

Calculation of comparative utilisation and cost: a South African perspective on intravenous vs. inhalational anaesthesia for procedures of differing duration

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Abstract

Objectives: The cost of various anaesthetic techniques fluctuates and is seldom transparent, because of complicated anaesthetic protocols. The theoretical costs of different anaesthetic techniques were compared in this study.

Design: This comparative study utilised protocols that determined the cost of inhalational anaesthesia, based on evidence from relevant literature. Propofol target-controlled infusion (TCI) was used as the intravenous protocol [Alaris® PK syringe pump (Schnider model), Cardinal Health, UK].

Setting and subjects: No patients were involved in this theoretical cost analysis.

Outcome measures: The calculated costs of high- vs. low-flow inhalational anaesthesia and inhalation vs. intravenous anaesthesia with propofol, with or without N₂O, and procedures of a longer and shorter duration were compared.

Results: Trends were noted. High-flow inhalational anaesthesia tended to be more expensive than low-flow inhalational anaesthesia. The savings that were gained by implementing low-flow anaesthesia increased with the duration of procedure. The savings were greater when less soluble inhaled anaesthetics were used. Isoflurane and halothane anaesthesia cost more when N₂O was added. Inhalational anaesthesia with isoflurane was the most cost-effective option consistently. Anaesthesia with desflurane was always the most expensive option. Propofol TCI was less expensive than sevoflurane for long procedures.

Conclusion: Anaesthetic drugs account for only 3-4% of the total cost of a surgical procedure, but economic use thereof frees up resources for other essentials in financially challenging times. Isoflurane should be used widely. N₂O should probably be used conservatively as it increases the anaesthetic cost and contributes to pollution and ozone depletion. Propofol TCI can be considered instead of sevoflurane inhalational anaesthesia for longer procedures.

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Introduction

Increasing economic and environmental awareness necessitates that the costs of daily anaesthetic practice are elucidated, and then minimised. Generally, it is accepted that anaesthetic drugs comprise a relatively small part of the overall cost of most surgical procedures. According to pharmacoeconomical reviews, the total anaesthetic drug cost accounts for < 5% of the total hospital pharmacy budget and only 3-4% of the total cost of a surgical procedure.¹

Inhalational agents that have been introduced over the past few decades (sevoflurane and desflurane) have distinct advantages over the older agents (halothane and isoflurane). Their lower solubility in blood leads to shorter wash-in and wash-out processes. This translates to faster induction and emergence, which could mean speedier turnover in the operating theatre and ultimately cost savings. The cost of these drugs per millilitre is greater, but adjustments in anaesthetic practice can reduce the volume that is consumed.

Table I: Characteristics of inhalational agents (cost as per government tender, March 2011)

Agent	Molecular weight (g)	Density (g/ml)	MAC ¹⁵	Cost per ml (ZAR)	Cost based on the following prices
Sevoflurane	200.05	1.52	1.85	R4.19	R1 047.90 for 250 ml
Isoflurane	184.50	1.50	1.15	R1.00	R250 for 250 ml
Desflurane	168.04	1.47	7.25	R5.14	R1 234.42 for 240 ml
Halothane	197.38	1.87	0.74	R1.62	R404.73 for 250 ml

MAC: mean alveolar concentration

Low flow anaesthesia (≤ 1 l/minute) was described decades ago and modern monitoring equipment has led to a resurgence in the popularity of this technique.² Its main advantages are a reduction in the consumption of anaesthetic vapours, cost savings and reduced environmental pollution. Total intravenous anaesthesia (TIVA) may be another way to reduce environmental pollution from general anaesthesia.

A number of studies in the UK, USA and Europe have compared the cost and clinical efficacy of propofol TIVA and inhalational anaesthesia.³⁻¹¹ However, study protocols vary with regard to premedication, inhalational agents, fresh gas flow rates, additional opioids, prophylactic antiemetic usage and the type and duration of surgery. The direct costs of propofol TIVA, including the cost of waste, have invariably been found to be higher than those of the inhalational agents. When indirect costs that are associated with specific outcomes (length of post-anaesthesia care unit stay and postoperative nausea and vomiting) and the need for additional medications (vasoactive drugs, antiemetics and analgesics) are compared, the results vary.

To the best of our knowledge, no studies have compared TIVA and inhalational anaesthesia in shorter vs. longer procedures.

