Brief Reports

Total intravenous anesthesia with remifentanil, propofol and cisatracurium in end-stage renal failure

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Purpose: To compare recovery parameters of total intravenous anesthesia (TIVA) with remifentanil and propofol, hemodynamic responses to perioperative events, and pharmacodynamic parameters of cisatracurium in 22 end-stage renal failure and 22 normal renal function patients.

Methods: Anesthesia was induced with 2-3 $mg \cdot kg^{-1}$ propofol and 1 $\mu g \cdot kg^{-1}$ remifentanil and maintained with 75 $\mu g \cdot kg^{-1} \cdot min^{-1}$ propofol and propofol initial infusion of 0.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$ propofol. Arterial pressure and heart rate were maintained by remifentanil infusion rate adjustments. The first twitch (T1) was maintained at 25% by an infusion of cisatracurium.

Results: There was no difference in the time to maintenance of adequate respiration, date of birth recollection, first analgesic administration, between the renal failure (4.8 ± 2.5, 7.8 ± 3.2, 12.3 ± 5.3 min respectively) and the control group (5.2 ± 2.8, 8.1 ± 3.1, 12.7 ± 5.5 min): nor were there any differences in the time to 25% T1 recovery, T1 recovery from 25% to 75%, or cisatracurium infusion rate between the renal failure group (32.1 ± 10.8 min, 18.2 ± 5.5 min, 0.89 ± 0.29 $\mu g \cdot kg^{-1} \cdot min^{-1}$ respectively) and the control group (35.9 (7.9 min, 18.4 ± 3.8 min, 0.95 ± 0.22 $\mu g \cdot kg^{-1} \cdot min^{-1}$).

Conclusion: End-stage renal failure does not prolong recovery from TIVA with remifentanil and propofol, or the recovery from cisatracurium neuromuscular block.

Objectif : Comparer les paramètres de la récupération après une anesthésie exclusivement intraveineuse (AEI) avec du rémifentanil et du propofol, les réponses hémodynamiques aux circonstances périopératoires et les paramètres pharmacodynamiques du cisatracurium chez 22 patients au stade d'insuffisance rénale terminale (SIRT) et chez 22 patients sans problème rénal.

Méthode : L'anesthésie a été induite avec 2-3 $mg \cdot kg^{-1}$ de propofol et 1 $\mu g \cdot kg^{-1}$ de rémifentanil et maintenue avec 75 $\mu g \cdot kg^{-1} \cdot min^{-1}$ de propofol et une perfusion initiale de 0,2 $\mu g \cdot kg^{-1} \cdot min^{-1}$ de propofol. La tension artérielle et la fréquence cardiaque ont été maintenues par des ajustements de la vitesse de perfusion de rémifentanil. La première stimulation musculaire (twitch T_1) a été maintenue à 25 % par une perfusion de cisatracurium.

Résultats : Aucune différence n'a été notée, quant au temps nécessaire au maintien d'une respiration adéquate, au rappel de sa date de naissance et à l'administration d'un premier analgésique, entre les groupes SIRT (4,8 ± 2,5; 7,8 ± 3,2; 12,3 ± 5,3 min respectivement) et témoin (5,2 ± 2,8; 8,1 ± 3,1; 12,7 ± 5,5 min). Également, aucune différence de temps nécessaire à la récupération d'un T_1 à 25 %, d'un T_1 de 25 % à 75 %, ou de vitesse de perfusion du cisatracurium, entre les groupes SIRT (32,1 ± 10,8 min; 18,2 ± 5,5 min; 0,89 ± 0,29 $\mu g \cdot kg^{-1} \cdot min^{-1}$ respectivement) et témoin (35,9 ± 7,9 min; 18,4 ± 3,8 min; 0,95 ± 0,22 $\mu g \cdot kg^{-1} \cdot min^{-1}$).

Conclusion : Le stade d'insuffisance rénale terminale ne prolonge pas la récupération après l'AEI avec du rémifentanil et du propofol ou la récupération après un blocage neuromusculaire avec du cisatracurium.

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Accepted for publication April 11, 1999

PATIENTS with end-stage renal failure require anesthesia for an increasing number of surgical procedures. An ideal total intravenous anesthesia (TIVA) would comprise drugs independent of renal function, such as remifentanil and cisatracurium. The purpose of this study was to compare the recovery parameters from TIVA with remifentanil and propofol, the hemodynamic responses to perioperative events, and the pharmacodynamic parameters of cisatracurium in 22 end-stage renal failure patients with those in a control group.

