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Inhalation versus intravenous anaesthesia for day surgery[☆]

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Abstract

Opinion is often fiercely divided over the relative merits of intravenous or inhaled anaesthesia for day case procedures. Advocates of intravenous anaesthesia claim superior recovery and minimal side effects, yet inhalational agents remain popular and are widely used for their excellent operative conditions and low costs. This review will consider the recent evolution in both inhalation and intravenous anaesthesia and will describe what are probably the optimal techniques for the delivery of each. Possible advantages and disadvantages of these approaches will be discussed and the outcomes examined. In reality, recovery characteristics are very similar with either of the two techniques and where differences do exist, they are of minimal importance. Costs may differ, but again the differences are small and frequently absorbed within the far greater overall costs of the procedure. Postoperative nausea and vomiting (PONV) is the most contentious outcome and this will be examined in some detail. While most evidence would favour intravenous anaesthesia in this respect, the magnitude of the advantage may be overestimated and strategies for reducing side effects after inhalation anaesthesia to acceptable levels will be presented. Finally, the future of day case anaesthesia will be considered, with the unfortunate conclusion that the supply of exciting new anaesthetic agents appears to be exhausted, at least for the present.

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1. Introduction

There has long been a vigorous debate between anaesthetists over whether inhalational anaesthetics or intravenous anaesthesia techniques are best for day case patients. The principal issues concern speed and quality of recovery, side effects (especially nausea and vomiting) and costs. These discussions usually occur between individuals who are enthusiasts for one or other technique and who may well have ‘vested interests’ in the form of research funding or speaker fees. While I cannot consider myself free from such bias, I will attempt to present a relatively balanced view.

Historically, the earliest anaesthetics were of course inhalation agents and some of the first anaesthetics were

given for day case procedures. Much has changed since then, and enthusiasm for inhaled and intravenous anaesthetics has oscillated as new drugs have been developed. For its time, cyclopropane was an excellent day case anaesthetic [1], allowing rapid induction and short recovery times from a ‘total inhalation’ anaesthetic. The demise of this highly explosive drug was partly brought about by the increasing use of electrical equipment, otherwise it might have retained its place for longer.

With the advent of propofol, there was renewed interest in intravenous anaesthesia; indeed it looked as if halothane, enflurane and isoflurane would become obsolete [2]. While propofol and total intravenous anaesthesia (TIVA) retain an important place, they failed to gain as widespread popularity as was initially thought. With the advent of relatively insoluble inhaled anaesthetics, such as desflurane and sevoflurane, the pendulum has again swung back towards the inhalation side, although it currently rests somewhere in the middle.

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2. Where are we now—the state of the art

2.1. Inhalation anaesthesia

Modern inhaled anaesthetics suitable for day surgery have low blood:gas solubilities. As a result, they have a fast onset of effect and allow for a rapid recovery. Although general anaesthetics have a multitude of actions, the newer agents are relatively ‘clean’ drugs, producing minimal depression of respiratory and cardiovascular systems. They relax voluntary muscles to a useful degree. They are safe in most patient groups, although they can still trigger malignant hyperpyrexia. A further advantage of these agents is that they permit excellent control of anaesthetic ‘depth’. This is primarily a result of their low solubility, allowing changes in delivered concentration to rapidly achieve the desired effect. This is enhanced, in the case of sevoflurane, by low airway irritability, permitting the delivery of high concentrations without provoking coughing or laryngospasm. Good control allows the level of anaesthesia to be closely matched to the level of surgical stimulation, so that the patient is ‘as deep as necessary, but as light as possible’. This helps to minimise adverse effects and promote rapid recovery.

In my opinion, the optimum inhaled day case anaesthetic involves the use of sevoflurane in a ‘total inhalation’ technique, sometimes referred to as Volatile Induction and Maintenance of Anaesthesia (VIMA). With VIMA, patients can undergo a smooth and painless induction of anaesthesia. While not always quite as rapid as intravenous propofol, this technique minimises hypotension and maintains spontaneous ventilation [3]. As equilibration with the inhaled anaesthetic occurs during the induction phase, the level of control is enhanced compared with the use of inhaled agents after an intravenous induction [3]. Opioid analgesics are rarely needed to suppress intraoperative responses; indeed their use may be detrimental in preventing spontaneous ventilation and, more importantly, increasing the incidence of postoperative nausea and vomiting (PONV) [4]. Immediate recovery may be faster than when an intravenous induction agent is used, at least after relatively short procedures [3,5]. This benefit has not been observed after operations lasting approximately 30 min, however, [6]. Although early comparative trials suggested a moderate level of patient dissatisfaction [3], increasing experience has shown the technique to be popular with most patients. Above all, the VIMA technique has an elegant simplicity which appeals to this author. It can be used with tracheal intubation, but works delightfully with the laryngeal mask airway (LMA).