The aim of this study was to compare the theoretical costs of different anaesthetic techniques, specifically high- vs. low-flow inhalational anaesthesia (four different inhalational vapours) and inhalational (four different vapours) vs. intravenous anaesthesia with propofol with or without N₂O in each category and for procedures of differing duration (20 minutes, one hour and three hours) in each category.

Method

The protocol for this comparative study was approved by the local ethics committee. No patients were involved. Instead, mathematical calculations were carried out. All calculations were based on a 40-year-old man weighing 70 kg and measuring 170 cm tall.

Table II: Fresh gas flow composition variation over time¹⁶

N ₂ O:O ₂	Duration
0.5:0.5	For the first 20 minutes
0.4:0.6	For the next 20 minutes
0.3:0.7	For the next 30 minutes
0.2:0.8	Thereafter

Inhalational anaesthesia

To calculate the inhaled anaesthetic costs, protocols were adapted from published works that suggested ideal time frames and fresh gas flows during induction and the maintenance of low-flow anaesthesia with and without N₂O.¹²⁻¹⁴ An intravenous propofol bolus at 2 mg/kg (140 mg) was used in the calculation of the induction of all the inhalational anaesthesia protocols. Mean alveolar concentration (MAC) values are referred to in individual protocols, and are listed in Table I.

Low flow anaesthesia with N₂O

An initial 10-minute period of high fresh gas flow [4.5 l/minute, N₂O to oxygen (3:1.5)] allowed for the following:

- The desired gas composition to be washed into the circuit.
- Elimination of nitrogen from the functional residual capacity.
- Establishment of a sufficient end-tidal concentration of inhalational agent to provide adequate depth of anaesthesia.
- The initial rapid uptake of N₂O to take place without the risk of accidental gas volume deficiency.^{13,14}

After 10 minutes, with inspired concentration set at 2.5% sevoflurane, 1.5% isoflurane, 4% desflurane and 1.5% halothane, respectively, an expired agent concentration of 0.8 MAC was obtained.¹² This, together with a N₂O concentration of 65%, resulted in an additive effect which equalled the AD₉₅ (the agent concentration that guarantees that 95% of patients will not move following a standard skin incision). Fresh gas flow was then reduced to 1 l/minute.

N₂O uptake decreases with time, which could lead to an accumulation of N₂O and the delivery of a hypoxic mixture

of fresh gas. Therefore, if used as a carrier gas providing approximately 0.66 MAC, its inflow to the circuit had to be reduced (see Table II) when using low-flow anaesthesia to maintain circuit F_{IO_2} at approximately 30%.¹⁵

When the fresh gas flow was reduced to 1 l/minute, vaporiser settings were increased to 3% sevoflurane, 2% isoflurane and 2% halothane, but maintained at 4% desflurane. For longer protocols, the vaporiser setting was changed again to 1.5% at 30 minutes of isoflurane and 1.5% at 35 minutes for halothane.¹²

Provided low flow is maintained, the anaesthetic vapour can be switched off 15-30 minutes prior to the end of the surgical intervention.¹² The lower the flow, the slower the decrease in anaesthetic concentration. Anaesthetic vapour was stopped 10 minutes prior to the end of the protocol period for all low flow inhalational protocols, except those of a 20-minute duration. The fresh gas flow was changed to 5 l/minute to wash out anaesthetic gases [oxygen to air (2.5:2.5)] for the last five minutes.

Anaesthetic vapours, sevoflurane, isoflurane and halothane were switched off after 15 minutes, and fresh gas flow increased to 5 l/minute in the case of the shortest protocol (20 minutes). Anaesthetic vapour was continued at 4%, because the time to emergence after discontinuation of the vapour was short in the desflurane protocol. Fresh gas composition was changed as above in order to wash out N_2O .

Low flow anaesthesia without N_2O

During inhalational anaesthesia without N_2O , the initial high flow phase is significantly shortened, determined only by the time needed to establish the agent concentration required to guarantee sufficient anaesthetic depth. Omitting N_2O necessitates an increase in volatile agent concentration

to compensate for the loss of the hypnotic effects of N_2O . Protocols for low flow anaesthesia without N_2O were based on work carried out on a simulation model by Mapleson.¹⁴

An initial fresh gas flow of 5.5 l/minute [oxygen to air (2:3.5)] was used. Vaporisers were set to 3 MAC, except for desflurane, where the maximum vaporiser setting was 2.7 MAC. This increased the end-expired partial pressure to 1 MAC in one minute (sevoflurane and desflurane), 1.5 minutes (isoflurane) and 4 minutes (halothane). The fresh gas flow was reduced and vaporiser settings were changed as illustrated in Table III. (Similar tables are available for all protocols, but not included here, because of space constraints).

