Control of emergence hypertension after craniotomy for brain tumor surgery

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ABSTRACT

الأهداف: مقارنة تأثير كل من الاسملول والريميفنتانيل في التحكم في ارتفاع ضغط الدم.

الطريقة: أُجريت دراسة شملت 20 مريضاً في عمليات جراحة المخ والأعصاب – مستشفى القصر العيني التعليمي – كلية طب جامعة القاهرة – جمهورية مصر العربية، خلال الفترة مابين 2006م وحتى 2008م. تم تقسيم المرضى إلى مجموعتين احتوت كل مجموعة على 10 مرضى، المجموعة الأولى: تم إعطائهم الريميفنتانيل شكل حبة iv (ug/kg) في 30–60 ثانية، تلاها استخدمنا طريقة التسريب الوريدي بمعدل (0.25–0.5ug/kg) في الدقيقة حتى وصل ضغط الدم إلى (<140mm Hg). المجموعة الثانية تم إعطائهم الاسملول بطريقة التسريب الوريدي (500ug/kg) في 30 ثانية، تلاها استمرارية في إعطاء المحلول الوريدي (100–300ug/kg) في الدقيقة حتى وصل ضغط الدم إلى (<140mm Hg). استمر المرضى بتلقي التسريب الوريدي حتى خروجهم من PACU.

النتائج: أظهرت الدراسة أن بداية انخفاض ضغط الدم كان اقصر في المجموعة الثانية (40±0.010) في الثانية، عنه في المجموعة الأولى (52.5±4.47) في الثانية. كانت مدة بقاء المرضى في غرفة الإفاقة PACU ومدة الإقامة في المستشفى متقاربة بين المجموعتين.

خاتمة: يمكن استخدام عقار الريميفنتانيل للتحكم في الحالات الطارئة لارتفاع ضغط الدم أثناء إفاقة المريض من التخدير بعد إجراء عملية استئصال الأورام من المخ، حيث يتميز بسرعة استعادة أكثر من الاسملول أو أية مخدر آخر. كما يمكن استخدامه عندما يكون الاسملول محظور في مرضى القلب، الربو، داء الرئة المزمن والسيدات الحوامل. كما انه يقلل من الحاجة لمسكنات الألم ما بعد العملية الجراحية، ويمكن من التخدير في حالة استمر التسريب ومرضى العمليات منومين في قسم العناية المركزة ICU.

Objectives: To compare the anti-hypertensive effects of both remifentanil and esmolol infusion.

Methods: This prospective comparative study was conducted on 20 patients (10 patients in each group), in the Neurosurgical Theater of Kasr Elaini Hospital, Cairo, Egypt from 2006 to 2008. The patients were divided into 2 equal groups. In group one, remifentanil was used as a bolus of one ug/kg intravenous (iv) in 30-60 seconds, followed by infusion at a rate of 0.25-0.5 ug/kg/min until the systolic blood pressure was <140 mm Hg. In group 2, esmolol was given as a 500 ug/kg iv bolus in 30 seconds followed by continued infusion of 100-300 ug/kg/min until systolic blood pressure was <140 mm Hg. Infusion was continued until the patients left the post anesthesia care unit (PACU).

Results: The onset time of decreasing blood pressure was shorter in group 2 (40±0.01 seconds) than group one (52.5±4.47 seconds). The PACU and hospital stay were comparable between both groups.

Conclusion: Remifentanil can be used to control blood pressure during emergence of anesthesia after craniotomy for brain tumors. It has higher rapid recovery score than esmolol and other narcotics. In addition, it can be used when esmolol is contraindicated such as in cardiac patients, asthmatics, chronic obstructive pulmonary disease, or during pregnancy. Also, it decreases the need for postoperative analgesia and allows sedation if the infusion is continued as surgical patients are admitted to the ICU.