2.2. Intravenous anaesthesia

There is really only one modern intravenous anaesthetic worth considering for day surgery and that is propofol. It is far removed from the early barbiturates, with a rapid onset and a short duration of action. Anaesthesia can be maintained for as long as necessary by an infusion, but recovery is rapid once this is terminated. Again, this short duration facilitates adjustments to anaesthetic depth, thereby enhancing control. Propofol is also a relatively ‘clean’ drug with few unwanted side effects. It rarely provokes allergic actions and is safe in epilepsy, porphyria and malignant hyperpyrexia. Indeed, unlike inhaled anaesthetics, which tend to produce a degree of analgesia (especially nitrous oxide) and relaxation of muscles in addition to hypnosis, propofol is a more specific hypnotic. As a result, a balanced approach is generally adopted, adding opioids for analgesia and neuromuscular blocking drugs, if and where required.

The optimum intravenous anaesthetic probably involves the combination of propofol and remifentanyl. Both hypnotic and analgesic components are short-acting, necessitating delivery by continuous infusion. Target-controlled infusion (TCI) systems, using a syringe driver programmed with population pharmacokinetic data, simplify the delivery of propofol [7]. Remifentanyl has such a short half life that changes to the infusion rate will rapidly produce a proportional change in the blood concentration, ensuring good control. This means that bolus administration is almost never required and manual infusion schemes are quite satisfactory. However, prototype TCI systems have been developed for remifentanyl.

A variety of combinations of propofol and remifentanyl are possible. At one extreme, a high propofol concentration will achieve a relatively deep level of anaesthesia, supplemented by a small analgesic component. At the other extreme, a high opioid concentration will block arousal resulting from noxious stimuli, requiring only a low concentration of propofol to ensure unconsciousness. While most combinations produce adequate anaesthetic conditions, recovery is fastest following high-opioid, low-hypnotic combinations; a consequence of the very rapid metabolism of remifentanyl. Care must be taken not to reduce the hypnotic component too much, however, or awareness is possible [8]. This may be difficult to detect, as remifentanyl blocks most clinical signs of light anaesthesia.

The brief duration of remifentanyl is due to its metabolism by non-specific blood and tissue esterases. Recovery from remifentanyl is virtually independent of infusion duration, age, hepatic or renal function and genetic disposition [9]. Propofol is short lasting more by virtue of redistribution, but its kinetics are also relatively unaltered by moderate levels of organ dysfunction. Both

drugs can decrease blood pressure, but hypotension can be minimised by the use of infusions rather than bolus administration. Remifentanyl is a potent respiratory depressant, but ventilation can be readily controlled in combination with propofol. The airway can usually be managed with the LMA, but tracheal intubation is possible at higher remifentanyl infusion rates (with propofol). Neuromuscular blocking drugs are seldom required for day surgery. Perhaps the greatest advantage of this technique is that it can be adapted to virtually any procedure which is likely to be performed on an ambulatory basis.

Loss of the spontaneous respiratory rate and pattern reduce the level of clinical monitoring of anaesthetic 'depth'; a disadvantage in this author's opinion. This TIVA technique is also inherently more complex, placing reliance on mechanical ventilation, infusion pumps and drug infusion lines. It is important to remember that there is no measure of drug delivery with TIVA (as there is with inspired anaesthetic agent monitoring), making regular inspection of infusion lines and syringe pumps mandatory.

3. Advantages and disadvantages

Despite claims to the contrary by enthusiasts, emergence, recovery and discharge times differ little, irrespective of whether day case anaesthesia is maintained by intravenous or inhaled anaesthetics [10]. The newer inhaled agents may result in more rapid emergence compared with propofol [11–13], but the differences are small in magnitude and of little significance. Rarely, PONV resulting from inhalation-based anaesthetics (see below) may delay discharge [13], but this is unusual, even when these symptoms occur substantially more frequently compared with propofol [5,12,14].

Some comparative studies have shown inferior operating conditions with intravenous techniques compared with inhalation anaesthesia [13,15,16]. However, this was probably the result of sub-optimal analgesia in the intravenous group, a consequence of trying to achieve a 'fair' comparison between fundamentally different techniques. With the optimal drugs, both techniques achieve satisfactory operating conditions and good control. Both end-tidal concentration and predicted blood propofol levels provide some guide to anaesthetic adequacy. While the former is measured and the latter calculated, the correlation with actual blood concentrations is similar for each and titration to clinical signs is essential. As mentioned previously, however, the measured end-expired concentration does provide a useful confirmation of drug delivery.

