Obstetrical and Pediatric Anesthesia

Remifentanil induces consistent and sustained controlled hypotension in children during middle ear surgery

[Le rémifentanil induit de l'hypotension constante et prolongée chez des enfants pendant une opération de l'oreille moyenne]

Christian S. Degoute MD PhD,* Marie J. Ray MD,* Pierre Y. Gueugniaud MD PhD,* Christian Dubreuil MD†

Purpose: To determine in children whether remifentanil combined with sevoflurane, could induce controlled hypotension, reduce middle ear blood flow (MEBF) measured by laser-Doppler, and provide a satisfactory operative field.

Methods: Forty children undergoing middle ear surgery and anesthetized with sevoflurane were randomly assigned to receive either 1 $\mu g \cdot kg^{-1}$ remifentanil *iv* followed by a continuous infusion of 0.2 to 0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$ or 0.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$ nitroprusside *iv* and alfentanil *iv* ($n = 20$ in each group).

Results: Controlled hypotension was achieved at the target mean arterial pressure (MAP) of 50 mmHg ($P < 0.01$) within 121 ± 21 and 62 ± 9 sec for remifentanil and nitroprusside respectively. MEBF decreased by 22 ± 4 and 20 ± 6% and preceded the decrease in MAP within 20 ± 7 and 10 ± 3 sec for remifentanil and nitroprusside respectively. Remifentanil, and nitroprusside decreased MEBF autoregulation (0.41 ± 0.2 and 0.37 ± 0.3 respectively). Controlled hypotension was sustained in both groups throughout surgery, and the surgical field rating was good. Nitroprusside increased $PaCO_2$ slightly, and there were no postoperative circulatory, neurological or metabolic complications in any of the groups.

Conclusion: Remifentanil combined with sevoflurane in children enabled controlled hypotension, reduced MEBF and provided good surgical conditions for middle ear surgery with no need for additional use of a specific hypotensive agent.

Objectif : *Déterminer si le rémifentanil, combiné au sévoflurane, peut permettre une hypotension contrôlée, une réduction du débit sanguin de l'oreille moyenne (DSOM) mesuré par Doppler à laser, et assurer un champ opératoire exsangue chez l'enfant.*

Méthode : *Quarante enfants opérés à l'oreille moyenne et anesthésiés par du sévoflurane, ont été répartis par randomisation en deux groupes ($n = 20$) recevant soit 1 $\mu g\ kg^{-1}$ de rémifentanil iv suivi d'une perfusion continue de 0,2 à 0,5 $\mu g\ kg^{-1}\ min^{-1}$, soit 0,25 $\mu g\ kg^{-1}\ min^{-1}$ de nitroprussiate iv, associé à de l'alfentanil iv.*

Résultats : *Tout d'abord, l'hypotension contrôlée a été obtenue au niveau souhaité de 50 mmHg ($P < 0,001$) en 121 ± 21 et 62 ± 9 sec pour le rémifentanil et le nitroprussiate respectivement. Le DSOM a diminué de 22 ± 4 et de 20 ± 6 % et a précédé la chute de pression de 20 ± 7 et de 10 ± 3 sec pour le rémifentanil et le nitroprussiate respectivement. Le rémifentanil et le nitroprussiate ont diminué l'autorégulation (0,41 ± 0,2 et 0,37 ± 0,3). Ensuite, l'hypotension contrôlée a été maintenue dans les deux groupes tout au long de l'opération, et l'état du champ opératoire a été excellent. Le nitroprussiate a augmenté modérément la $PaCO_2$. Il n'y a eu aucune complication circulatoire, neurologique ou métabolique postopératoire dans chacun des groupes.*

Conclusion : *Le rémifentanil associé au sévoflurane chez l'enfant a permis de réaliser une hypotension contrôlée, de réduire le débit sanguin de l'oreille moyenne et d'assurer de bonnes conditions opératoires pour l'opération de l'oreille moyenne sans recourir à un hypotenseur spécifique.*

From the Department of Anesthesiology,* and ENT Surgery,† Centre Hospitalo- Universitaire Lyon-Sud, France.