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Strict control of blood pressure is very important during neurosurgical procedures. Authors postulated that the brief periods of hypertension during neurosurgery or emergence from anesthesia may result in the occurrence of postoperative bleeding and cerebral edema.[1,2] It is generally preferable to avoid the occurrence of hypertension by preemptive

therapy. There are many drugs that can be used to control emergence hypertension, such as labetalol and esmolol. The common drug used is esmolol, which is a beta selective blocking drug. This drug may be preferable in patients with obstructive pulmonary diseases and peripheral vascular disease, Raynaud's phenomenon, and diabetes mellitus. Remifentanil is an ultra short recent opioid. It is a synthetic mu receptor agonist with a very short half life. The onset of action is within one minute, and the duration of action is 5-10 minutes following discontinuation of infusion or even less after a single dose. Remifentanil is metabolized by cholinesterase found in plasma and tissue. Therefore, metabolism of remifentanil is not affected by hepatic impairment. The metabolite has minimal sedative and analgesic effects and is excreted by the kidney, with no risk of accumulation during renal impairment. Regarding the use of remifentanil in neurosurgery, it may result in oxidative cerebral metabolism and intracranial pressure and minimal change in cerebral blood flow perfusion pressure. Its short half life means that it can be temporarily discontinued for residual sedation obscuring results. Another benefit of the use of remifentanil in neurosurgical patients is it can be continued as a sedative drug if the patient is admitted to the intensive care unit (ICU) postoperatively, without the need to start another sedative agent such as propofol after emergence from anesthesia. When there are high incidences of renal and hepatic failure the potential benefits of using remifentanil in the ICU are obvious. Patients can be weaned and extubated quickly and so may speed up discharge from the ICU.[3] The aim of this study was to compare remifentanil and esmolol as regards controlling of emergence hypertension, and the effect of these drugs on post operative recovery.

Methods. After approval of the Local Ethics Committee of the Anesthesia Department of Cairo University in the form of Registration of Research, which was signed by the head of department, and after obtaining informed written consent, 20 patients were included in this study at the Neurosurgical Theater, Kasr Elaini Hospital, Cairo University, Cairo, Egypt from 2006 to 2008. They were admitted for craniotomy for removal of intracranial tumor. Exclusion criteria included pregnancy, chronic obstructive pulmonary disease, cardiac disease as heart failure, ischemic heart disease, valvular disease, drug addiction, extensive intracranial tumors that may affect recovery of patients, and drugs affecting minimum alveolar concentration of volatile anesthetics. Surgical procedures exceeded 300 minutes in duration. Patients were divided into 2 equal groups, group one included 10 patients that received remifentanil infusion. Group 2 included 10 patients that received esmolol infusion.

Anesthesia. No premedication was used. Induction was carried out with intravenous (iv) sodium thiopental (5mg/kg) and vecuronium (0.15/kg). Patients were monitored by echocardiography, pulse oximeter, end tidal CO_2, noninvasive blood pressure, and intra-arterial blood pressure through indwelling catheter placed in the radial artery before and/or immediately after induction of anesthesia. Anesthesia was maintained with isoflurane (0.5-1.0) in N_2O/O_2 (70-30) mixture and vecuronium (0.03 mg/kg/h). Ventilation was set to maintain arterial CO_2 partial pressure between 20-25 mm Hg. After closure of the dura, remifentanil infusion was started in group one. Remifentanil given as one microgram (mic)/kg iv over 30-60 seconds, followed by continuous infusion of 0.25-0.5 mic/kg/min until systolic blood pressure was less than 140 mm Hg. Group 2 received esmolol as 500 mic/kg iv over 30 seconds followed by continuous infusion of 100-300 mic/kg/min until systolic blood pressure was less than 140 mm Hg, and the infusion was continued until the patients left the Post Anesthesia Care Unit (PACU). Postoperative nausea and vomiting were treated by 0.15 mg/kg metoclopramide. Patients were discharged to the ward (a) if they had stayed in the PACU 30 minutes, (b) nausea and vomiting was controlled. Heart rate systolic blood pressure (SBP), mean arterial blood pressure (MBP) and O_2 saturation were recorded every 5 minutes after admission from the PACU. Total doses of drugs administered to the patients in the operating room (OR) and PACU were recorded. No narcotics were given in the PACU for controlling pain. Recovery was evaluated as follows: early recovery signs such as eye opening, spontaneous breathing, extubation, stating name, and date of birth, while late recovery signs included PACU stay (minutes), oral intake <3 hours, ambulation, and hospital stay (days).

