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Review

The clinical pharmacology of remifentanil: a brief review

TALMAGE D. EGAN

Department of Anesthesiology, University Health Sciences Center, 50 North Medical Dr., Salt Lake City, UT 84132, USA

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Introduction

Remifentanil is a new congener of the fentanyl family of opioids that was approved for use as a supplement to general anesthesia by the United States Food and Drug Administration in 1996 [1]. Remifentanil is now available in numerous countries internationally, but it is still in the early stages of clinical application and development [2].

Pharmacodynamically, remifentanil is in most regards indistinguishable from the other fentanyl congeners, producing analgesia, respiratory depression, and other effects typical of the fentanyl derivatives. The unique feature of remifentanil is its short-acting pharmacokinetic profile. The ester structure of remifentanil renders it susceptible to widespread ester hydrolysis, resulting in very rapid metabolism. Remifentanil thus constitutes the first true "ultra-short-acting" opioid.

The aim of this review is to describe briefly the clinical pharmacology of remifentanil and to discuss its clinical application.

Physicochemical properties

Remifentanil is related to the phenylperperidine compounds. Known in its early development as GI87084B, it is the hydrochloride salt of 3-[4-methoxycarbonyl-4-[(1-oxopropyl)phenylamino]-1-piperidine]propanoic acid methyl ester.

The physicochemical properties of remifentanil have important implications for clinical use [2,3]. Like the other fentanyl congeners, remifentanil is a weak base that is quite lipid soluble (octanol/water partition coefficient of 19.9 at pH 7.4). With a p*K*a of 7.1, it exists mostly in the un-ionized form at physiologic pH. It is highly bound (70%–80%) to plasma proteins, mostly α_1-acid glycoprotein. Some of the physicochemical properties of remifentanil are listed in Table 1.

Despite the fact that remifentanil is highly protein bound, remifentanil's comparatively low p*K*a means that the diffusible fraction (the unbound, un-ionized portion) is high. A high diffusible fraction, in combination with moderate lipid solubility, makes remifentanil a rapid-onset opioid.

Remifentanil free base is formulated with glycine. Because glycine is an important inhibitory neurotransmitter in the central nervous system of mammals, in addition to having typical opioid effects, remifentanil causes a reversible motor weakness when administered intrathecally in rodents [4,5]. Thus, remifentanil is not approved for intrathecal or epidural use.

Remifentanil is supplied as a white powder that readily dissolves in water, normal saline, or lactated Ringer's solution (or these same solutions containing dextrose). Because remifentanil is not stable in solution for long periods of time, it must be reconstituted within 24 h prior to use.

Analytical methods

Before the pharmacokinetics and pharmacodynamics of a new drug can be characterized, an accurate assay method must be available. A method for determining remifentanil blood concentrations using capillary gas chromatography/high resolution mass spectrometry/selected ion monitoring (GC-HRMS-SIM) has been developed and validated [6]. The quantitation range of the assay is 0.1 to 250 $ng \cdot ml^{-1}$. Collection tubes are spiked beforehand with tetradeuterated remifentanil as an internal standard to correct for variations in recovery and stability among samples.

Table 1. Representative physicochemical properties and pharmacokinetic parameters of remifentanil

Property or parameter	Value
pK_a	7.1
% un-ionized at pH 7.4	67
Octanol/H_2O partition coefficient	17.9
% bound to plasma protein	80?
Diffusible fraction (%)	13.3?
$t_{1/2}$ alpha (min)	0.5–1.5
$t_{1/2}$ beta (min)	5–8
$t_{1/2}$ gamma (h)	0.7–1.2
Vdc ($l \cdot kg^{-1}$)	0.06–0.08
Vdss, ($l \cdot kg^{-1}$)	0.2–0.3
Clearance ($ml \cdot min^{-1} \cdot kg^{-1}$)	30–40

$t_{1/2}$ alpha, first distribution half-life; $t_{1/2}$ beta, second distribution half-life; $t_{1/2}$ gamma, elimination half-life; Vdc volume of distribution of central compartment; Vdss, volume of distribution at steady state; ? indicates not yet well known.

