Total intravenous anaesthesia techniques for ambulatory surgery

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Purpose of review

The purpose of the present review is to provide an updated discussion on the use of total intravenous anaesthesia (TIVA) for ambulatory surgery, based on results from recent studies put into the context of issues already known.

Recent findings

The current use of TIVA for ambulatory surgery seems to be abundant. It is encouraged by the simplicity of the method, increased experience and declining costs with the propofol and remifentanil combination. The TIVA methods are well tolerated and perceived to give good quality patient care; with rapid, clear-headed emergence and low incidence of postoperative nausea and vomiting. Cost-efficacy and other benefits of recovery from TIVA versus alternative techniques of anaesthesia seem to depend more on the patient and the individual perioperative setting than on the TIVA concept *per se*. Further development of TIVA will include the refinement of target control systems, the introduction of new drugs and adjuvants and advanced equipment for automatic drug delivery, as well as improved effect monitoring.

Summary

TIVA is well tolerated and simple. It is associated with less postoperative nausea and vomiting than inhalational anaesthesia and has no residual paralyses as are possible with locoregional techniques. Propofol with remifentanil seems to be the dominating TIVA technique, delivered either by conventional pumps or by target control systems.

Keywords

ambulatory anaesthesia, ambulatory surgery, postoperative nausea and vomiting, propofol, recovery, remifentanil, target control infusion

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Introduction

When general anaesthesia is provided only with intravenous (i.v.) agents, this is called total i.v. anaesthesia (TIVA). The characteristics of TIVA compared with alternative techniques (i.e. locoregional anaesthesia, inhalational anaesthesia) have to do both with the concept *per se*, but also with the characteristics of the drugs which are used.

The TIVA concept is simple. An i.v. line is the only prerequisite, and everything you need for general anaesthesia will be supplied through this line. This means that there is no need for sophisticated gas delivery systems or scavenger equipment. There is no need for time consuming procedures such as establishing regional blocks or neuraxial blocks, and no risk of block failure and unpredictable duration of residual paralyses.

The TIVA drugs are generally less toxic than inhalational agents, with less risk of malignant hyperthermia and no pollution of environmental air or the athmosphere. TIVA usually implies giving dedicated component therapy with different drugs for different effects, typically one drug for the hypnotic effect (propofol, ketamine, methohexital, midazolam) and another drug for analgesia and antinociception (remifentanil, other opioids, ketamine).

The development of ambulatory surgery brings with it increasing demands for a smooth anaesthetic service. In recent years more extensive procedures have been introduced into the ambulatory setting and more frail patients, such as stable American Society of Anesthesiologists (ASA) III and even ASA IV patients, are accepted for ambulatory care. Also, ambulatory surgery is expanding from the fully equipped operating rooms into diagnostic suites and office-based settings, with less proximity to adequate backup and rescue facilities. Still, the basic requirement for anaesthetic care is to provide optimal safety, quality and cost-efficacy.

This review will focus on the recent international literature on TIVA in the ambulatory setting, adressing TIVA compared with alternative techniques of anaesthesia. The clinical issues in focus will be rapid induction, smooth maintenance, rapid emergence and adequate

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pain control, with the patients being fully awake without side effects such as nausea, vomiting and shivering.

We also looked at recent developments in TIVA techniques and potential future aspects, such as automatic systems and upcoming drugs.

Total intravenous anaesthesia versus alternatives

The success of any TIVA technique will be based on its clinical characteristics evaluated against any potential alternative technique in the individual setting of one specific patient for one specific procedure. Whereas a lot of the characteristics of different techniques are well known from older literature, there are still aspects which may be important to document further.

Total intravenous anaesthesia versus locoregional anaesthesia

In a study of open haemorrhoidectomy, local anaesthesia was associated with less overall costs and less pain at days 1–10, whereas general anaesthesia had less pain at 90 min after surgery [1]. In a study of knee arthroscopy, the use of TIVA with propofol resulted in a shorter time to micturition, but otherwise had quite similar results to a regional anaesthetic technique of femoral nerve and sciatic nerve block [2]. In a more extensive study of ambulatory brachytherapy of the prostate, Flaishon *et al.* [3] found less urinary retention and faster discharge with TIVA than with inhalational anaesthesia and two different techniques of spinal anaesthesia.

Total intravenous anaesthesia versus nitrous oxide supplementation

In most reviews nitrous oxide is associated with increased risk of postoperative nausea and vomiting (PONV; [4]). This was recently confirmed in a large study of more than 2000 in-patients reported by Leslie *et al.* [5•]. However, in a study of ambulatory orthopaedic patients, Mathews *et al.* [6•] found no significant side effects of nitrous oxide when compared with remifentanil as an adjunct to general anaesthesia. The time to emergence was also similar in the two groups. Nitrous oxide is associated with rapid emergence and minor influence on respiratory function, and may be used as an adjunct to reduce the required dose of propofol. In a study of oocyte retrieval, Handa-Tsutsui *et al.* [7] found a 20% reduction in the required dose of propofol when nitrous oxide was used, without any obvious clinical benefits or drawbacks.