High flow inhalational anaesthesia

During high fresh gas flows, the rebreathing of exhaled gas, which is partially depleted of inhalational agent, is reduced. Therefore, the difference between inhaled and alveolar gas concentrations is reduced. Initial protocols with and without N_2O remain the same as for those for low flow. After wash-in periods, fresh gas flows were reduced to 3 l/minute [oxygen, N_2O or air (1:2)], and vaporiser settings were reduced to 0.4 MAC (with N_2O) and 1 MAC (without N_2O), respectively. Wash-out of the anaesthetic agent, and therefore emergence, was faster at high flow, so the vaporiser was only switched off and high flow given five minutes prior to the end of the study period.

Intravenous anaesthesia

To calculate the intravenous anaesthetic costs, the Schnider model was used, in effect-site concentration mode, on an Alaris® PK syringe pump (Cardinal Health, UK). Volumes of propofol that were used during target-controlled infusion (TCI) were read from the syringe driver at appropriate elapsed times after running the protocol.

Table III: Inhalational protocols without N_2O at low flow for one hour

Without N_2O	Induction duration (minutes)			Wash-in duration (minutes)			Maintenance duration (minutes)						Emergence duration (minutes)			Wash-out duration (minutes)		
	O_2	Air	P	O_2	Air	IA	O_2	Air	IA	O_2	Air	IA	O_2	Air	IA	O_2	Air	IA
Sevoflurane	2			1			6			43			5			5		
	2	3.5	140	2	3.5	6	0.5	0.5	4.5	0.5	0.5	3.3	0.5	0.5	0	2.5	2.5	0
Isoflurane	2			1.5			5.5			43			5			5		
	2	3.5	140	2	3.5	3.5	0.5	1	3.5	0.5	0.5	2.8	0.5	0.5	0	2.5	2.5	0
Desflurane	2			1			9			40			5			5		
	2	3.5	140	2	3.5	18	0.5	0.5	11	0.5	0.5	8.7	0.5	0.5	8.7	2.5	2.5	0
Halothane	2			4			6			40			5			5		
	2	3.5	140	2	3.50	2.3	0.5	1	2.3	0.5	0.5	2.3	0.5	0.5	0	2.5	2.5	0

Air: air (l/minute), IA: percentage of inhalational agent set on vapouriser (%), O_2 : oxygen (l/minute), P: propofol (mg)

The effect-site target was set at 8 µg/ml for induction and reduced to 6 µg/ml for maintenance. Similar to inhalational protocols, two minutes were allowed for induction and airway management to calculate fresh gas flows. Propofol was discontinued five minutes prior to the end of the study protocol. One 50-ml syringe, one extension line and one three-way tap were included in the cost calculations for the 20-minute protocol. One extension line, one three-way tap and two 50-ml syringes, to facilitate easy exchange of the syringes when one was empty, were included in the cost calculations (see Table IV) for the one-hour and three-hour protocols.

Calculations were carried out with and without N₂O for all TCI protocols. Without N₂O, fresh gas flow during induction was 5.5 l/minute [oxygen to air (2:3.5)], which was similar to that of the inhalational protocols. Maintenance flows were reduced to 1 l/minute [oxygen to air (0.5:0.5)] and maintained during the last five minutes as there was no need to wash out the inhalational agent or N₂O.

The propofol effect-site target for the maintenance of anaesthesia was reduced by 25% to 4.5 µg/ml for the protocols including N₂O. Induction was maintained at 8 µg/ml, as the N₂O additive effect would only commence after 10 minutes of wash-in. The fresh gas composition remained the same as that for the inhalational protocols for the reasons mentioned above. The last five minutes of the protocol was used to wash out N₂O with 5 l/minute fresh gas flow while stopping the propofol infusion.

Cost calculations

Carrier gases

Gases may be acquired in cylinders of different weights and are priced accordingly. The content in litres and cost per litre

Table IV: Cost of disposables and propofol (prices as per government tender, March 2011)

Item	Cost
Propofol (20 ml)	R8.30
Syringe (50 ml)	R20
Extension	R1.25
Three-way tap	R3.88

Table V: Cost of the carrier gases (prices as per government tender, March 2011)

Gas	Cylinder weight (kg)	Cost (ZAR)	Molecular weight (g)	Volume (l)	Cost per litre (ZAR)
O ₂	11.52	69.41	32.00	8.06	0.009
Air	8.60	26.03	28.97	6.65	0.004
N ₂ O	31.3	844.58	44.00	15.94	0.053

were determined (see Table V) using Avogadro's hypothesis and the molecular weights of the different gases.