Because of remifentanil's rapid metabolism, special processing is necessary to prevent continued metabolism of remifentanil prior to assay. This consists of immediate arrest of esterase activity in the blood, followed by liquid extraction of remifentanil into an organic solvent. Blood esterase activity is initially inactivated by the addition of acetonitrile (a water-soluble compound that rapidly precipitates plasma proteins). The organic solvent methylene chloride is subsequently added to the blood-acetonitrile mixture to extract the remifentanil.

A second assay method that does not require the use of volatile solvents at the time of sample collection has also been developed [7,8]. This method relies on the inhibition of remifentanil hydrolysis in whole blood by the addition of 20 µl of 50% citric acid per milliliter of blood immediately after sample collection, followed by liquid extraction of the chilled blood with butylchloride and back extraction into hydrochloric acid. Remifentanil concentrations are then determined by high-pressure liquid chromatography with ultraviolet detection. An internal standard of GI97559 (an ethyl analogue of remifentanil) is used in the assay. This method has been validated in human whole blood over a range of 1 to 200 $ng \cdot ml^{-1}$.

Metabolism

Remifentanil undergoes widespread extrahepatic hydrolysis by nonspecific esterases in blood and tissue. Incubation of remifentanil in fresh human whole blood demonstrates that remifentanil can undergo ester cleavage in vitro, suggesting that the same metabolic pathway is operative in vivo [9].

The primary metabolic pathway for remifentanil is de-esterification to form a carboxylic acid metabolite, GI90291. About 90% of the drug is recovered in the urine in the form of this acid metabolite [10]. GI90291 is excreted unchanged in the urine and is therefore dependent on renal clearance mechanisms (see Special Populations).

The metabolic pathway of remifentanil is shown in Fig. 1. Although most remifentanil hydrolysis probably occurs in tissue (perhaps because it is distributed so quickly), the site of remifentanil metabolism within the vasculature appears to be inside the red cell [11].

The body's capacity to metabolize esters like remifentanil is very substantial and does not appear to be influenced by coadministration of drugs that are metabolized by the same enzyme systems, such as esmolol [12]. However, whether this applies to other commonly used esters such as succinylcholine remains to be demonstrated.

Pharmacodynamics

Remifentanil is a pure mu receptor agonist whose opioid receptor activity has been demonstrated in vitro. Remifentanil inhibits electrically evoked contraction in guinea pig ileum and rat and mouse vas deferens, three isolated animal tissues commonly used to demonstrate opioid receptor activity [13]. In these studies remifentanil exhibited its effect at the mu subtype of opioid receptor, as evidenced by the complete reversibility of the effects by naloxone. Naloxone antagonism of the effects of remifentanil has also been demonstrated in humans [14].

As a pure mu agonist, remifentanil produces all the opioid effects characteristic of the fentanyl family of opioids. Its therapeutic effects therefore include dose-related analgesia and sedation.

The effects of remifentanil on the central nervous system are reflected in the raw electroencephalograph (EEG). At high doses, remifentanil produces a slowing in frequency and an increase in amplitude that translates into a decrease in the spectral edge parameter [15]. These changes are regarded as the EEG fingerprint of this drug class [16]. Figure 2 illustrates the typical spectral edge changes observed when human volunteers receive a brief but high-dose infusion of remifentanil.

Remifentanil is substantially more potent than alfentanil and slightly less potent than fentanyl. These potency estimates have been made using MAC (minimum alveolar concentration) reduction and EEG methods [15,17–19]. Figure 3 contrasts the potency of remifentanil with that of alfentanil using the EEG as the measure of drug effect.

The adverse effect profile of remifentanil is also essentially indistinguishable from that of the previously marketed fentanyl congeners. Most importantly,

