

## Anaesthesia with remifentanil infusion in diabetic versus non-diabetic patients undergoing vitrectomy. A Holter-controlled study

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**Summary :** Diabetic patients are known to have additional risks in surgery. We evaluated haemodynamic profiles, incidence of arrhythmias and post-operative recovery when remifentanil infusion was used for vitrectomies. We compared 22 diabetics with 22 age-matched controls undergoing vitrectomy. ECG Holter monitoring was continued throughout the operation and until 20 hours postoperatively. Autonomic tests including breathing and stand up were performed in the beginning of Holter-monitoring. Anaesthesia was induced with a bolus of remifentanil (1 µg/kg) and continued with 0.4 µg/kg/h. Thereafter, propofol, 0.5 mg/kg, was given with additional doses of 0.25 mg/kg if needed. Anaesthesia was maintained with 40% oxygen in air and 0.5% isoflurane. After the operation time to obey commands, pain scores, nausea and vomiting, and haemodynamic parameters were registered. Both breathing and stand up tests differed statistically between the groups ( $p = 0.001$  and  $p = 0.000$ , respectively). Diabetic patients needed less remifentanil ( $p = 0.039$ ) than controls. Hypotensive periods were more frequent in diabetic patients ( $p = 0.013$ ) and they needed more etilefrine than controls ( $p = 0.014$ ). Holter recordings revealed no ischaemic episodes in either group. Periods of short ventricular and supraventricular extra beats occurred without any clinical relevance in both groups. Time to obey commands or need for pain medicine postoperatively did not differ between the groups. Diabetic patients were haemodynamically more instable with more frequent hypotensive periods during anaesthesia despite of less amount of remifentanil compared to controls. On the other hand, during remifentanil infusion no ischaemic or clinically significant arrhythmic episodes occurred in either group.

**Key words :** Analgesics opioid : remifentanil ; Complications : diabetes mellitus.

Most of the patients undergoing vitrectomy are diabetics which are known to be at increased risk of perioperative mortality and morbidity (5). Diabetics are four-to five times as likely to have coronary heart disease than non-diabetics (1). In addition, neuropathic and renal complications of diabetes mellitus may affect the outcome from surgery due to increased incidence of arrhythmias, sudden death and renal failure (6, 9). In these

patients smooth and stressfree anaesthesia is essential. On the other hand, postoperative period after vitrectomy is not painful, and therefore an ultra short-acting opioid, remifentanil, would be ideal for this type of surgery. No studies exist about the use of remifentanil-infusion in diabetic compared to non-diabetic patients. Using perioperative Holter-monitoring we studied the effect of remifentanil infusion on haemodynamics, arrhythmias, ischaemic episodes and postoperative recovery in diabetic vs non-diabetic patients undergoing vitrectomies. We tested the hypothesis that remifentanil-infusion is suitable to be used in diabetics as well as healthy controls undergoing vitrectomies.

### METHODS

After institutional ethics approval and informed patient consent, 22 diabetics and 22 age-matched (ASA I-II) controls undergoing vitrectomy were recruited for the study. Holter recording (Daltex Biomedical™) of ECG was started the evening before surgery and continued 20 hours postoperatively. Recordings were analyzed by the blinded physician in the Department of Clinical Physiology with special regard to the occurrence of arrhythmias and ischaemic attacks. Autonomic tests including breathing and stand up were performed before Holter monitoring was started.

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Patients were given oxazepam, 15 to 30 mg, and paracetamol 1 g, for premedication. In the beginning of anaesthetic induction glycopyrrolate, 0.005 mg/kg i.v., was given to prevent oculocardiac reflex. Remifentanyl 1 µg/kg, was given and an infusion of 0.4 µg/kg was started. One minute after the administration of remifentanyl, propofol 0.5 mg/kg was given with additional doses of 0.25 mg/kg every 30 sec until the eyelashreflex had disappeared. Rocuronium, 0.6 mg/kg was used as muscle relaxant. Anaesthesia was continued with 40% O<sub>2</sub> in air and isoflurane 0.5%. During the anaesthesia remifentanyl-infusion was adjusted to maintain mean arterial pressure (MAP) > 60 mmHg.

We monitored ECG, non-invasive blood pressure, pulse oxymetry, end-tidal CO<sub>2</sub> and end-tidal isoflurane concentrations (Capnograph™, Datex, Finland). We also recorded "light anaesthesia" periods when MAP was > 15 mmHg or heart rate was > 20% over the baseline. A bolus of 0.5 µg/kg of remifentanyl was then given and the infusion was increased in steps of 0.2 µg/kg every five min. "Deep anaesthesia" periods were defined as MAP < 60 mmHg. The infusion was then decreased by 0.2 µg/kg. Etilefrine 2-3 mg was given if MAP did not increase over 60 after 5 min.