Total intravenous anaesthesia versus inhalational anaesthesia

This is an area in which numerous studies are currently being performed, and have also been performed during the past 1–2 years. Inhalational anaesthesia usually implies inhalational maintenance, with or without opioid supplement, after an i.v. induction. In a study of septo-rhinoplasty, Gokce *et al.* [8] did not find any significant differences between desflurane and remifentanil maintenenance versus propofol and remifentanil. In a more detailed study of microsurgical vertebral disc resection, Gozdemir *et al.* [9] found shorter emergence and less nausea, but more shivering and postoperative pain in the propofol and remifentanil group than in the desflurane and nitrous oxide group. Increased incidence of postoperative shivering was also found after remifentanil and propofol in Röhm *et al.*'s [10] comparison with desflurane and fentanyl. Moore *et al.* [11•] confirmed the well known benefit of reduced PONV after TIVA with propofol in mixed-case day surgery. Similarly, reduced PONV was found by Hong *et al.* [12] after breast biopsy with propofol and remifentanil anaesthesia. However, their result may be biased by the use of a longer acting opioid, fentanyl, in the control group. Inhalational induction with sevoflurane and nitrous oxide was slower, but smoother (i.e. less bradycardia and apnoea) and associated with slower emergence and less postoperative pain than the TIVA technique in this study [12]. In their large study of 1158 adults in ambulatory mixed surgery, Moore *et al.* [11•] compared different methods of sevoflurane with/without nitrous oxide induction and/or maintenance versus propofol TIVA. They found more injection pain and hiccups with propofol and more breathholding and recalled discomfort with sevoflurane induction. Sevoflurane was associated with more PONV, but the major outcome results, such as time to discharge and unplanned hospital admissions, were similar in both groups [11•].

The problem of coughing during emergence and extubation was addressed specifically in a study of lumbar disc surgery by Hohlrieder *et al.* [13]. They found significantly less coughing with propofol and remifentanil than with sevoflurane, nitrous oxide and fentanyl. Aspects of early and late PONV were adressed by White *et al.* [14] in a study of day-case gynaecological surgery. They reported similar predischarge PONV incidence when dolasetron was added to sevoflurane maintenance and compared with propofol and remifentanil. However, as discussed by the authors, the dolasetron effect is prolonged compared with propofol, explaining why the dolasetron and sevoflurane patients had less PONV after discharge [14].

Gastric emptying may also have an impact on PONV incidence. This was looked upon by Walldén *et al.* [15] in a study of ambulatory laparoscopic cholecystectomies. They found generally delayed and variable gastric emptying rate in their patients, but no difference between the propofol plus remifentanil group and the sevoflurane group [15].

As inhalational agents may be used in low-flow re-breathing systems, they may be more cost-effective than propofol. This was demonstrated in a study of sevoflurane and sufentanil versus propofol and sufentanil for laparoscopic cholecystectomy [16•].

There have been some reports on sevoflurane-induced convulsions [17] and potential negative effects in brain trauma patients [18], but these concerns do not seem to be very relevant in ambulatory procedures. Similarly, the benefits of preconditioning and protection against cardiac ischaemia with inhalational agents have not been demonstrated to be of clinical importance in ambulatory surgery so far, and may be disputed even for major surgery [19•]. More clinically important are the reports of emergence agitation in children, which are more frequent after sevoflurane than propofol anaesthesia [20].

Developments, adjuncts and trends in total intravenous anaesthesia

In recent years the combination of propofol as a hypnotic agent with remifentanil as an analgesic and antinociceptive agent seems to have emerged as the most popular TIVA technique. In many places this combination is synonymous with TIVA. Both drugs are supplied as a continuous infusion. Propofol may be titrated against an electroencephalogram (EEG)-based hypnotic monitor [e.g. bispectral index (BIS) or other] or kept at a fairly constant level to ensure sleep, whereas remifentanil delivery may be adjusted more frequently and vigorously according to surgical stimulation and nociceptive input.

Methohexital is a cheaper alternative to propofol. It was recently compared with propofol and midazolam for oral and maxillofacial surgery [21]. The methohexital patients had more adverse events, especially nausea. Propofol was better in this aspect, also when compared with midazolam.

As pump technology is expensive, there may still be an option for ketamine as a single all-purpose drug in settings of limited resources [22]. Ketamine is traditionally associated with slower emergence and some incidence of unpleasant hallucinations even when given in moderate doses for sedation [23•]. However, Friedberg *et al.* [24,25] have repeatedly reported a high success rate for ketamine sedation during plastic surgery under local anaesthesia. Propofol with an increasing supplement of ketamine for light or profound sedation during spontaneous ventilation gave no hallucinations and virtually no PONV. Recent publications in the ambulatory setting partly support this conclusion [26,27]. However, Aouad *et al.* [28] reported more agitation, Goel *et al.* [29] reported delayed recovery and a review from Slavik and Zed [30] concluded that there are no specific benefits with this technique. A recent interest has also been in low-dose ketamine infusion for the reduction of postoperative pain and hyperalgesia [31]. Still, the clinical relevance of this, if any, needs to be further tested in ambulatory anaesthesia.