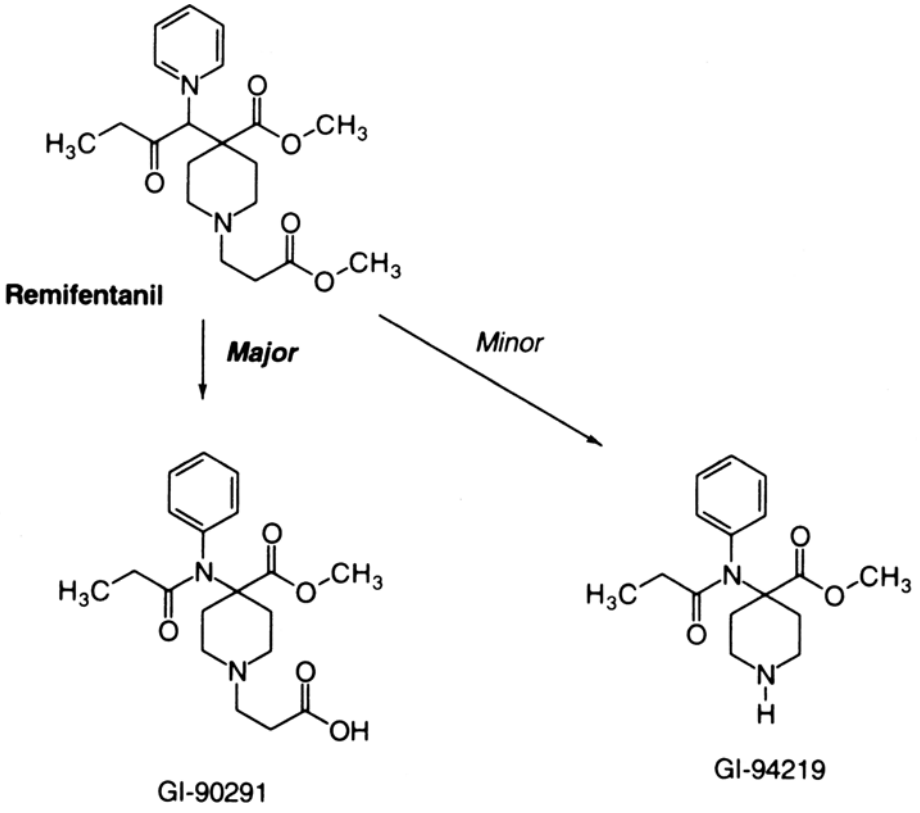

Fig. 1. Metabolic pathway of remifentanil. De-esterification by non-specific blood and tissue esterases to form a carboxylic acid metabolite (GI90291) is the primary metabolic pathway. N-dealkylation of remifentanil to GI94219 is a minor metabolic pathway (from [2], with permission)

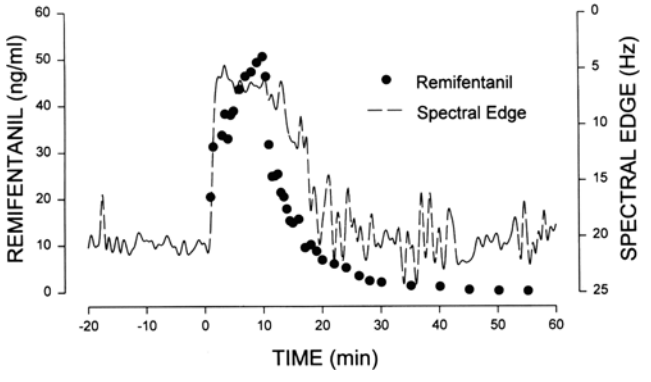

Fig. 2. Representative changes in remifentanil blood concentrations and the EEG spectral edge parameter produced by a 10-min infusion of remifentanil at $3\,\mu g \cdot kg^{-1} \cdot min^{-1}$. Note the very close relationship between changes in blood concentration and changes in the spectral edge, with a rapid return of the spectral edge to baseline values as the remifentanil concentration declines (from [15], with permission)