Postoperatively the episodes of nausea and vomiting were recorded. Patients were given ondansetron, 4 mg, i.v. twice if needed. In addition, droperidol 0.75 mg/kg was administered in case of prolonged vomiting. Patients were given oxycodone, 0.06 mg/kg i.v. for additional pain relief if needed.

In statistical analyses we used General Linear Model for repeated measurements, t-test, Chi-square and Mann-Whitney U-test when appropriate. A p-value < 0.05 was considered significant.

## RESULTS

The mean age of diabetics was 50 (SD 14) yr and 53 (10) yr of controls. The mean duration of diabetes was 23 (11) years. All diabetic patients had already organ complications. The median for the incidence of organ complication was 2.2 (range 1-4). The results from the autonomic tests are shown in Table I. Based on these tests only four diabetics did not show evidence of autonomic neuropathy.

Heart rate and MAP did not differ between the groups during induction of anaesthesia. Diabetics needed less remifentanyl during the operation than non-diabetics when steady state infusion rates were compared (Table I). Hypotensive periods occurred

Table I

Results from autonomic tests and the use of remifentanyl and etilefrine during surgery. Also hypotensive periods and time to obey commands are shown. Results are given as mean (SD) or range

	Diabetics	Controls	p-value
Breathing (beats)	12 (9)	23 (8)	0.001
Stand-up (beats)	17 (7)	30 (9)	0.000
Remifentanyl (µg/kg)	0.29 (0.075)	0.35 (0.075)	0.039
Hypotensive periods (n)	2.0 (0-5)	0.86 (0-3)	0.013
Etilefrine (mg)	1.3 (1.5)	0.32 (0.57)	0.014
Time to obey commands (min)	8 (5)	8 (4)	ns

more often in diabetic than in control patients and they also needed more etilefrine (Table I). Immediate recovery from the anaesthesia did not differ between the groups (Table I). Diabetics tended to require more antiemetics than controls ( $p = 0.052$ ). No difference was observed in pain scores postoperatively. The need for pain medicine did not differ between the groups either. No patient had any recall when asked on the first day after surgery.

Holter recordings were technically acceptable in 20 diabetics and 18 controls. No ischaemic episodes were observed in either group. Episodes of short ventricular and supraventricular extra beats without any clinical relevance were observed in both groups. Diabetic patients tended to have higher mean heart rates throughout the study than controls, possibly due to autonomic neuropathy, but it did not reach statistical significance.

## DISCUSSION

Our study showed that diabetics are more prone to the hypotensive effects of remifentanyl infusion than control patients undergoing vitrectomies. Holter recordings revealed no ischaemic episodes or clinically meaningful arrhythmias in either group. All patients recovered quickly and were soon well orientated after the remifentanyl-infusion was stopped.

The haemodynamic effects of remifentanyl are mild bradycardia and a decrease of 15-20% in arterial blood pressure (2). In addition, remifentanyl has been shown to cause more hypotension than alfentanil (8) or fentanyl (7). Autonomic neuropathia has been suggested to be the cause of haemodynamic instability in diabetics (9) which may explain the results seen in this study. It is also known, that diabetic patients having suffered from diabetes over

twenty years often have hypertension which may have produced haemodynamic instability as well when a potent and fast acting opioid was used. On the other hand, no differences in haemodynamics was seen during and after induction of anaesthesia, which confirms the finding of KEYL and colleagues that autonomic neuropathy does not necessarily cause haemodynamic instability (4). Although hypotensive episodes occurred more frequently, no ischaemic episodes during Holter monitoring were observed suggesting that remifentanil-infusion could be used in diabetics as well.

We did not use bispectral index monitoring (BIS). The use of BIS is unreliable and inconvenient in ophthalmologic surgery, because the surgeon is leaning on the forehead while operating.

Remifentanil has been shown to be a suitable drug also in renal failure (3). The pharmacokinetics and pharmacodynamics of remifentanil are not altered in patients suffering from renal failure (3). This is an advantage for diabetic patients who often develop renal failure. In our study, immediate recovery was not delayed in diabetics compared to controls and all patients were responding adequately and quickly after the infusion was stopped. Vitrectomy is not a painful operation and additional pain medicine were not often needed postoperatively. Therefore, remifentanil seems to be an ideal opioid to be used in ophthalmologic operations.

Our study showed that diabetic patients are more sensitive to the opioid effects of remifentanil needing less amount of remifentanil and having slightly more hypotensive periods during anaesthesia than healthy controls. Recovery was not delayed

in diabetics and Holter-recordings did not reveal ischaemia or clinically meaningful arrhythmias. Remifentanil seems to be a suitable anaesthetic for ophthalmologic surgery but less amount of remifentanil should perhaps be used when diabetic patients are anaesthetized.

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