SUMMARY

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Remifentanil is a fentanyl derivative with an ester linkage (3-[4-methoxycarbonyl-4-{(1-oxopropyl)phenylamino}-1-piperidine]propanoic acid, methylester). It is a pure μ agonist and the rapid breakdown of the ester linkage by non-specific tissue and plasma esterases is responsible for its unique characteristics.

The speed of onset of action of Remifentanil is similar to that of Alfentanil.

Remifentanil is extremely fat soluble with a steady-state volume of distribution of 25-40 L, total clearance 4.2-5 L/min. and terminal half-life (T½) 10-21 min. Clearance was not affected significantly by body weight, sex or age, and it is likely to be independent of renal or hepatic function. Furthermore, Remifentanil is a poor substance for butyrylcholinesterases (Pseudocholinesterases) in vitro and clearance should be unaffected by cholinesterase deficiency or administration of anticholinesterases.

The main metabolic product of ester hydrolysis is a carboxylic acid derivative (GI90291) which is mainly excreted unchanged by the kidney with a terminal half-life of 1.5-2 hs.

Although elimination of GI90291 is delayed in renal failure, significant pharmacological effects are unlikely as its potency relative to Remifentanil is only 0.1-0.3%.

Rapid biotransformation to minimally active metabolites should be associated with a short predictable duration of action with no accumulation of effect on repeated dosing or with continuous infusion. Because of its pharmacokinetics, similar properties were expected of Alfentanil. However, clinical experience has shown that prolonged infusion of Alfentanil may be associated with prolonged recovery time. It is now appreciated that the offset of the clinical effect is not simply a function of the half-life, particularly in the multicompartmental systems. It may be affected by rate of equilibration between plasma and effector site, method of administration (e.g. continuous infusion, intermittent boluses, . . . etc.) and duration of infusion.

Pharmacodynamically, Remifentanil possesses all the features of a Mu-receptor agonist. It produces analgesia and sedation. Also it shows all the complications associated with opioids such as respiratory depression, nausea and vomiting, bradycardia, hypotension, muscle rigidity and pruritus. It has an onset time of 1.1 min.

Significantly fewer patients who received Remifentanil responded to tracheal intubation, skin incision and surgery. Also during surgery, fewer patients receiving Remifentanil showed any responses compared to those receiving Alfentanil. However, the incidence of hypotension and bradycardia reported as adverse events was significantly commoner in the Remifentanil group. There was no difference in the time to return of spontaneous ventilation, adequate respiration, response to command and discharge from recovery room; time to extubation was shorter in the Remifentanil group. (The haemodynamic findings were broadly similar to those described in patients under abdominal hystrectomy.)

The adverse events that occurred perioperatively were typical of Mu-agonist drugs and the overall incidence was similar in both groups, but the occurrence of apnea and muscle rigidity were significantly higher in patients who received Remifentanil.

It has been confirmed that the effects of Remifentanil are anatgonized by Naloxone. Its potency is similar to that of Fentanyl, and 15-30 times that of Alfentanil.