Controlled hypotension during middle ear surgery: hemodynamic effects of remifentanil vs nitroglycerin

Ann. Ital. Chir., 2018 89, 3: 283-286
pii: S0003469X18027641

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INTRODUCTION: *Controlled hypotension is a well-known technique used by anesthesiologists to limit intraoperative bleeding in patients undergoing middle ear surgery and improve visibility of the surgical field. Nitroglycerin and remifentanil are among the drugs used to induce controlled hypotension.The aim of our study was to compare the hemodynamic effects of remifentanil and nitroglycerin in this patient population.*
METHODS: *All consecutive patients who underwent middle ear surgery between January and December 2016, at the University Hospital Vittorio Emanuele in Catania were included in a retrospective study. Patients who were given nitroglycerin to induce controlled hypotension were compared to those given remifentanil. The following parameters were measured systolic and diastolic blood pressure, heart rate, peripheral (capillary) oxygen saturation, and fraction of expired carbon dioxide. A mean arterial pressure of 50-70 mmHg was considered optimal.*
RESULTS: *Thirty patients who underwent stapedioplasty and tympanoplasty, 25 men and 5 women,with a mean age of 43 years (range 32-58 years) were included in the study. Fifteen patients had received nitroglycerin (group A) and 15 patients remifentanil (group B). The target blood pressure was reached in all patients and no significant difference was found between the groups with regard to the level of systolic and diastolic blood pressure, heart rate, peripheral (capillary) oxygen saturation, and fraction of expired carbon dioxide. However the heart rate of 2 younger patients in group A rose to > 100 bpm after the administration of nitroglycerin.*
CONCLUSION: *Both remifentanil and nitroglycerin are effective in inducing controlled hypotension.*
In younger patients administration of nitroglycerin is associated with an increase in heart rate.

KEY WORDS: Controlled hypotension, Middle ear surgery, Nitroglycerin, Remifentanil

Introduction

In middle ear surgery careful control of intraoperative bleeding is essential. Minimizing bleeding provides the surgeon with a clearer view of the surgical field and thus leads to better outcomes and shorter operating times. Controlled hypotension, reducing the patient's mean arterial pressure to approximately 50-70 mmHg, can be used to achieve this goal. Although both nitroglycerin and remifentanyl have been shown to be safe and effective for creating controlled hypotension, the hemodynamic effects of the 2 drugs have not been fully elucidated.
The aim of the present study was to compare the hemodynamic effects produced by nitroglycerin and remifentanyl using non-invasive monitoring.

Materials and Methods

Consecutive patients who underwent middle ear surgery consisting of stapedioplasty or tympanoplasty at our insti-

Pervenuto in RedazioneLuglio 2017 Accettato per la pubblicazione Ottobre 2017
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tution between January and December 2016 were included in the present study. None of the patients had heart disease, renal insufficiency or anemia. They were all classified as American Society of Anesthesiologists (ASA) class I or class II.

The patients were divided into 2 groups depending on whether they received nitroglycerin (group A) or remifentanil (group B).

The following anesthetic protocol was used for both groups: induction with propofol 2,5 mg/kg, 100% O_2 and atracurium 0,5 mg/kg, maintenance with 2.5% sevoflurane in an O_2/air mixture [50% fraction of inspired oxygen (FiO_2)] at 6L/min. Muscle relaxation was maintained with fractionated doses of atracurium in both groups.

Patients in group A also received repeat boluses of fentanyl, 2.5 mg/kg for analgesia and for controlled hypotension a continuous infusion of nitroglycerin, at 0,03-0,06 mg/kg/hr depending on the hypotensive effect obtained.

Patients in group B received remifentanil for both analgesia and to induce hypotension. After an initial bolus of 0,5-1 μg/kg, remifentanil infusion was started at a rate of 0,25-0,5 μg/kg/min and titrated according to patient's response.

The target systolic blood pressure was 70-80 mmHg.

During surgery there was continuous non-invasive monitoring of systolic and diastolic blood pressure heart rate,end-tidal carbon dioxide ($EtCO_2$) via capnography, peripheral capillary oxygen saturation (SpO_2) via pulse oximetry, and hourly monitoring of diuresis.