Inhalational anaesthetic agents

The cost of inhaled agents was determined by using the formula quoted by Dion in the *Canadian Journal of Anaesthesia*:¹⁷

$$\text{Cost} = \frac{P \times F \times T \times M \times C}{2142 \times d}$$

P: vaporiser (%), F: fresh gas flow (l/minute), T: duration (minutes), M: molecular weight (g), C: cost (rands/ml), D: density (g/ml)

The molecular weight, cost and density are agent specific, and are provided in Table I. Vaporiser settings, fresh gas flows and durations differ according to protocol (as mentioned earlier). Dion's formula has been accepted in the anaesthetic and pharmacological communities and has been widely used to calculate cost analyses for over a decade.¹⁸⁻²⁴

Propofol for TCI

The cost of propofol was R8.30 for a 20-ml ampoule. The volumes that were used were calculated and the costs determined. The volume (number of millilitres) was rounded off to the next 20 ml (ampoule). Whatever was left of a 20-ml ampoule was added as waste cost.

Disposables

One or two 50-ml syringes, a three-way tap and an extension were added to the TCI protocols as the cost of the disposables.

Statistics

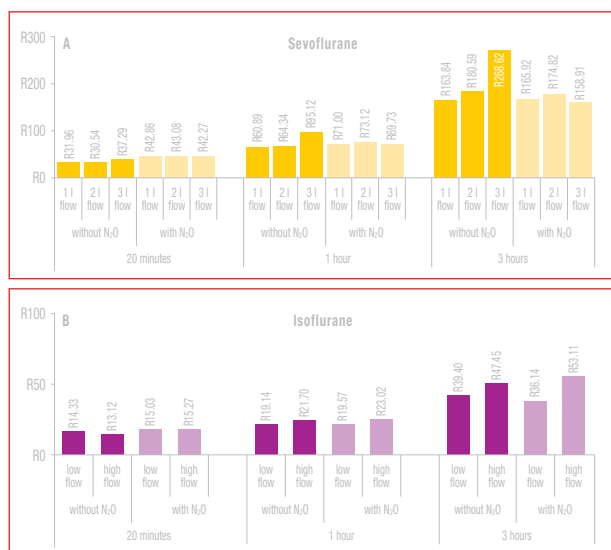
Spreadsheets were designed in Microsoft Excel® 2007 to effect the calculations. A template that contains different settings was created for future use. The different costs for the various anaesthetic techniques and duration of anaesthesia are described in the results section. No statistical analysis was performed.

Results

The calculated costs of inhaled anaesthesia (including oxygen and air/N₂O) are illustrated in Figures 1 a-d.

The following were noted:

- High flow inhalational anaesthesia tended to be more



Figures 1 a-d: Calculated cost of inhalational anaesthetics at different fresh gas flow rates, with and without N₂O, for different durations



Figure 2: Cost of propofol TCI, with and without N₂O, for different durations

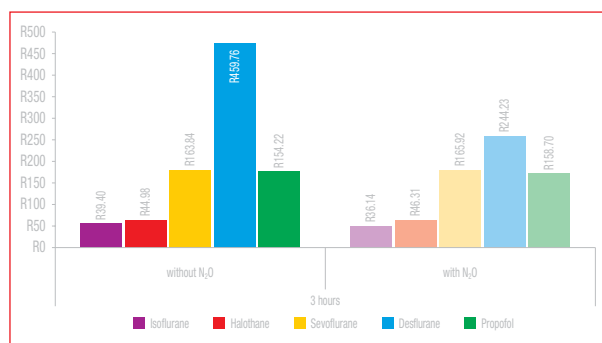


Figure 3: Cost of low flow inhalational anaesthesia with different agents, as well as propofol TCI, with and without N₂O, for three hours

expensive than low-flow inhalational anaesthesia.

- As the length of the procedure increased, so did the saving when using low-flow inhalational anaesthesia.
- The savings were greater when less soluble anaesthetic agents were used.
- Anaesthesia with isoflurane and halothane cost more when N₂O was added. This is because the fresh gas is more expensive, even though lower volumes of inhaled anaesthetic were used. When the potent hypnotic became more expensive [sevoflurane (but only at high flow for one or three hours) and desflurane and propofol], the addition of N₂O to fresh gas, and subsequent decreased use of the expensive hypnotic, translated to a cost saving, compared to the same duration of anaesthetic without N₂O.