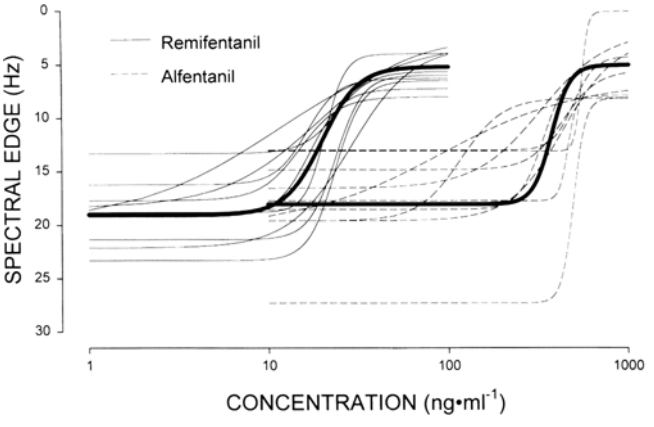

Fig. 3. A comparison of remifentanil and alfentanil potency as determined by the EEG. Ten adult males received infusions of remifentanil and alfentanil on separate occasions at dosages sufficient to produce maximal changes on the EEG. *Each curve* represents the concentration-effect relationship for a single volunteer. The *bold curves* represent the mean concentration-effect relationship for each drug. As measured by the EEG, remifentanil is about 20–30 times more potent than alfentanil (from [15], with permission)

remifentanil produces a dose-dependent increase in the partial pressure of carbon dioxide as a result of ventilatory depression. Remifentanil's respiratory depression closely parallels remifentanil blood concentrations and has thus been exploited as a measure of drug effect for pharmacodynamic modeling purposes [20].

The hemodynamic effects of remifentanil are also characteristic of the fentanyl series of opioids. Remifentanil causes dose-dependent decreases in heart rate, arterial blood pressure, and cardiac output [21]. At high

doses, severe bradycardia has been reported secondary to remifentanil [22]. These cardiovascular effects are thought to be at least in part related to a centrally mediated increase in vagal tone [23]. Unlike morphine, the decrease in arterial blood pressure observed with remifentanil is not secondary to histamine release [24].

Other side effects that are expected with mu agonists have also been reported in association with remifentanil. These adverse effects include nausea, vomiting, pruritus, and muscle rigidity [2]. Intraoperative awareness has also been reported in association with remifentanil [25].

Pharmacokinetics

Remifentanil's short-acting pharmacokinetic profile is its unique pharmacologic feature. In terms of the rapidity with which concentrations fall after stopping an infusion, remifentanil is dramatically different from the other fentanyl congeners.

The pharmacokinetics of remifentanil are best described by a three compartment model [15,17,26,27]. Its clearance is several times greater than hepatic blood flow, which is consistent with widespread extrahepatic metabolism [28]. As with the other fentanyl congeners, remifentanil is widely distributed in body tissues, with a steady-state distribution volume of approximately 20–401 [15,17,26,27]. Unlike the other fentanyl congeners, remifentanil is not sequestered or taken up by the lung to any substantial degree [29].

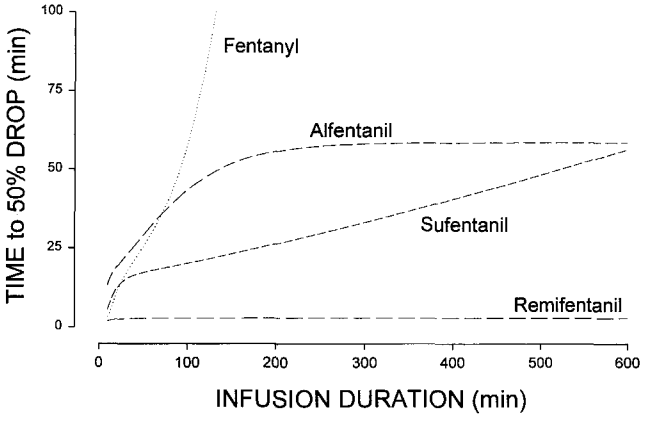

Fig. 4. Graphic representation of the context-sensitive half-times ($CST_{1/2}$) for remifentanil and the other fentanyl congeners using pharmacokinetic parameters from the literature. $CST_{1/2}$ simulates the time required for a 50% decrease in plasma concentration after termination of a continuous infusion targeted to a steady-state level. Note the short, time-independent $CST_{1/2}$ of remifentanil (from [26], with permission)