Methods

Patients

The study was approved by Karl-Franzens University Ethics Committee. Patients who agreed to participate in the study gave written informed consent, were 20-59 yr old and within ±20% ideal body weight. The renal failure group consisted of 22 patients with end-stage renal disease undergoing the creation of end-to-side arteriovenous fistulas in the arm. An equal number of patients with normal renal function, ASA I-II, undergoing elective surgical procedures in the upper extremities, served as a control group. All renal failure patients had undergone hemodialysis within 24 hr prior to operation and were receiving human recombinant erythropoietin (rh-Epo) therapy.

Anesthetic technique and neuromuscular monitoring

Anesthesia was induced with 2-3 $mg \cdot kg^{-1}$ propofol, followed by 1 $\mu g \cdot kg^{-1}$ remifentanil. Based on effective anesthesia in previous studies,[1,2] anesthesia was maintained with 75 $\mu g \cdot kg^{-1} \cdot min^{-1}$ propofol by infusion and remifentanil initial infusion of 0.2 $\mu g \cdot kg^{-1} \cdot min^{-1}$.

Neuromuscular function of the adductor pollicis muscle was monitored using the Relaxometer® mechanomyograph (Groningen University Holland). The ulnar nerve was stimulated supramaximally at the wrist with train-of-four (TOF) stimuli (2 Hz for 2 sec) at 12-sec intervals. Intubation of the trachea was attempted 180 sec after 0.1 $mg \cdot kg^{-1}$ ($2 \times ED_{95}$) cisatracurium, and was graded as; excellent, good or poor.[3] From the beginning of cisatracurium administration, the onset time (time to the first twitch, T1, 100% depression) or time to maximum T1 depression and Dur_{25} (time until 25% T1 recovery) were recorded.

Remifentanil infusion rate was adjusted by ±0.02 $\mu g \cdot kg^{-1} \cdot min^{-1}$ once every three minutes if systolic arterial pressure (SAP) or heart rate (HR) changed >15% from baseline (average of measurements obtained on the day before surgery, within two hours and before induction of anesthesia). Rescue protocols for light anesthesia (lacrimation, mydriasis, sweating or grimacing), or hypotension not controlled by two successive remifentanil infusion rate reductions, consisted of 50 mg propofol or 10 mg ephedrine *iv* respectively.

Following T1 recovery to 25%, if relaxation was required for mechanical ventilation, an initial infusion of 0.75 $\mu g \cdot kg^{-1} \cdot min^{-1}$ cisatracurium was started. The T1 was maintained at 25% by 3-min adjustments of ±0.075 $\mu g \cdot kg^{-1} \cdot min^{-1}$. Twenty minutes before the anticipated end of surgery, cisatracurium infusion was stopped, and recovery $interval_{25-75}$ (time of T1 recovery from 25% to 75%) was recorded. At the end of the operation, if TOF ratio was < 0.8, residual neuromuscular block was antagonized. Remifentanil and propofol infusions were stopped, and this was taken as the start of calculation of

TABLE I Patient demographics and preoperative blood investigations. Means ± SD.

	Control Group *n* =22	*Renal Failure Group* *n* =22
Age (yr) [range]	50.86 ± 12.1 (22-59)	53.09 ± 14.7 (27-59)
Weight (kg) [range]	73.5 ± 16.3 (56-85)	67.85 ± 11.2 (55-82)
Male/Female	10/12	13/9
Operation duration (min)	75.1 ± 37.94	83.6 ± 35.46
Creatinine ($\mu mol \cdot l^{-1}$)	97.35 ± 8.85	557.52 ± 41.59
Urea ($mmol \cdot l^{-1}$)	6.01 ± 0.24	22.16 ± 1.52
Hemoglobin $\mu g \cdot dl^{-1}$)	14.3 ± 0.47	11.0 ± 0.21
Potassium ($mmol \cdot l^{-1}$)	4.2 ± 0.11	4.9 ± 0.15

TABLE II TIVA recovery parameters and cisatracurium pharmacodynamics. Means ± SD.

Time (min) to:	*Control Group* *n* =22	*Renal Failure Group* *n* =22	*P*
Spontaneous respiration	4.2 ± 3.1	3.7 ± 2.5	0.15
Adequate respiration	5.2 ± 2.8	4.8 ± 2.5	0.20
Open the eyes	4.8 ± 3	4.7 ± 2.5	0.86
Lift the arm	5.7 ± 3.2	5.6 ± 2.8	0.75
Extubation	6.2 ± 3	5.6 ± 2.3	0.49
Date of birth recollection	8.1 ± 3.1	7.8 ± 3.2	0.40
Discharge to PACU	9.7 ± 4.1	9 ± 3.2	0.17
First analgesic	12.7 ± 5.5	12.3 ± 5.3	0.82
Onset time	6 ± 2.3 (*n* =19)	7.3 ± 1.8 (*n* =18)	0.04
Dur_{25}	35.9 ± 7.9	32.1 ± 10.8	0.20
RI_{25-75}	18.4 ± 3.8	18.2 ± 5.5	0.92

Adequate respiration: respiratory rate ≥ 8 bpm or $P_{ET}CO_2$ < 45 mm Hg.