The cost of propofol TCI is illustrated in Figure 2.

Inhalational vs. intravenous anaesthesia

When low flow inhalational anaesthesia was compared with propofol TCI, the results tended to follow the trends that are depicted in Figure 3 (the results of the three-hour protocols).

The following was observed:

- Inhalational anaesthesia with isoflurane was consistently the most cost-effective option.
- Anaesthesia with desflurane was consistently disproportionately more expensive than the other inhalational techniques, as well as propofol TCI.
- One exception was evident. Propofol TCI was less expensive than sevoflurane inhalational anaesthesia for longer procedures (three hours). This was not true for the shorter procedures (20 minutes or one hour). Propofol TCI is still more expensive than isoflurane and halothane anaesthesia for long procedures.

Discussion

Volatile anaesthetics are partially halogenated chloro-fluorocarbons. These play a role in the destruction of the ozone layer and promote the greenhouse effect.¹⁵ Although anaesthetic vapours are minor contributors to environmental decline currently, the cumulative consequences of their continued emission are not known. It is our moral obligation to minimise this contribution to pollution by utilising all

available technical facilities, including low flow anaesthesia and TIVA.

The advantages of low flow anaesthesia have been described. They include economic savings, environmental benefits and heat and humidity conservation in breathing circuits.^{4,12,16,17} In this study, the results of the calculations served to confirm and quantify the theoretical savings of low flow inhalational anaesthesia in a local context. The potential risks of low flow anaesthesia, i.e. accidental hypoxia, hypercapnia, inadequate depth of anaesthesia and the accumulation of potentially toxic trace gases, can be minimised by having basic knowledge of the uptake and distribution of anaesthetic gases and of appropriate patient monitoring, including pulse oximetry, capnography, inspired oxygen monitoring and anaesthetic gas analysis. These requirements are identical to those of any other anaesthetic technique.

N₂O is not suitable for use as a sole anaesthetic agent because of a high MAC of approximately 104%.²⁵ It may be used to reduce the amount of more potent anaesthetic if the latter is needed. During inhalational anaesthesia, the reduction in the required end-tidal concentration of a potent anaesthetic agent is equal (as a proportion of its MAC value) to the MAC of N₂O that is delivered.²⁶ The relationship is not as well defined for the propofol-sparing effect, but administration of 65-67% N₂O has been estimated to reduce propofol requirements by up to 25%.^{27,28}

Although N₂O has an important place in the history of anaesthesia, there is continuing debate over any associated clinical advantages in modern anaesthetic practice. Apart from any disadvantages, the reduced effectiveness of N₂O at altitude may negate the perceived main advantage of its use: reduced awareness while under general anaesthesia.^{13,29} Our calculations also showed an increased cost when N₂O was added to commonly used inhalational agents (isoflurane and sevoflurane). If the cost to the environment is added to this, as a consequence of venting scavenged gas into the atmosphere, the following should be considered: is this adjuvant finally becoming too costly to justify its continued use?

Several authors have compared the cost of intravenous propofol for the maintenance of anaesthesia with different inhalational agents. In general, the relative cost of propofol exceeds the cost of inhaled anaesthetics.^{3-5,7-10,30,31} This was true in our study, with the exception of desflurane for procedures of any duration, and sevoflurane for longer procedures (three hours).

This may be explained by a number of factors:

- Desflurane is comparatively more expensive locally than

it is overseas.

- Propofol is more expensive internationally.
- Many of the quoted studies were carried out using propofol TIVA. TCI infers a more tightly regulated dosing regimen and may translate to a decreased use of propofol.

A few problems exist when extrapolating the findings of this study to clinical practice.

The required depth of anaesthesia varies between patients, and in an individual patient, depending on the intensity of surgical stimuli. In practice, this would be accommodated by adjusting the vaporiser setting or the effect site target value during TCI, leaving the stated protocols as an oversimplified rendition of clinical practice. The strict one-minute intervals that are used in inhalational protocols are unlikely to be used in practice. The propofol waste cost may vary. We took the approach of theoretical "as good as they are likely to get" protocols and aimed to make them comparable, if not precisely clinically accurate.

Using cylinder-supplied fresh gas may alter the calculated costs vs. oxygen produced by oxygen generators on site.