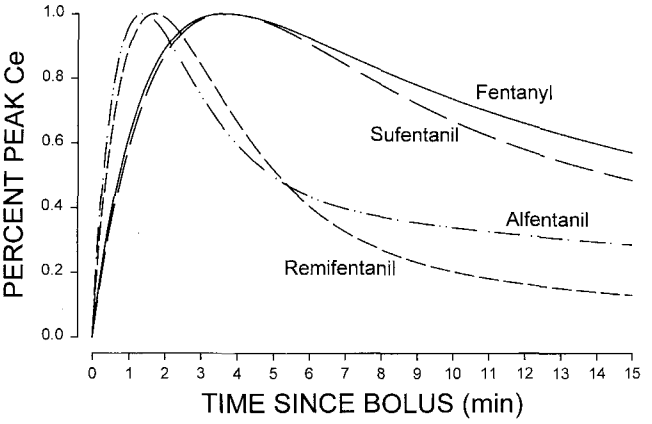

Fig. 5. Computer simulation of the time required to reach peak effect site concentration after bolus administration of fentanyl, alfentanil, sufentanil, and remifentanil using pharmacokinetic parameters from the literature. This is a graphic illustration of the plasma-biophase equilibration process for these drugs. Ce is the effect site concentration; a bolus injection was made at time 0 (from [32], with permission)

Numerous "high-resolution" studies have confirmed remifentanil's short acting pharmacokinetic profile [15,17,26,27]. Table 1 lists some parameters that are representative of remifentanil's pharmacokinetics [17].

A graphic representation of the context-sensitive half-time ($CST_{1/2}$) of remifentanil is perhaps the most clinically meaningful way of representing the pharmacokinetics of remifentanil. Defined as the time required to achieve a 50% decrease in concentration after stopping an infusion targeted to steady state, $CST_{1/2}$ is a useful means of contrasting the clinical implications of multicompartment pharmacokinetic parameters [30,31]. Figure 4 illustrates the $CST_{1/2}$ of remifentanil compared with the other members of the fentanyl series of opioids. Remifentanil's $CST_{1/2}$ is short (approximately 3–4 min) and is independent of infusion duration [15,17,26,27]. The robustness of remifentanil's $CST_{1/2}$ has been confirmed prospectively [20]. Thus, remifentanil can be viewed as a truly rapid-offset opioid.

The latency-to-peak effect of remifentanil is also rapid and is comparable with that of alfentanil. The $t_{1/2}k_{e0}$ of remifentanil, the parameter used to characterize the delay between peak drug levels in the plasma (or blood) and peak drug effect, is similar to that of alfentanil as reported in several human volunteer studies, some using the EEG and others using an experimental pain method [10,15,17]. Figure 5 depicts the time required to reach peak effect site concentration (and therefore peak effect) after bolus administration of the fentanyl congeners. Like alfentanil, remifentanil

reaches peak effect site concentration within 1–2 min after bolus injection and then begins to decline [32]. This means that remifentanil can be regarded as a rapid-onset agent.

Special populations

Age

Advancing age has an important influence on the pharmacokinetics and pharmacodynamics of remifentanil [17]. The clearance and central distribution volume of remifentanil decline with age. Similarly, EC_{50}, the concentration necessary for 50% of maximal effect as measured by the EEG, also declines substantially with age. This means that remifentanil is significantly more potent in the elderly and that it is not cleared as quickly (the blood and effect site also equilibrate more slowly). These age-related changes translate into a 50%–70% dosage reduction in the elderly (i.e., patients over approximately 60 years of age) [33]. Figure 6 illustrates the change in potency as a patient ages.

Comparatively little is known about remifentanil in the pediatric population. However, the available data indicate that remifentanil is also a short-acting drug in children and newborns [34,35].

Weight

Body weight is another important factor in the formulation of remifentanil dosage regimens. Remifentanil pharmacokinetic parameters are more closely related to lean body mass than to total body weight [36]. In other words, patients who weigh more do not necessarily have a weight-proportional increase in metabolic capacity. This is consistent with the observation that over 90% of metabolic processes are thought to occur in lean tissue [37].

This means that obese patients, particularly morbidly obese patients, do not need to receive a higher dose (i.e., a weight-normalized dose). Remifentanil dosages should be calculated on the basis of lean body mass or ideal body weight and not total body weight. Truly obese patients who receive a total body weight-based dosage are more likely to suffer bradycardia, hypotension, and other adverse effects [36].