Response to verbal command: open the eyes, lift the arm and date of birth recollection.

PACU: post anesthesia care unit.

Onset time: time to 100% T1 depression

Dur_{25}: time until 25% T1 recovery.

RI_{25-75}: time of T1 recovery from 25% to 75%.

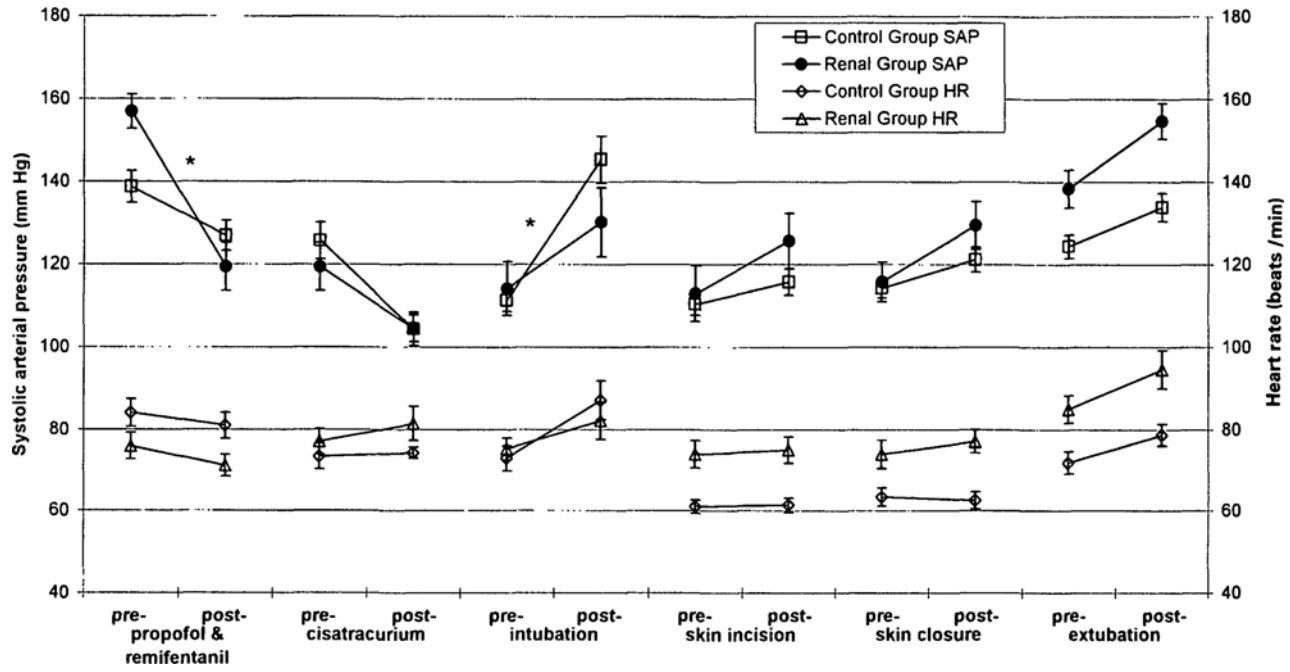

FIGURE 1 Systolic arterial pressure and heart rate at specified perioperative events.