The variables used to compare the effects of nitroglycerin and remifentanil were: systolic and diastolic blood pressure, heart rate, SpO_2 and $EtCO_2$, at the following time points: before induction of anesthesia; intraoperatively once the desired degree of hypotension was reached; and when the patient was taken to the recovery room upon completion of the operation.

Statistical Analysis

Quantitative data were expressed as mean ±standard deviation. Student's t-test was used for comparison of continuous variables.…

The alpha level was set at 0.01. A p-value <0.01 was considered statistically significant.

Results

There were 30 patients, 15 in the nitroglycerin group (13 males, mean age 45±13 years), and 15 in the remifentanyl group (12 males, mean age 42±10 years). Patient characteristics of the groups were similar (Table I). There were no significant differences between the groups in mean systolic or diastolic blood pressure and heart rate either preinduction, intraoperatively or in the recovery room (Figs. 1, 2, 3, Table II).

Table I - *Comparison of demographics and clinical parameters in the two groups*

Parameters*	Nitroglicerin (n=15)	Remifentanil (n=15)	P value
Age (years)	45 (±13)	42 (±10)	0,766
Sex(M/F)	13(M), 2(F)	12(M), 3(F)	1
Preinduction:			
Systolic BP (mm/Hg)	135 (±20)	131,8 (±16,8)	0,722
Diastolic BP (mm/Hg)	85,4 (±10,4)	83,4 (±8,4)	0,733
Heart rate (bpm)	85 (±13)	83,6 (±11,6)	0,553
SpO_2 (%)	97,9 (±1,9)	97,8 (±1,8)	0,405
$ETCO_2$ (%)	33,8 (±1,8)	33,9 (±1,9)	0,405
During controlled hypotension:			
Systolic BP (mm/Hg), mean (±SD)	77,8 (±9,8)	83,.2 (±8,.2)	0,982
Diastolic BP (mm/Hg)	59,9 (±5,9)	57,.3 (±10,.3)	0,.794
Heart rate (bpm)	73 (±11)	67,.5 (±7,.5)	0,.985
SpO_2 (%)	98,3 (±2,3)	98,.5 (±1,5)	0,.707
$EtCO_2$ (%)	33,9 (±1.,9)	32,.5 (±2,.5)	0,994
In recovery room:			
Systolic BP (mm/Hg)	135,1 (±17.,1)	129,5 (±9,5)	0,934
Diastolic BP (mm/Hg)	85,7 (±7.,7)	70,5 (±5,5)	1
Heart rate (bpm)	84,2 (±15,2)	82,7 (±7,7)	0,583
SpO_2 (%)	98,2 (±2.,2)	98,5 (±1,5)	0,773

* values reported as mean (±SD) BP= Blood pressure; SD= standard deviation;
SpO_2: Peripheral (capillary) oxygen saturation; EtCO2=Extra-tidal carbon dioxide.

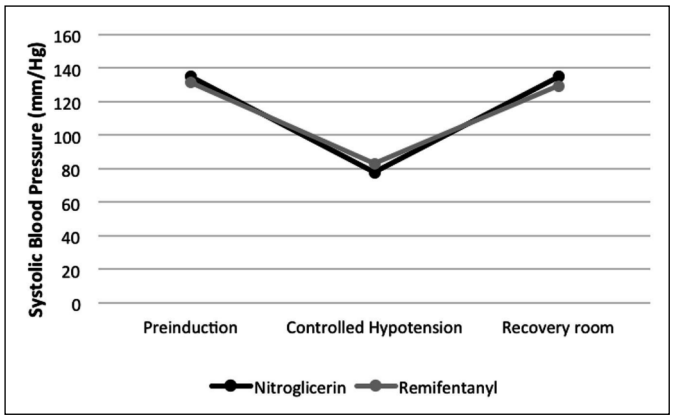

Fig. 1: Comparison of systolic blood pressure.