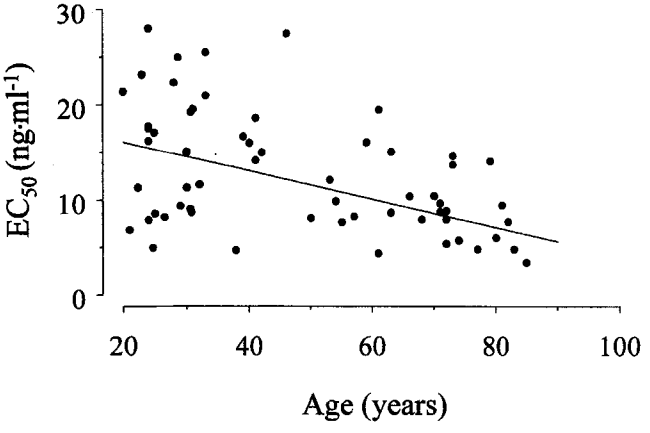

Fig. 6. Relationship of age and remifentanil potency as measured by the EEG. As with the other fentanyl congeners, as age increases the concentration required to achieve 50% of maximal brain depression (EC_{50}) on the EEG decreases (from [17], with permission)

Gender

Gender does not appear to have an important influence on the pharmacokinetics or pharmacodynamics of remifentanil. In a large, high-resolution study, Minto showed that neither the pharmacokinetic nor the pharmacodynamic parameters significantly changed with gender [33]. Remifentanil dosage regimens can therefore be formulated irrespective of the patient's gender.

Kidney function

The pharmacokinetics of remifentanil are not influenced by renal function. The pharmacokinetics of remifentanil administered by infusion for 4 h to renal dialysis patients have been compared to those in control subjects [38]. The pharmacokinetics of remifentanil in renal impairment are not appreciably different from those in normal subjects.

Because it is cleared by the kidney, concerns have been raised regarding the fate of the metabolite GI90291 in renal failure [2,39]. With a potency that is several orders of magnitude less than that of the parent compound, current evidence suggests that even though GI90291 may rise to levels that are 25 times those of remifentanil in the face of renal failure, it is unlikely to exert any pharmacodynamic activity [38].

Hepatic failure

Like renal failure, hepatic failure does not appear to alter the pharmacokinetics of remifentanil. The pharmacokinetic behavior of remifentanil in patients awaiting liver transplantation for end-stage liver disease has been investigated [40]. Remifentanil pharmacokinetics were unchanged by severe liver disease at doses up to 0.25 μg·kg^{-1}·min^{-1}. The findings of this study are bolstered by the observation that remifentanil clearance continues unchanged during the anhepatic phase of orthotopic liver transplantation [41]. Interestingly, patients with end-stage liver disease may be

pharmacodynamically more sensitive to remifentanil [40].

Pharmacogenetics

Because of the esterase-dependent metabolic pathway of remifentanil, questions regarding remifentanil metabolism in pseudocholinesterase-deficient patients inevitably arise. In vitro tests indicate that remifentanil is not a good substrate for butylcholinesterase (i.e., pseudocholinesterase) [11], suggesting that no dosage reduction will be necessary in patients with any subtype of pseudocholinesterase deficiency. When remifentanil is introduced in vitro into plasma harvested from pseudocholinesterase-deficient volunteers, its rate of metabolism is not different from that observed in the plasma of normal controls [42].

Some of the other fentanyl congeners are subject to pharmacokinetic alterations as a result of genetic aberrations in hepatic enzyme activity. For example, alfentanil metabolism may be predominantly, if not exclusively, by cytochrome P450 3A3/4 [43,44]. Cytochrome P450 3A3/4 is one of a family of cytochrome P450 isoenzymes that have distinct but overlapping substrate specificities [45]. This enzyme is known to display at least an eightfold difference in activity in humans. This may be why occasional patients are found to have a very low alfentanil clearance and a very prolonged effect from standard doses. To date, similar genetic abnormalities that alter remifentanil pharmacokinetics have not been encountered.

Clinical applications

Although it is still too early to predict with confidence what clinical niche remifentanil will ultimately occupy, remifentanil is obviously best suited for cases in which its responsive pharmacokinetic profile can be exploited. Remifentanil is perhaps best applied to cases in which rapid recovery is desirable, the anesthetic requirement rapidly fluctuates, opioid titration is unpredictable or difficult, there is a substantial danger to opioid overdose, or a "high-dose" opioid technique is advantageous but the patient is not going to be mechanically ventilated postoperatively.