Address correspondence to: Dr. Christian S. Degoute, Secrétariat de consultation d'anesthésie CHU de Pointe-à-Pitre/Abymes, 97159 Pointe-à-Pitre cedex, France. Phone: 33 0590 89 13 44; Fax: 33 0590 89 17 90; E-mail: christian.degoute@wanadoo.fr

This study was sponsored by departmental funds only. It was presented in part at the Annual Meeting of the French Society of Anesthesiology, Paris, September 2002.

Accepted for publication September 26, 2002.

Revision accepted November 11, 2002.

CONTROLLED hypotension is commonly used as a means of limiting intraoperative blood losses or avoiding the need for homologous blood transfusions; it is also used to achieve a bloodless operative field which is needed for successful middle ear microsurgery.[1] Several different agents have been used in children to provide controlled hypotension including direct acting vasodilators (sodium nitroprusside,[2] nitroglycerin,[3] prostaglandin E_1,[4] nicardipine,[5,6] fenoldopam),[7] or inhalational agents (sevoflurane).[8] Some adverse effects have been reported for these techniques including resistance to vasodilators,[9] tachyphylaxis,[10] cyanide toxicity for nitroprusside,[2] long postanesthetic recovery for halothane,[11] renal tubular function disturbance for sevoflurane;[12] these adverse effects incite authors to seek a new agent which would correspond to the ideal agent for controlled hypotension, i.e., easy to administer, with a fast onset, with a rapid elimination, without toxicity, with a predictable and dose dependant effect. Recently, remifentanil, an ultrashort-acting μ-agonist opioid receptor, has demonstrated its ability in inducing controlled hypotension and in achieving a bloodless operative field with no need for additional potent hypotensive agents and with no described adverse effects in adults when combined with propofol.[13] Since remifentanil was authorized in children and we have replaced alfentanil by remifentanil in our clinical practice, we noted that its hypotensive effect led us to stop the use of nitroprusside or nicardipine for controlled hypotension. The hypotensive effect of remifentanil for intraoperative controlled hypotension in children remains unclear.

Accordingly, the current study was designed: a) to determine whether remifentanil with sevoflurane anesthesia can induce controlled hypotension to a target mean arterial pressure (MAP) of 50 mmHg; b) to determine whether remifentanil-induced hypotension is accompanied by a reduction in middle ear blood flow (MEBF) measured by laser-Doppler; and c) to evaluate its effect on the quality of the operative field in children undergoing middle ear surgery. Concomitantly, the expected effects of sodium nitroprusside combined with alfentanil were studied. This article presents the results of a pilot study designed to show how controlled hypotension can be obtained using remifentanil and avoiding nitroprusside during middle ear surgery in children.

Methods

Patients

From May 2001 to February 2002, 40 ASA physical status I children undergoing middle ear surgery for chronic otitis media were studied. After adequate information was provided and after the child's assent (for older children) was obtained, parents signed consent forms approved by the Institution's Human Research Review Committee. Children were randomly assigned by blocks of five in two groups. Twenty children, 8.4 ± 3.2 yr undergoing middle ear surgical repair not exceeding one hour for chronic otitis media that had provoked cholesteatoma and tympanic membrane perforation, received remifentanil as the primary drug for inducing hypotension along with sevoflurane anesthesia. During the same period, 20 children, 9 ± 4.1 yr, undergoing middle ear surgical repair (54 ± 5 min of duration) for the same indication received sodium nitroprusside and alfentanil instead of remifentanil.