The use of neuromuscular blocking agents (NMBAs) seems to be declining in ambulatory care, also when endotracheal intubation is used. Gravningsbraten *et al.* [32] did not use NMBAs for ear, nose and throat (ENT) surgery and Paek *et al.* [33•] did without them for intubation in laparoscopic surgery without any problems. However, intubation without muscle relaxants requires a high dose of opioid to be successful. Thus, some cases of severe hypotension may be seen, especially in old and frail patients. Injury of the vocal cords has been described after intubation without NMBAs, but clinical studies have not been able to show fewer symptoms of airway trauma with curare than without [34,35].

Beta-blockers are adjuncts that are strongly recommended for surgery in patients with coronary disease, although their perioperative benefits in beta-blocker naive patients are disputed and controversial [36]. Beta-blockers will stabilize the haemodynamics during surgery [37], but may also have other interesting effects in ambulatory surgery. In a study of cholecystectomies, Collard *et al.* [38••] used esmolol infusion instead of opioids, that is, remifentanil or fentanyl, during laparoscopic surgery. The results are remarkable as the beneficial effects of beta-blockers were evident throughout early recovery: less nausea, less pain and more rapid discharge [38••].

Future development of total intravenous anaesthesia

The future of TIVA may change, as a result of both upcoming new drugs and more sophisticated delivery and monitoring equipment.

Already, in most countries, the target control systems for TIVA have been launched. Initially, only the Diprifusor (AstraZeneca Pharmaceuticals, London, United Kingdom) with the Marsh pharmacokinetic model for plasma propofol was available. Now, the open target control infusion (TCI) systems are provided by many manufacturers, and there is a choice of different dosing models for propofol, remifentanil and other opioids. The idea of TCI is to deliver drug intravenously to maintain a precise drug level, either in the plasma (plasma TCI) or at the brain effect site (effect site TCI). The drug is infused automatically from a pump progammed with the patient's demographic data (e.g. weight, height and age). The anaesthesiologist may adjust target levels according to variable clinical need during the procedure [39•]. Also, new monitoring devices are being introduced, in which

the combined anaesthetic effect of different TIVA drugs is simulated, added and displayed on the monitor [40]. A further development of TCI is the automatic, closed loop system which applies registration of effect by EEG or auditory evoked potential (AEP) and haemodynamics to adjust the TCI pumps automatically. Successful reports of such systems are emerging [41•,42,43]. Such systems may simplify dosing further, but they all have a delay from clinical response to dose adjustment, and will certainly never be able to predict increased dose need ahead of especially painful surgical procedures.

Dexmedetomidine has already been launched in many countries as a promising analgesic and anxiolytic drug for sedation, both for minor procedures in children and for intensive care settings [44•]. The potential of dexmedetomidine in ambulatory general anaesthesia is also being explored, but so far the prolonged recovery after high doses needed for anaesthesia compared with propofol may be a clinical limitation [45,46]. However, as the need for opioid may be reduced or even eliminated with dexmedetomidine, the incidence of PONV is also reduced. This point was shown in a study of laparoscopy with dexmedetomidine and desflurane by Salman *et al.* [46].

Propofol 5 mg/ml has recently been introduced and has shown less aching during induction in children compared with the present 10 mg/ml propofol, both solved in mixed long and medium chain triglyceride [47]. A prodrug of propofol, fospropofol, has been launched as a water-soluble alternative for sedation, but the prolonged induction time and increased rate of vein pain may limit the potential for replacing the original propofol [48]. The ongoing attempts to make an esterase-degraded, ultra-short-acting propofol analogue may be more interesting, but so far this drug (THRX-918661) has not come into published trials. Results from animal studies of the new, short-acting esterase-degraded benzodiazepine (CNS-7056) seem very promising [49]. The first human clinical study is in progress and seems to confirm an ultra-short duration combined with otherwise traditional benzodiazepine characteristics (G. Kilpatrick, personal communication).

Conclusion

The current use of TIVA for ambulatory surgery seems to be abundant. It is encouraged by the simplicity of the method, increased experience and declining costs with the propofol and remifentanil combination. The TIVA methods are well tolerated and perceived to give good quality patient care; with rapid, clear-headed emergence and low incidence of PONV. Cost-efficacy and other benefits of recovery from TIVA versus alternative techniques of anaesthesia seem to depend more on the patient and the individual perioperative setting than on the TIVA concept *per se*. Further development of TIVA will include the refinement of target control systems, the introduction of new drugs and adjuvants and advanced equipment for automatic drug delivery, as well as improved effect monitoring.

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