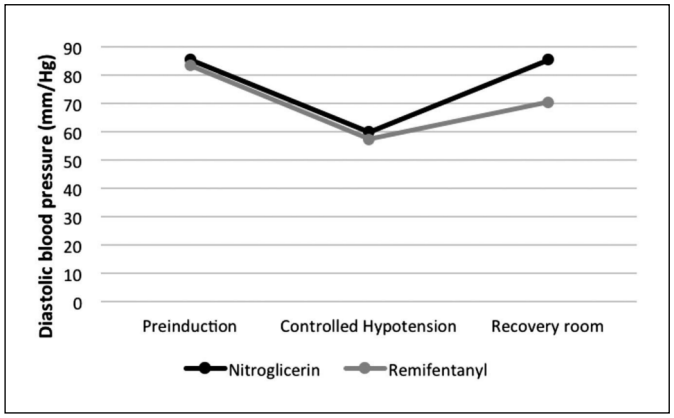

Fig. 2: Comparison of diastolic blood pressure.

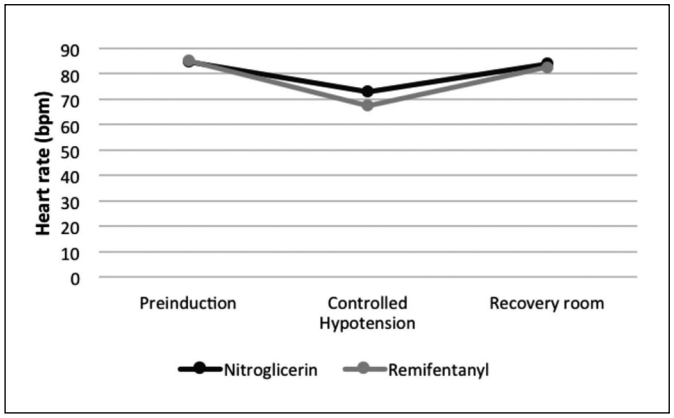

Fig. 3: Comparison of heart rate.

Two patients in group A (32 and 34 years old) had a heart rate > 80 bpm (107 and 105 bpm respectively) after administration of nitroglycerin although these findings did not reach statistical significance (Fig. 3). These patients were given atenolol (tenormin) 5 mg/10 ml at 1 ml/minute until their heart rate fell to <70 bpm. The SpO_2 and $EtCO_2$ were similar in the 2 groups as shown in Figs. 4, 5.

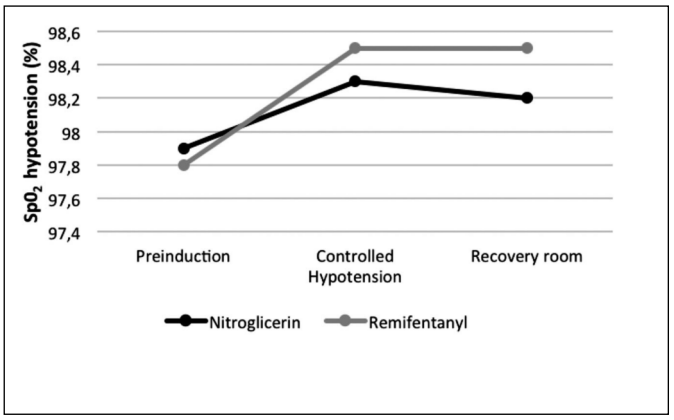

Fig. 4: Comparison of peripheral capillary oxygen saturation (SpO_2).

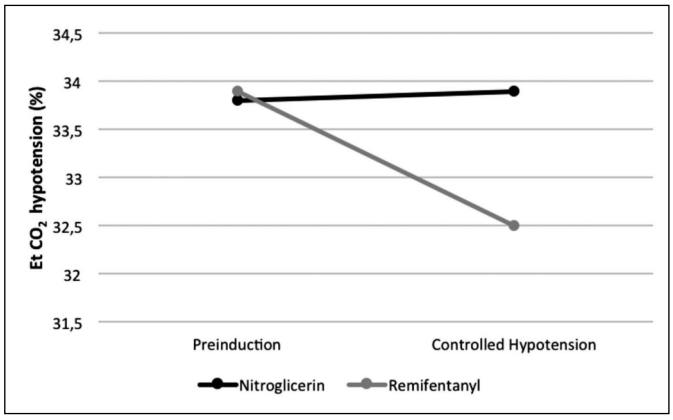

Fig. 5: Comparison of end-tidal carbon dioxide ($EtCo_2$).