All children were admitted on the day before surgery and fasted for at least five hours prior to surgery. All children received an oral medication for sedation (1 $mg \cdot kg^{-1}$ hydroxyzine) one hour before anesthesia. All children received 20 $mg \cdot kg^{-1}$ propacetamol *iv* intraoperatively for postoperative analgesia and received 0.2 $mg \cdot kg^{-1}$ nalbuphine postoperatively according to verbal or visual analogue scale. Children were instrumented and studied while supine. The study was performed in two parts: in the first, hypotension and MEBF were investigated when no surgical stress was applied. In the second, hypotension and surgical field were investigated during surgery.

Hemodynamic variables

After induction of sevoflurane anesthesia, a 24-gauge catheter was inserted into a radial artery for direct determination of arterial blood pressure (mean, MAP) and heart rate (HR), which were recorded continuously. The arterial cannula allowed serial blood gas determinations. Functionality of the palmar arch of the hand had been verified with Doppler ultrasound prior to radial artery cannulation.[14] A 24-gauge catheter was inserted into a forearm vein for fluid and drug administration.

Metabolic variables

Arterial blood samples enabled us to determine changes in partial pressures of oxygen (PaO_2) and carbon dioxide ($PaCO_2$), pH and lactate concentration. Arterial blood lactate concentration was determined by an enzymatic method using the oxidation of lactate to pyruvate (DuPont Instruments Aca SX, Wilmington, Delaware, USA) which gave a coefficient of variation of 5.6% at 1.79 $\mu mol \cdot L^{-1}$ and 1.3% at 13.1 $\mu mol \cdot L^{-1}$. Samples were taken at control (see further) and every 15 min until 20 min after end of surgery in the recovery room.

MEBF changes

MEBF changes, measured by a validated laser-Doppler flowmetry method,[8,15] were continuously recorded by a commercially available laser-Doppler instrument (Periflux PF3, Perimed KB, Sweden). The optic fibre is inserted through the tympanic perforation and is put in place by the surgeon on the mucosa of the promontorium cavi tympani. The MEBF was calibrated before the study so that a true zero indicated that the flux was null. MEBF and arterial blood pressure were recorded continuously and simultaneously. The relative changes in MEBF (MEBF) and in MAP from their respective baselines were considered for statistical analysis. The MEBF autoregulatory responses to controlled hypotension were quantified by the closed-loop gain factor of autoregulation (Ga) calculated from the equation Ga = 1- (%MEBF/ %MAP). A Ga value of 1 implies perfect flow autoregulation, Ga > 1 indicates excessive, and Ga close to 0 indicates impaired autoregulation. When Ga = 0, autoregulation is abolished and MEBF follows MAP passively.[16]

Quality of the surgical field and blinding

The quality of the surgical field, in terms of blood loss and dryness, was rated every ten minutes by the attending surgeon who was unaware of the pharmacological procedure and treatments, using a six-point scale (0 = no bleeding, virtually bloodless field; 5 = uncontrolled bleeding).[17] The anesthesiologist administering the drugs was unblinded to the specific agent being used.

Anesthesia

Anesthesia was induced and maintained with sevoflurane in all cases. Children breathed through a face mask connected to a semi-closed anesthetic circuit. Fresh gas flow into the anesthetic circuit was 6 $L \cdot min^{-1}$.[18] The concentrations of carbon dioxide, sevoflurane and oxygen were measured using an infrared anesthetic gas analyzer (Capnomac, Helsinki, Finland), which was calibrated before anesthesia for each patient using a standard gas mixture. Anesthesia was induced with 4% sevoflurane in oxygen until loss of consciousness and loss of movement, and anesthesia was maintained by inspired concentrations of sevoflurane adjusted to obtain sevoflurane end-tidal concentrations near 2%. A laryngeal mask allowed controlled ventilation which was adjusted to an end-tidal CO_2 concentration of 35 mmHg and to ensure SpO_2 over 97% with 65% air in oxygen. Children assigned to receive sodium nitroprusside received 25 $\mu g \cdot kg^{-1}$ alfentanil *iv* followed by a constant infusion of 0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$.