In this context, one unique aspect of remifentanil is that its use mandates a change in the traditional pharmacologic ratios of "balanced anesthesia" [46]. Because it is so pharmacokinetically evanescent, remifentanil can be infused to a profound level of opioid effect and yet permit the return of spontaneous ventilation only a few minutes later. This means that it is possible to do a "high-dose" opioid technique, such as is commonly used for cardiac anesthesia (for any kind of case), without committing a patient to mechanical ventilation postoperatively.

In practical terms, the clinician must answer a few simple questions in deciding whether remifentanil might be appropriate for any given case: Is rapid recovery absolutely essential (e.g., neuroanesthesia, outpatient procedures)? Is the control of autonomic responses to noxious stimuli important and perhaps problematic with longer-acting opioids (e.g., patient with severe coronary artery disease for a brief outpatient procedure)? Will determination of the proper opioid dosage be difficult (e.g., children, elderly, hepatic disease patients)? Is there a substantial danger associated with opioid overdose (e.g., during fiberoptic intubation of the difficult airway)? When the answers to these questions are yes, remifentanil may be helpful.

General anesthesia

Remifentanil can be infused as a supplement to general anesthesia in combination with either inhaled vapor or intravenous sedative hypnotics, such as propofol. It has been used successfully for both inpatient and outpatient general anesthesia [47–49].

Interestingly, remifentanil in combination with propofol for anesthetic induction can reportedly produce adequate conditions for tracheal intubation without muscle relaxants [50]. Remifentanil at low doses has also been successfully used as a supplement to inhaled anesthetic without muscle relaxants in patients spontaneously ventilating through a laryngeal mask airway for outpatient surgery [51].

Remifentanil, like the other opioids, should not be regarded as a complete anesthetic. It is not suitable as a sole induction or maintenance agent [52].

Conscious sedation-analgesia

Remifentanil is also approved by the United States Food and Drug Administration as the analgesic component of conscious sedation during monitored anesthesia care. It can be infused in combination with propofol (by infusion) or midazolam (by bolus dosing) to provide relief of anxiety and pain during procedures in which local anesthetic is infiltrated at the site of the operation (or for procedures where no local anesthesia is necessary). It can also be infused as an adjunct to procedures performed under regional block [53].

For practical purposes, remifentanil should not be viewed as an appropriate single agent for monitored anesthesia care when significant sedation is desired. It is difficult to produce substantial sedation with remifentanil alone without producing significant respiratory

depression. Although remifentanil can be used alone, optimal conscious sedation and analgesia is more easily achieved with remifentanil in combination with a sedative-hypnotic such as propofol or midazolam [54,55].

Neuroanesthesia

Rapid emergence from anesthesia is a priority after neurosurgical procedures so that a neurologic assessment can take place before leaving the operating room. Remifentanil's short-acting pharmacokinetic profile can be exploited to promote a quick return of consciousness after neurosurgical procedures to allow for a neurological exam shortly after the surgeons have finished their work.

The effects of remifentanil on cerebral physiology appear to be similar to those of other fentanyl congeners, although they are shorter-lived [56]. When ventilation is controlled, remifentanil does not cause an increase in intracranial pressure when infused to patients undergoing craniotomy [57].

Remifentanil has been used successfully as an alternative to fentanyl as part of a balanced anesthetic technique for resection of supratentorial lesions. In a series of 63 adult craniotomy patients who were randomized to receive either remifentanil or fentanyl, remifentanil was thought to help promote a rapid emergence that did not require the administration of naloxone [58]. Remifentanil in combination with propofol has also been reported to provide excellent conditions for awake craniotomy [59].

Cardiac anesthesia

Comparatively little is known about the pharmacokinetics of remifentanil during cardiopulmonary bypass (CPB). For example, how much remifentanil is sequestered by the CPB circuit is unknown. It is clear, however, that remifentanil remains a very short-acting drug despite CPB [29]. During the hypothermic portion of CPB, the clearance of remifentanil decreases by about 20% and then returns to pre-bypass levels after rewarming [60].

Remifentanil has been used successfully as a means of promoting "fast-track" anesthesia (i.e., early extubation of the trachea) after CPB operations [61]. Although the preliminary indications have been promising, the results of ongoing work in this area will be required to establish the utility of remifentanil for cardiac anesthesia.