When analysing the cost of anaesthesia, the costs of the anaesthetic drugs are important, as well as the fixed and variable costs that are associated with their delivery and which relate to their effects.¹

Fixed costs that were common to both anaesthetic techniques (the building, the staff and the anaesthesia machine) can be ignored. The vaporiser and infusion pump are not common to both techniques, but are both on loan from specific companies who service them regularly. In exchange, our institution uses their products.

Indirect and variable costs are often more difficult to define, for example:

- The indirect costs that result from the consequences of a particular treatment, such as hemodynamic changes that require treatment, or postoperative nausea and vomiting (PONV).
- Staff costs, which may be influenced by recovery characteristics.
- Patient satisfaction could be included here, but it is difficult to measure.

In 2005, Sneyd et al compared the costs of sevoflurane and propofol anaesthesia and found significantly more haemodynamic events in the sevoflurane group which required more vasoactive or rescue drugs.⁸ The overall cost and recovery were no different in the two groups. Others have found that fewer additional drugs were required and lower additional drug costs incurred in the post-anaesthesia care unit in TIVA vs. inhalational anaesthesia.⁹

Several studies have noted the incidence of PONV in inhalational vs. intravenous anaesthesia. However, results differ. PONV occurred more frequently with the use of inhalational anaesthesia in some studies,^{5,9-11,32,33} while no significant difference between intravenous and inhalational anaesthesia was noted in others.^{6,7,30,31} A meta-analysis that was carried out by Sneyd et al in 1998 included 96 trials (80 in adults and 16 in children). It was found that maintenance of anaesthesia with propofol had a significantly lower incidence of PONV in comparison with the use of inhalational agents, regardless of the induction agent that was used, the choice of inhalational agent, the presence or absence of N₂O, the age of the patient or the use of an opiate.³⁴ It is doubtful that the use of antiemetic rescue therapy would lead to sufficient additional costs that would make inhalational anaesthesia more expensive than an intravenous propofol anaesthetic. However, it would most certainly affect patient satisfaction.

Faster emergence from anaesthesia may allow shorter operating room turnover time and more efficient use of resources. A shorter recovery room stay could cut indirect costs by decreasing the number of recovery room nursing staff who are needed, or by reducing overtime payments. Bypassing the recovery room altogether has been shown to be more likely after a sevoflurane or desflurane anaesthetic, rather than after an intravenous propofol anaesthetic in outpatient surgery.⁶ Other studies have shown no statistically significant differences in the recovery characteristics of inhalational vs. intravenous anaesthesia.^{8,11,31,32} Recovery times were shorter with TIVA than with an inhalation anaesthetic in other studies.^{9,10} In 2004, a systematic review by Gupta et al concluded that early recovery was significantly different, but only marginally quicker with sevoflurane or desflurane, compared to isoflurane or propofol anaesthesia.³⁵ Any inferred saving in this category should be viewed with caution as it is unlikely to be sufficient to warrant the appointment of one less recovery room staff member or to accommodate one more patient on a routine list per day.

In 2001, Epple et al devised a strategy with which to measure patient satisfaction.³ They found that although the drug cost of propofol-remifentanyl anaesthesia was more expensive than that of isoflurane-fentanyl, the total anaesthetic cost was higher for isoflurane-fentanyl anaesthesia because of higher anaesthetist and anaesthetic nurse costs. Patient satisfaction was found to be lower following isoflurane-fentanyl anaesthesia. The cost per completely satisfied patient (a patient who would have the same anaesthetic again) was less in the propofol-remifentanyl group. This was confirmed by a prospective, multi-centre randomised controlled trial by Hofer et al in 2003. It compared inhalational and intravenous anaesthesia.³³ They showed improved early

postoperative patient well-being in the total intravenous anaesthesia group, as measured by the Adjective Mood Score and State-Trait-Anxiety Index. As stated earlier, it is difficult to put a price on patient well-being and satisfaction.

Conclusion

Different anaesthetic techniques bear different costs, but these are seldom transparent because of complicated protocols. Although anaesthetic drugs only account for 3-4% of the total cost of a surgical procedure, economic use thereof would free resources for other essentials in financially challenging times.

Isoflurane should be used widely. Nitrous oxide should probably be used conservatively, as it may increase anaesthetic costs and contribute to pollution and ozone depletion. Propofol TCI may be considered instead of sevoflurane inhalational anaesthesia in longer procedures.

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