Procedures

After induction of anesthesia and insertion of a laryngeal mask were performed, the laser-Doppler optic fibre was inserted. A five-minute rest period was observed and was followed by a two-minute period of hemodynamic measurements and blood sampling for blood gas analysis (control). Then, at T_0 children underwent the treatment protocol. Drugs were delivered in order to induce controlled hypotension, which was considered effective when MAP reached the target pressure of 50 mmHg. Infusion rate was adapted in order to maintain hypotension.

Children assigned to the remifentanil group (R) received 1 $\mu g \cdot kg^{-1}$ remifentanil *iv* in 30–60 sec, followed by a continuous infusion of 0.20 to 0.50 $\mu g \cdot kg^{-1} \cdot min^{-1}$ until MAP was 50 mmHg, then the infusion rate was adapted to maintain hypotension at this level. Children assigned to the sodium nitroprusside group (N) received a continuous *iv* infusion of sodium nitroprusside at a rate of 0.25 $\mu g \cdot kg^{-1} \cdot min^{-1}$ until MAP was 50 mmHg and was adapted to maintain hypotension at this level. Delay in onset of hypotension and delay in start of variations in MEBF were measured from T_0.

During the first part of the study, no surgical stress was applied during 15 min after initiating hypotension. The laser-Doppler fibre was withdrawn at T_{+15} min of experimentation to allow surgery. During the second part of the study, direct visual evaluation of the surgical field was performed from T_0 until the end of surgery. All drugs were discontinued at least ten minutes before the end of surgery.

Statistical analysis

For each child variations in MEBF, MAP and HR were calculated from baseline values. All results are expressed as mean ± SE. Results were averaged before statistical analysis. Intragroup comparisons were conducted using one-way analysis of variance for repeated measures. Where indicated, Bonferroni's corrections were used to identify significant differences. Relationships between MEBF and MAP, MEBF and HR were studied by least squares linear regressions. The threshold for statistical significance was taken as $P < 0.05$.

Results

Demographic data, duration of hypotension, duration of anesthesia, duration of surgery and baseline hemodynamic data are shown in Table I. Doses and time delays for hemodynamic effects of the drugs and end-tidal concentrations of sevoflurane are shown in Table II.

In the first part of the study, when surgical stress was avoided, controlled hypotension was achieved at the target MAP of 50 mmHg in the R group ($P < 0.01$)

TABLE I Demographic data, duration of hypotension, duration of anesthesia, duration of surgery and baseline hemodynamic data

	Remifentanil group n = 20	*Nitroprusside group n = 20*
- Patient		
Gender F/M	11/9	12/8
Age (yr)	8.4 ± 3.2	9 ± 4.1
Weight (kg)	29.1 ± 9.8	30.2 ± 8.6
- Duration of hypotension (min)	46 ± 4	45 ± 5
- Duration of anesthesia (min)	58 ± 10	63 ± 11
- Duration of surgery (min)	52 ± 5	54 ± 5
- Baseline mean arterial pressure (mmHg)	72 ± 6	75 ± 6
- Baseline heart rate (beats·min^{-1})	102 ± 8	100 ± 6

Results are mean values ± SE.

TABLE II Doses and time delay for hemodynamic effects of drugs used for controlled hypotension in the two groups

	Remifentanil group n = 20	*Nitroprusside group n = 20*
- Infusion rate (μg·kg^{-1}·min^{-1})	0.30 ± 0.05	0.81 ± 0.25
- Total dose (μg)	415 ± 30	1162 ± 277
- Delay in onset of hypotension (sec)	47 ± 4	29 ± 2
- Time delay MEBF–MAP (sec)	23 ± 7	13 ± 3
-$Sevo_{et}$ %	2 ± 0.2	2 ± 0.2

MAP = mean arterial pressure; Time delay MEBF–MAP (sec) = time delay between start of variations in middle ear blood flow and onset of hypotension; $Sevo_{et}$ = sevoflurane end-tidal concentration. Results are mean values ± SE.

and in the N group ($P < 0.01$) within 121 ± 21 sec in R group and 62 ± 9 sec in N group. HR decreased significantly from baseline by 17 ± 4% ($P < 0.01$) in the R group and increased by 32 ± 7% ($P < 0.01$) in the N group.