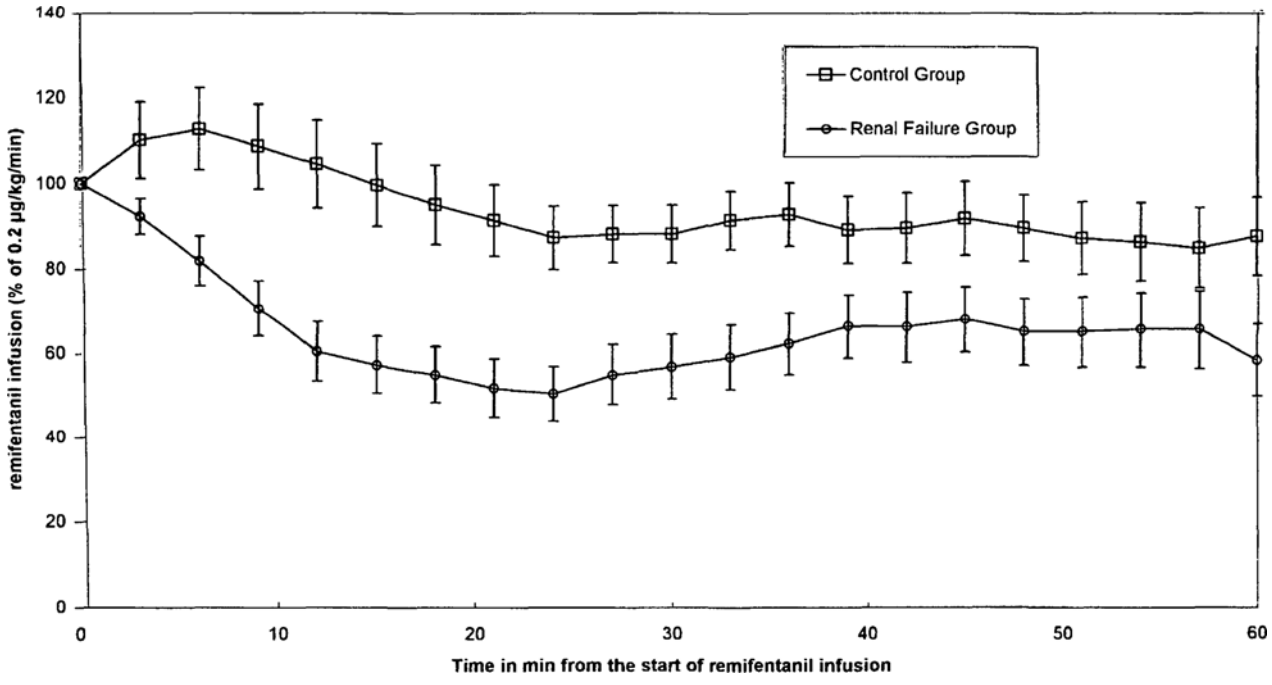

FIGURE 2 Remifentanil infusion rate expressed as percentage of initial rate.

all recovery parameters. At the first occurrence of discomfort or pain, patients were given 0.25 mg·kg^{-1} piritramid *iv*.

Statistical analysis

The paired t test was used for parametric data analysis and Mann-Whitney U test for non-parametric data. Repeated measures ANOVA was used for SAP and HR analysis. Data were expressed as means ±SD. P values < 0.05 were considered statistically significant.

Results

The two groups were comparable with respect to age, weight, sex and duration of operation. The blood investigations in the renal failure group were typical of patients undergoing regular dialysis (Table I).

Hemodynamic responses are presented in Figure 1. Remifentanil infusion rate was lower in the renal failure group (0.13 ± 0.05 μg·kg^{-1}·min^{-1}), than in the control group (0.19 ± 0.07 μg·kg^{-1}·min^{-1}) (Figure 2).

Recovery parameters for TIVA and cisatracurium pharmacodynamics are presented in Table II. There was no difference in the number of propofol rescue interventions per hour between the two groups. When assessed on the first postoperative day, no incidents of dreaming, awareness or recollection of the intraoperative period were reported by any of the patients.

There was no difference in intubation conditions between the renal failure group (9 excellent, 10 good and 3 poor) compared with the control group (12 excellent, 7 good and 3 poor) and there was no difference between the infusion rate of cisatracurium in the renal failure group (0.89 ± 0.29 μg·kg^{-1}·min^{-1}, n =11) and the control group (0.95 ± 0.22 μg·kg^{-1}·min^{-1}, n =13).

Discussion

In the renal failure group, the decrease in the SAP and DAP following propofol and remifentanil administration, and the number of ephedrine rescue interventions (1.05 ± 1.4 hr^{-1}) were greater than in the control group (0.13 ± 0.4 hr^{-1}) perhaps because end-stage renal failure patients appear to have an impaired compensatory vasoconstrictor responses as well as vascular volume depletion following recent dialysis.[4,5]

The increase in the SAP and DAP in response to intubation, skin incision and skin closure in both groups suggests that, the infusion rate of remifentanil used in our study, combined with 75 μg·kg^{-1}·min^{-1} propofol, were less than that required for the complete abolition of all intraoperative responses.[2,6]

The renal failure patients were all undergoing rh-Epo therapy, leading to correction of their anemia and probably improvement of their cognitive functions.[7] Although these patients are perhaps not typical end-stage renal failure patients, remifentanil did not appear to have any detrimental effect on recovery of their cognitive functions or their resumption of adequate respiration.[8]

Renal failure is often associated with generalised muscle fatigability, chronic metabolic acidosis and electrolyte disturbances.[9] This had no apparent effect on the behaviour of cisatracurium in the renal failure patients. However, the prolongation of the onset time could be a result of the lowering of the cardiac output in the sicker renal failure group following induction of anesthesia.[10]

In conclusion, end-stage renal failure and its associated biochemical and physiological changes do not prolong the recovery from TIVA with remifentanil and propofol, or the recovery from cisatracurium neuromuscular block.

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