Personal preference is undoubtedly important in determining the selection of intravenous and inhaled techniques. Considerations include previous experience

and biases, an inclination towards a simple or complex approach and the choice of controlled or spontaneous ventilation. Mask and needle phobias amongst patients and availability of suitable infusion pumps and vaporisers may further influence the choice of technique. Some concern has been raised about the possible polluting effect of inhaled anaesthetics. Occupational exposure remains at safe levels in operating areas equipped with efficient scavenging systems, even when inhalation induction is practised [17]. The effect on the wider environment is more debatable, but modern inhaled anaesthetics have little impact on ozone levels and are not greenhouse gasses. Nitrous oxide (N_2O) is not so benign, however, [18]. The impact of discarded plastic syringes and infusion lines should also be considered when this subject is debated.

4. Postoperative nausea and vomiting

PONV is the issue most frequently raised when intravenous and inhaled anaesthetics are discussed. It is also one of the outcomes most feared by patients and should not be taken lightly. Aside from the unpleasantness, its management may increase costs, distract nursing staff from other duties, delay discharge and even necessitate overnight admission. The vast majority of comparative studies show a reduction in vomiting with propofol anaesthesia compared with the use of inhaled agents [19]. What is in dispute is the magnitude and significance of this phenomena and whether simple measures can limit the occurrence of PONV with inhalation anaesthesia.

One meta-analysis revealed a 20% reduction in PONV occurring within the first 6 h when propofol was used in patients at relatively high (20–60%) risk of emetic symptoms [20]. In patients already at low risk ($\leq 20\%$), the effect was negligible [20]. In contrast, one recent large study failed to find a protective effect of propofol in high-risk patients [21], seeing only a small benefit in those already at low probability of PONV. Furthermore, propofol may only have an effect on early PONV, perhaps due to its relatively brief half-life. The effect of propofol on late PONV was too small to be considered clinically relevant [22]. This may explain why reductions in PONV following propofol rarely translate into earlier discharge times.

A further problem compounding this issue is that comparisons between intravenous and inhalation anaesthetics seldom have PONV as their main focus. Individually, they lack sufficient power to rule out false positive results and other perioperative risk factors for PONV have rarely been controlled for. With broadly similar results obtained from a great many trials, we can be more confident in our conclusions, but the possibility of error cannot be excluded. Perhaps more importantly,

direct comparisons rarely deliver an optimum technique to each group. For example, in some of my own studies, the retention of spontaneous ventilation was desirable to facilitate blinded observation [13] or clinical comparison of anaesthetic adequacy [5]. In consequence, the intravenous groups received only small bolus doses of fentanyl, which may have artificially lowered the incidence of PONV. In contrast, opioids were also given to the inhalation groups, in whom they were not clinically required. Subsequent experience has shown that the mandatory administration of opioids in association with a VIMA technique results in a 25% incidence of PONV compared with only 8% when opioids are avoided [4]. Furthermore, opioids appear to increase the severity and duration of PONV, with 12% requiring antiemetic therapy in the presence of opioids compared with only 2% in their absence [4].

The incidence of PONV may be further diminished by the use of prophylactic antiemetics. The need for such preventative measures needs to be balanced against the underlying incidence of PONV in the population(s) of interest and the risk:benefit ratio of the particular antiemetic. Recent evidence suggests that dexamethasone is an effective and long lasting antiemetic agent, which is relatively inexpensive and virtually free from adverse effects at the doses used (typically 4–8 mg) [23]. It may also contribute some analgesia, a useful benefit. At present, there are no studies comparing PONV following optimised intravenous anaesthesia with that following VIMA plus dexamethasone.

5. Costs of inhaled and intravenous anaesthesia

Another area of contention concerns the costs of these anaesthetic techniques. It must be remembered that the cost of anaesthetic drugs is extremely low in relation to the overall cost of an ambulatory surgical procedure [24]. Nevertheless, anaesthetists may only be concerned with their own budgets, in which case differential costs assume greater importance. The cost of intravenous drugs are directly proportional to dose, which in turn is related to patient weight. A further factor is the degree of wastage occurring from packaging of intravenous anaesthetics in discrete sizes of ampoule or prefilled syringe. In contrast, inhaled anaesthetic costs are largely related to fresh gas flow rates. Gas flows can readily be reduced to 1 l/min without any noticeable disadvantage, while providing considerable savings. With the use of such low fresh gas flows, the direct cost of inhaled anaesthetics have always been lower than those of propofol. Recently, the situation has changed somewhat, in that the cost of both isoflurane and propofol have reduced substantially in most markets, through the availability of generic products. The newer anaesthetics, sevoflurane and desflurane, still retain patent protec-

tion, so their costs have remained higher. The direct cost of a generic propofol anaesthetic may now be lower than anaesthesia with sevoflurane. However, prefilled syringes of propofol, which are required by commercial TCI systems, are somewhat more expensive (and may result in considerable waste) and the use of remifentanyl may also increase direct costs.