MEBF decreased from baseline by 22 ± 4% ($P < 0.01$) in the R group, by 20 ± 6% ($P < 0.01$) in the N group.

Delay in onset of hypotension was 47 ± 4 sec in the R group and 29 ± 2 sec in the N group (Table II). Delay in onset of variation of MEBF was 16 ± 4 sec and 18 ± 5 sec in the R and N groups, respectively, and was shorter than the delay in onset of hypotension in the two groups ($P < 0.01$ in each group). Time delay between onset of variations of MEBF and onset of hypotension was 23 ± 7 sec in R group, 13 ± 3 sec in N group (Table II). No relationships were found between hemodynamic data within the groups (Table III). The

TABLE III Relationships between MBEF and mean arterial pressure or heart rate. Least squares regression analysis, $P < 0.05$ significant

		Remifentanil group n = 20	*Nitroprusside group n = 20*
- MEBF as a function of MAP			
at MAP 50	r	0.32	0.17
	P	0.31	0.80
- MEBF as a function of HR:			
at MAP 50	r	0.45	-0.33
	P	0.23	0.37

The slopes are not significantly different from zero. MEBF = middle ear blood flow; HR = heart rate; MAP 50 = mean arterial pressure of 50 mmHg.

MEBF coefficient of autoregulation Ga decreased to 0.41 ± 0.2 in the R group and decreased to 0.37 ± 0.3 in the N group.

In the second part of the study, during surgery, hypotension was sustained at the target MAP of 50 mmHg in the two groups (Table IV). The surgical field rating decreased significantly from baseline in the two groups ($P < 0.01$; Table IV).

$PaCO_2$ was significantly higher and pH was significantly lower compared with control values ($P < 0.05$) in the N group during hypotension and in the recovery room (Table V).

There were no postoperative circulatory, respiratory, neurological, or metabolic complications in any group, and all children were normally discharged the first postoperative day.

Discussion

The main findings of the current study were that remifentanil combined with sevoflurane in children undergoing middle ear surgery enabled: a) convenient controlled hypotension in children at a level of 50 mmHg of MAP; b) a significant reduction of MEBF; and c) a satisfactory and bloodless operative field, with no adverse effects and no need for additional use of a potent hypotensive agent or adjunct agents. This decrease in arterial pressure or in MEBF was in the range of that observed with sodium nitroprusside. The current randomized, pilot study, with a small sample size, does not have sufficient power to show a difference of efficacy between remifentanil and nitroprusside to control arterial pressure, and even less to demonstrate comparable efficacy but this was not the aim. The sample size is small but was sufficient to show that

TABLE IV MAP and SFR

	T_{-10}	T_0	T_{+1}	T_{+2}	T_{+15}	T_{+20}	T_{+30}	T_{+40}	T_{+50}
MAP mmHg									
R	73 ± 6	72 ± 6		50 ± 2*	51 ± 2*	51 ± 3*	49 ± 2*	52 ± 4*	54 ± 5*
N	75 ± 7	75 ± 6	49 ± 2*		50 ± 3*	51 ± 2*	51 ± 3*	53 ± 5*	52 ± 4*
SFR (0–5)									
R		3.2 ± 0.19			1.1 ± 0.2*		0.97 ± 0.17*		0.94 ± 0.14*
N		3.1 ± 0.21			1.0 ± 0.15*		0.96 ± 0.21*		0.94 ± 0.16*

Mean arterial pressure (MAP), and surgical field rating (SFR) were plotted against time in minutes for patients receiving either remifentanil (R), or sodium nitroprusside (N) for controlled hypotension at a MAP of 50 mmHg. T-10, T0, T+1, T+2, T+15, T+20, T+30, T+40, T+50; control values -10 min, 0 min, +1 min, +2 min, +15 min, +20 min, +30 min, +40 min, +50 min respectively. N = 20 in each group. Results are mean ± SE. *$P < 0.01$ different from baseline in each group.