Pediatric anesthesia

Compared with the adult population, relatively little information is available regarding the clinical pharmacology and clinical use of remifentanil in pediatric patients. As noted earlier, it appears that the pharmacokinetics of remifentanil are not markedly different in children (including neonates) than in adults. Because it can be difficult to determine how much opioid will provide the analgesic component of anesthesia without preventing the return of spontaneous ventilation at the end of a pediatric procedure, some have suggested that remifentanil may be the ideal opioid for use in pediatric anesthesia [62].

Obstetric anesthesia

As might be expected for a recently approved drug, there is very little information available about remifentanil in obstetric anesthesia. Only one study has documented the apparent safety of intravenous infusion of remifentanil during cesarean section under epidural anesthesia [63]. The data from this study suggest that remifentanil readily crosses the placenta, with an umbilical vein to maternal artery ratio of 0.88. This study also indicates that remifentanil probably has a short duration of action in a neonate whose mother received the drug just before delivery, because the umbilical artery to umbilical vein ratio was only 0.29, suggesting that the fetus is metabolizing (or distributing) the drug rapidly. Another report proposes that remifentanil may be useful by infusion as an adjunctive analgesic for labor pain, such as during epidural catheter placement [64].

It is important to emphasize that remifentanil is not approved for obstetric anesthesia by the United States Food and Drug Administration. The effect of remifentanil on uterine blood flow and contractility is unknown. Whether or not neonates whose mothers received remifentanil in substantial doses just prior to delivery would be adversely affected by remifentanil is also relatively unexplored. These and other issues may require full examination before widespread use of remifentanil in parturients can be advocated.

Acute pain management

Remifentanil is also approved for the treatment of acute postoperative pain in the postanesthesia care unit and the intensive care unit. Several studies have demonstrated the efficacy of remifentanil for this indication. With a remifentanil infusion ongoing in the recovery room at rates ranging from about 0.05 to $0.1\,\mu g \cdot kg^{-1} \cdot min^{-1}$, a high proportion of patients rate their pain as either mild or absent after major surgery [65,66].

Making the transition from remifentanil intraoperatively to a longer-acting analgesic postoperatively is one of the unique aspects of using remifentanil. Because remifentanil is metabolized so rapidly, there is the possibility of a rapid decline in analgesia during emergence from anesthesia unless an analgesic infusion of remifentanil is maintained or unless the transition to another longer-acting analgesic is made prior to emergence [2,65]. Anesthesiologists are accustomed to switching from the intraoperative opioid (usually one of the fentanyl congeners) to the postoperative opioid (usually morphine or meperidine) in the postanesthesia care unit. With remifentanil, it is necessary to make this transition before the end of anesthesia (e.g., 100 μg of fentanyl about 15 min before the end of the operation or 5–10 mg of morphine about 30 min before the end of the operation).

Future applications

In the future, remifentanil may be used for a host of other applications, including some outside the operating room. For example, remifentanil may be useful by bolus injection to provide analgesia during short, painful diagnostic or therapeutic procedures, such as lumbar puncture, central venous catheterization, or wound dressing changes. It may also be useful by continuous infusion in the intensive care unit for the conscious sedation-analgesia of mechanically ventilated patients. In the chronic pain arena, remifentanil may be useful as a diagnostic tool in the ambulatory clinic in determining whether a patient with a complex chronic pain syndrome is responsive to opioid analgesics. These and other potential applications for remifentanil are currently under study.

Summary

Because it is still in its clinical infancy, it is difficult to predict with confidence exactly what role remifentanil will ultimately play in the delivery of anesthesia (and in other settings). It is clear, however, that remifentanil is a new pharmacologic tool with exciting potential that was not possible with the longer-acting opioids. On the basis of its familiar, fentanyl-like pharmacodynamic behavior and its short-acting pharmacokinetic profile, remifentanil may well be advantageous in a variety of settings in which profound opioid effect with subsequent rapid return of spontaneous ventilation and consciousness is desirable. Ongoing research and widespread clinical use will be required before the theoretical advantages associated with a short-acting opioid can be fully explored and confirmed.

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