M, Hesselvik F, Jakobsson J. Brief review: Theory and practice of minimal flow anesthesia. Can J Anesth 2012 59: 785-797
4. Baxter AD. Low and minimal flow inhalational anaesthesia. Can J Anaesth 1997; 44: 643-52.
5. Foldes F, Ceravolo A, Carpenter S. The administration of nitrous oxide – oxygen anesthesia in closed systems. Ann Surg. 1952;136:978-81
6. Virtue R. Minimal flow nitrous oxide anesthesia. Anesthesiology 1974;40:196-8
7. Hargasser S, Mielke L, Entholzner E, Hipp R. Anesthesia with low fresh gas flow in clinical routine use (German). Anasthesiol Intensivmed Notfallmed Schmerzther 1995; 30: 268-75.
8. Baum JA, Aitkenhead AR. Low-flow anaesthesia. Anaesthesia 1995; 50(Suppl): 37-44.
9. I. Odin and P. Feiss. Best Practice & Research Clinical Anaesthesiology Vol. 19, No. 3, pp. 399–413, 2005
10. Boulogne P, Demontoux MH, Colin D & Feiss P. Financial advantages of using isoflurane in a closed circuit. Ann. Fr. Anesth. Réanim. 1987; 6: 54–56.
11. Cotter SM, Petros AJ, Doré JC et al. Low-flow anaesthesia practice, cost implications and acceptability. Anaesthesia 1991; 46: 1009–1012.
12. Pedersen FM, Nielsen J, Ibsen M & Guldager H. Low-flow isoflurane nitrous-oxide anaesthesia offers substantial economic advantages over high and

medium-flow isoflurane nitrous oxide anaesthesia. Acta Anaesthesiol. Scand. 1993; 37: 509–512.

13. Weiskopf RB & Eger II. EI. Comparing the costs of inhaled anesthetics. Anesthesiology 1993; 79: 1413– 1418.
14. Bach A. Kosten von sevofluran im gesamten perioperation umfeld. Anaesthesist 1998; 47: S87–S96.
15. Hendrickx J & De Wolf AM. Costs of administering desflurane or isoflurane via a closed circuit. Anesthesiology 1994; 80: 240–242.
16. Baum J, Enzenauer J, Krausse J & Sachs G. Soda lime service life, consumption and costs in relation to gas flow. Anesthesiol. Reanim. 1993; 18: 108–113.
17. BIS range and clinical state. Norwood, MA: Aspect Medical Systems. (Accessed February 19, 2008, at http://www. aspectmedical.com/assets/Documents/ pdf/New_BIS_Range.pdf.)