TABLE V Metabolic data

		T_0	$T_{+30\ min}$	$T_{+45\ min}$	$T_{recovery}$
PaO_2 mmHg					
	R	156 ± 16	167 ± 14	168 ± 9	120 ± 6
	N	160 ± 15	165 ± 16	160 ± 9	112 ± 8
$PaCO_2$ mmHg					
	R	37 ± 0.9	32 ± 1.1	32 ± 0.8	40.2 ± 0.6
	N	37 ± 0.5	41 ± 1.2*	42 ± 0.8*	44.7 ± 2.1*
pH					
	R	7.38 ± 0.04	7.39 ± 0.05	7.39 ± 0.04	7.4 ± 0.02
	N	7.38 ± 0.04	7.33 ± 0.03*	7.31 ± 0.03*	7.29 ± 0.05*
Lactate $\mu mol \cdot l^{-1}$					
	R	1 ± 0.3	1 ± 0.3	1 ± 0.2	1 ± 0.1
	N	1 ± 0.3	1.2 ± 0.3	1.1 ± 0.2	1 ± 0.1

*$P < 0.05$ = different from baseline; R = remifentanil group; N = sodium nitroprusside group; PaO_2 = partial pressure of oxygen; $PaCO_2$ = partial pressure of carbon dioxide. $T_{recovery}$ = 20 min after end of surgery in the recovery room. N = 20 in each group. Results are mean ± SE.

remifentanil was able to reduce blood pressure to the desired level, compared to control ($P < 0.01$). We are planning a large scale randomized study comparing the efficacy of these two agents for controlled hypotension. Remifentanil has recently been used successfully for inducing controlled hypotension in adults combined with propofol during tympanoplasty,[13] but its efficacy as a primary hypotensive agent in children remains unclear. Remifentanil, an ultra-short μ-agonist opioid, has been used for analgesia with sevoflurane/isoflurane anesthesia in children where fenoldopam was used for controlled hypotension as the primary agent.[7] It is interesting to note that the concentrations of remifentanil were the same than those used in the current study, and were the same than those commonly used for analgesia in adults or children (0.1–0.5 $\mu g \cdot kg^{-1} \cdot min^{-1}$). However, remifentanil was not used as the primary hypotensive agent in the study by Tobias[7] as it was in this one. Sevoflurane was used to induce and maintain anesthesia. It is commonly used in children because of rapid induction of anesthesia,[19,20] comfort, good airway tolerance causing minimal breath holding, coughing, excitement or laryngospasm.[21] It has also been used as a primary agent for controlled hypotension in children combined with sufentanil during spinal fusion but, as for other inhalational agents (isoflurane) with predominantly vasodilatory properties, reflex tachycardia was encountered, with the need for beta adrenergic antagonism to control HR.[8] High levels of expired concentrations (4%) of sevoflurane, which were necessary to ensure satisfactory blood pressures (55–65 mmHg), increased this phenomenon. The lower concentrations of sevoflurane (2%) used in our study did not ensure hypotension as attested by