It has often been argued that the higher direct costs associated with intravenous anaesthesia may be offset by indirect savings [25] due to faster recovery and reductions in PONV. In practice, faster recovery is seldom observed and, even when the expense of treating PONV is taken into account, drug costs are still considerably higher with intravenous anaesthesia [5,21]. Other indirect costs should be considered too, such as possible differences in staff workload resulting from postoperative side effects. Such issues are exceedingly complex [24], but there is little evidence that intravenous anaesthesia reduces staff costs in practice. Some have tried to suggest that scavenging systems and even anaesthetic machines would not be required if only intravenous anaesthesia was used, thereby significantly reducing costs. The requirement for controlled ventilation probably dictates the availability of some form of anaesthesia machine and the requirement to deliver just one inhalation anaesthetic would necessitate a scavenging system.

6. Anaesthesia of the future

The past two decades have seen phenomenal developments in day case anaesthetic drugs. Can we expect similar advances to continue and will the future favour intravenous or inhaled delivery?

In theory, there is great potential for new intravenous drugs. As the mechanisms underlying anaesthesia are elucidated, it should be possible to produce 'designer drugs', able to interact selectively with the appropriate receptors. It is likely that such complex molecules would have to be delivered intravenously. These future agents might be expected to produce the individual components of anaesthesia with little, if any, depression of other organ systems. Even current intravenous agents are more specific than their inhaled counterparts, although the 'one-drug-does-all' nature of volatile anaesthetics can be quite useful at times.

Intravenous steroid anaesthetics have long shown great potential, but their history is a sad one of anaphylaxis, difficulty in solubilisation and stability and unwanted side effects. Perhaps some of these problems may be solved in the future. GABA is certainly an important mediator in sleep and arousal, so better understanding of its receptors and development of new benzodiazepines may eventually lead to improved anaesthetics. Nevertheless, despite the considerable

potential for intravenous anaesthesia, there seems to be precious little currently undergoing clinical trials.

All of the current volatile anaesthetics were synthesised long ago. The many other drugs in these chemical series have all been subjected to basic screening and evaluation, so we should not expect any new agents soon. Nevertheless, desflurane and sevoflurane were both initially sidelined because of manufacturing difficulties and concerns over toxicity, respectively. These concerns were ultimately unfounded, so perhaps some other promising agent has been overlooked for similar reasons.

The only new general anaesthetic currently undergoing clinical investigation is an inhaled agent. Xenon, has long been known to possess properties which would make it an attractive day case anaesthetic. The blood:gas solubility of xenon may be as low as 0.115 [26], suggesting impressively rapid induction and recovery. The MAC of xenon, 71% [26], is quite high, preventing the effective use of overpressure. While inhalation induction with one MAC xenon is substantially faster than that with one MAC sevoflurane [27], the latter is typically administered at over four MAC and can result in even faster loss of consciousness [28]. Nevertheless, xenon is odourless and well-tolerated and combinations of sevoflurane and xenon for induction would be interesting. Recovery times are impressive, with emergence and orientation following prolonged inpatient procedures occurring considerably earlier following xenon anaesthesia compared with either isoflurane–N₂O or sevoflurane–N₂O [29].

Unfortunately, there are problems with xenon. As a noble gas, it is available only from natural sources and supplies are severely limited. The concentration of xenon in atmospheric air is 0.086 ppm and currently about 6 million l/year are produced by air liquification and purification [26]. Although collection is likely to increase, much is already earmarked for other medical uses and the aerospace industry. Consequently, the already high price is likely to increase further. The expense and rarity of xenon means that it is never likely to be widely used in anaesthesia, perhaps being reserved for patients with severe cardiac dysfunction, in whom it may be especially beneficial [26]. Sadly, xenon is unlikely ever to be cost-effective in day case surgery, since almost all the expense is incurred during the initial uptake phase [30], making it relatively more economical in longer procedures.

7. Summary

In conclusion, it appears that we already have excellent day case anaesthetics which can be delivered either by inhalation or intravenously. With an appropriate choice of drug and technique, there is probably

little to choose between the two routes of administration and personal preference and prior experience heavily influence the choice. Recovery characteristics are generally favourable with either technique and costs differ relatively little. Furthermore, when the cost of anaesthetic drugs are seen in relation to total expenditure, these agents all represent extremely good value for money.

TIVA with propofol usually does have an advantage in terms of PONV, although the differences may not be as great as is often suggested. Users of inhalation anaesthesia are obliged to take greater care in eliminating other, unnecessary, causes of PONV (especially opioids) and must regularly audit the outcome of their specific patient populations to ensure that the incidence of side effects remains acceptable. The use of prophylactic antiemetics may need to be considered, but should not always be necessary. We will probably all have plenty of time to fine-tune the delivery of our own particular favourite day case anaesthetics, since any new agents seem unlikely in the foreseeable future.

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