Discussion

Nitroglycerin has long been successfully used to induce controlled hypotension. It has a favorable pharmacokinetic profile since it has a rapid onset of action, a short half-life and metabolites that have only minimal pharmacological activity. Studies have shown that younger patients have a different response to nitroglycerin than older patients [1,2] and this should be kept in mind when using nitroglycerin to induce controlled hypotension. In our patients that there was a difference in heart rate: the heart rate of the two younger patients in the nitroglycerin group rose after administration of the drug. Because induced hypotension causes relative hypovolemia, in young patients, who have more pronounced aortic and carotid baroreceptor activity than older patients, hypotension causes reflex tachycardia which increases myocardial O_2 consumption in addition to reducing visibility of the surgical field. In older patients the Bainbridge, or "atrial "reflex, in which hypovolemia causes bradycardia, is dominant [2].
Therefore nitroglycerin must be administered with care to avoid undesired hemodynamic changes such as reflex tachycardia and rebound hypertension.

Remifentanil is a more recent addition to the anesthesiologists armamentarium for inducing controlled hypotension. The drug is rapidly metabolized not in the liver or kidney but by nonspecific esterases in both blood and tissue. The pharmacokinetics of the drug are independent of the total dose, as well as of the speed and duration of infusion. Since its elimination is independent of liver and kidney function remifentanyl doers not accumulate in patients with hepatic or renal insufficiency [3]. Its small apparent volume of distribution and its metabolism are responsible for its short duration of action which makes respiratory depression (typical of opioid agonists) easily reversible.

The administration of remifentanil is associated with a dose-dependent reduction of mean arterial pressure and heart rate [4,5] as well as reduced electroencephalographic activity because the drug lowers cerebral perfusion pressure, cerebral blood flow and cerebral metabolism. Though flow-metabolism coupling is preserved Intracranial pressure does not rise, in fact it tends to fall. Studies have shown that the above characteristics of remifentanil make it is especially suitable for achieving controlled hypotension without the undesired effects associated with nitroglycerin [6-8]. This is in line with our results which suggest that as regards hemodynamic effects, remifentanil is preferrable to nitroglycerin for younger patients

Limitations of our study are its retrospective nature and the small sample size.

Conclusion

Our results show that nitroglycerin and remifentanil are equally effective in inducing controlled hypotension in patients undergoing middle ear surgery, and have similar hemodynamic effects except as regards heart rate which may increase in younger patients after administration of nitroglycerin. Larger, randomized controlled studies are needed to confirm our results.

Riassunto

INTRODUZIONE: L'ipotensione controllata è una tecnica anestesiologica che permette nella chirurgia dell'orecchio medio una diminuzione del sanguinamento con una migliore visione del campo operatorio al chirurgo.

METODO DI STUDIO: È stata eseguita una revisione sistematica su 30 interventi di chirurgia dell'orecchio medio eseguiti presso l'Azienda Ospedaliero Universitaria Policlinico-Vittorio Emanuele di Catania nel 2016. Il campione aveva età compresa tra i 32 ed i 58 anni trattati con nitroglicerina o con remifentanil al fine di indurre ipotensione, considerando come valori ottimali di pressione media 50/70 mm/Hg.

RISULTATI: Esaminando i valori di pressione arteriosa misurati nel campione studiato non sono emersi variazioni significative dovute all'uso dei due farmaci. Gli effetti emodinamici sono risultati simili ad eccezione della frequenza cardiaca, che tende ad aumentare nei pazienti di giovane età in seguito a somministrazione di nitroglicerina.

CONCLUSIONI: Entrambi i farmaci utilizzati risultano efficaci nell'induzione dell'ipotensione controllata. La tachicardia indotta nei pazienti di giovane età rende più agevole l'utilizzo del remifentanil in questa categoria di pazienti.

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