control values. The bradycardia that occurred could be ascribed to remifentanil, whose effects on the heart have been shown to resemble those of esmolol, a short-acting *iv* beta adrenergic antagonist.[13,22] The hemodynamic data for nitroprusside are in agreement with those previously reported in middle ear surgery in adults,[13] and in spine, craniofacial or hepatic surgery in children.[3] Disadvantages of nitroprusside for deliberate hypotension in children, which include reflex tachycardia and potential for cyanide toxicity, were a light acidosis and hypercarbia in this and in a previous study,[2] and did not appear to be more important in children than in adults.[13,23] These disorders, beginning at the 30th intraoperative minute in spite of an adapted ventilatory mode, may be related to a disturbance of cellular breathing rather than a disorder of gaseous exchanges due to alveolar hypoventilation.[2] Though remifentanil appears to be safer than nitroprusside both in children and in adults, the risks of nitroprusside, when dosage rules are respected,[23] are weak in clinical practice. However, inobservance of dose limitations, resistance to the drug, or tachyphylaxis, can lead to increased doses of nitruprusside, excessive cyanide levels in plasma and death.[2,20] This justified the continuous monitoring of arterial blood pressure and metabolism by arterial cannulation.[24]

In the present study, MEBF was reduced by approximately 22%. As shown in adults,[13] the present study suggests that autoregulatory mechanisms for the control of MEBF, which act as local protective mechanisms to ensure minimal tissue metabolism despite important variations of blood flow, presumably exist in children, and were not suppressed by remifentanil or nitroprusside. To our knowledge the mechanisms of control of cochlear blood flow had never been studied in children previously, so that the limits of autoregulation are not defined in children. Further studies are needed to elucidate these mechanisms.

The concentration of sevoflurane and infusion rate of remifentanil used in the present study were those normally used for maintenance of anesthesia in children and showed efficacy and safety with no need for additional use of a potent hypotensive agent. This easy-to-use and reliable "hypotensive anesthesia" in children makes it possible to simplify and reduce monitoring.[24] In this study, an ethical consideration was that arterial cannulation may have added risks to the children. In an adult population, there may be an argument for taking an acceptable risk that subjects fully understand and agree with. With respect to safety, arterial cannulation is recommended by international experts for controlled hypotension, whatever the surgery, without distinction between adult and child.[24] The risks of the arterial cannulation are quite small,[25] and considerably reduced by the systematic examination of the arterial arch of the hand by Doppler ultrasound.[14] The risks of arterial cannulation appear to be less than the neurologic and metabolic risks associated with potent vasodilators. For these reasons, up to this day, we have been using arterial cannulation routinely in this patient population. The results of this study, i.e., a slow decrease in arterial pressure and hemodynamic stability during hypotension induced by remifentanil, suggest it may be possible to utilize noninvasive monitoring of blood pressure and respiratory variables and to abandon arterial catheterization with its constraints and its risks for this specific indication.

In conclusion, the present study showed that remifentanil, an ultra-short acting μ-opioid receptor agonist: a) was effective in inducing consistent and sustained controlled hypotension in children; b) was effective in reducing MEBF; and c) was effective in providing a satisfactory operative field during middle ear surgery for chronic otitis media in children anesthetized with sevoflurane.

References

1 *Smith C.* Haemostasis in ear surgery. Proc R Soc Med 1971; 64: 1225–6.

2 *Davies DW, Greiss L, Kadar D, Steward DJ.* Sodium nitroprusside in children: observations on metabolism during normal and abnormal responses. Can Anaesth Soc J 1975; 22: 553–60.

3 *Yaster M, Simmons RS, Tolo VT, Pepple JM, Wetzel RC, Rogers MC.* A comparison of nitroglycerin and nitroprusside for inducing hypotension in children: a double-blind study. Anesthesiology 1986; 65: 175–9.

4 *Aono J, Kataoka Y, Takimoto E, Ueda W, Manabe M.* Effect of deliberate hypotension with PGE1 on PaO2 in pediatric patients (Japanese). Masui 1993; 42: 515–7.

5 *Tobias JD, Hersey S, Mencio GA, Green NE.* Nicardipine for controlled hypotension during spinal surgery. J Pediatr Orthop 1996; 16: 370–3.

6 *Hersey SL, O'Dell NE, Lowe S, et al.* Nicardipine versus nitroprusside for controlled hypotension during spinal surgery in adolescents. Anesth Analg 1997; 84: 1239–44.

7 *Tobias JD.* Fenoldopam for controlled hypotension during spinal fusion in children and adolescents. Paediatr Anaesth 2000; 10: 261–6.

8 *Tobias JD.* Sevoflurane for controlled hypotension during spinal surgery: preliminary experience in five adolescents. Paediatr Anaesth 1998; 8: 167–70.

9 *Degoute CS, Dubreuil C, Ray MJ, et al.* Effects of pos-

ture, hypotension and locally applied vasoconstriction on the middle ear microcirculation in anaesthetized humans. Eur J Appl Physiol 1994; 69: 414–20.

10 *Amaranath L, Kellermeyer WF Jr.* Tachyphylaxis to sodium nitroprusside. Anesthesiology 1976; 44: 345–8.

11 *Saarnivaara L, Klemola UM, Lindgren L.* Labetalol as a hypotensive agent for middle ear microsurgery. Acta Anaesthesiol Scand 1987; 31: 196–201.

12 *Hara T, Fukusaki M, Nakamura T, Sumikawa K.* Renal function in patients during and after hypotensive anesthesia with sevoflurane. J Clin Anesth 1998; 10: 539–45.

13 *Degoute CS, Ray MJ, Manchon M, Dubreuil C, Banssillon V.* Remifentanil and controlled hypotension; comparison with nitroprusside or esmolol during tympanoplasty. Can J Anesth 2001; 48: 20–7.

14 *Mercier FJ, Basdevant C, De Tovar G, Fischler M.* Preoperative diagnosis with Doppler ultrasound of palmar arches functional anomalies in children (French). Ann Fr Anesth Reanim 1994; 13: 785–8.

15 *Miller JM, Bredberg G, Grenman R, Suonpaa J, Lindstrom B, Didier A.* Measurement of cochlear blood flow. Ann Otol Rhinol Laryngol 1991; 100: 44–53.

16 *Strebel S, Lam AM, Matta B, Mayberg TS, Aaslid R, Newell DW.* Dynamic and static cerebral autoregulation during isoflurane, desflurane, and propofol anesthesia. Anesthesiology 1995; 83: 66–76.

17 *Fromme GA, Mackenzie RA, Gould AB Jr, Lund BA, Offord KP.* Controlled hypotension for orthognatic surery. Anesth Analg 1986; 65: 683–6.

18 *Katoh T, Suzuki A, Ikeda K.* Electroencephalographic derivatives as a tool for predicting the depth of sedation and anesthesia induced by sevoflurane. Anesthesiology 1998; 88: 642–50.

19 *Smith I, Ding Y, White PF.* Comparison of induction, maintenance, and recovery characteristics of sevoflurane-N_2O and propofol-sevoflurane with propofol-isoflurane-N_2O anesthesia. Anesth Analg 1992; 74: 253–9.

20 *Johannesson GP, Floren M, Lindahl SGE.* Sevoflurane for ENT-surgery in children. A comparison with halothane. Acta Anaesthesiol Scand 1995; 39: 546–50.

21 *Patel SS, Goa KL.* Sevoflurane. A review of its pharmacodynamic and pharmacokinetic properties and its clinical use in general anaesthesia. Drugs 1996; 51: 658–700.

22 *Ebert TJ, Muzi M, Berens R, Goff D, Kampine JP.* Sympathetic responses to induction of anesthesia in humans with propofol or etomidate. Anesthesiology 1992; 76: 725–33.

23 *Tinker JH, Michenfelder JD.* Sodium nitroprusside: pharmacology, toxicology and therapeutics. Anesthesiology 1976; 45: 340–54.

24 *Van Aken H, Miller ED Jr.* Hypotension contrôlée. *In*: Miller RD (Ed.). Anesthésie. Paris: Flammarion; 1996: 1481–1503.

25 *Slogoff S, Keats AS, Arlund C.* On the safety of radial artery cannulation. Anesthesiology 1983; 59: 42–7.