For each patient, variation in SBP, MBP, and heart rate were calculated from baseline and were considered for comparison between the groups. All results were expressed as mean ± standard deviation, and averaged before statistical analysis. Inter group comparisons were evaluated using one-way analysis of variance for repeated measures; where indicated, Bonferroni correction was used to identify significant differences. Inter group comparison were made using the nonparametric Mann-Whitney U test for unpaired data. The threshold for statistical significance was set as $p<0.05$. All statistical calculations were carried out using Microsoft Excel version 7 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) statistical program.

Results. Patients and surgical characteristics are summarized in **Table 1**. There was no significant difference between the 2 groups. Doses and time delay

Table 1 - Demographic and operative data of study participants (values are presented as mean ± standard deviation).

Parameters	Remifentanil group (n=10)	Esmolol group (n=10)
Gender (M/F)	6/4	8/2
Age (years)	42±20	42±30
Weight (kg)	79±50	72±48
Duration of anesthesia (minutes)	104±8	102±7
Duration of surgery (minutes)	66±9	59±12

Table 2 - Doses and time delay for hemodynamic effects of drugs (values are presented as mean ± standard deviation).

Parameters	Remifentanil group (n=10)	Esmolol group (n=10)
Infusion rate (mic/kg/min)	0.3±0.04	210±33
Total dose (mg)	1.1±0.2	612±51
Delay onset of decreasing blood pressure (seconds)	52.5±4.47	40±0.01

for the hemodynamic effects of both drugs are described in **Table 2**. It shows the total dose and the infusion rate of both drugs. Also, it shows that there was a significant difference in onset time of decreasing blood pressure between the 2 groups, however, there was no significant difference in baseline SBP, MBP, and heart rate of both groups (**Figure 1**). The heart rate decreased from baseline by 21% in the remifentanil group, and by 10% in the esmolol group (no significant difference between the 2 groups). Patients in group one opened their eyes before group 2 (p=0.001). Time of extubation was shorter in group one than in group 2. Patients in group one could state their name and date correctly earlier than those of group 2, which was statistically significant. The PACU and hospital stay were comparable between both groups. More patients in group one took oral fluids and ambulated within 3 hours of discontinuation of anesthesia compared with group 2, which was clinically but not statistically significant. The recovery parameters are shown in **Table 3**. **Table 4** shows the post operative medications that were needed within the first 4 hours and the next 48 hours. No patients needed analgesia in group one, while all patients needed analgesia in group 2, which was statistically and clinically significant. All patients in both groups needed antiemetics, no patients in group one needed anti shivering drugs, while all patients in group 2 needed anti shivering drugs. After 48 hours all patients needed analgesics, 7 patients in group one, and 6 patients in group 2 needed anti emetics. No patients needed cardiovascular drugs in both groups, which were clinically but not statistically significant.

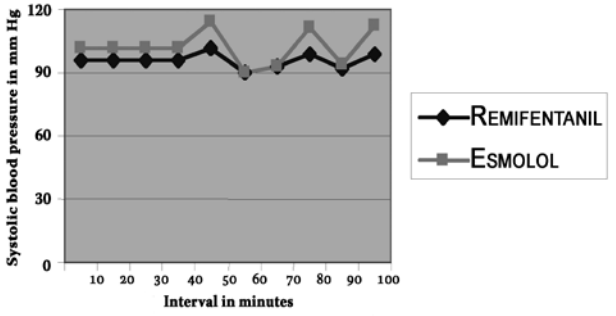

Figure 1 - Systolic blood pressure (mm Hg) changes in both groups.

Table 3 - Recovery characteristics (values are presented as mean ± standard deviation).

Characteristics	Remifentanil group (n=10)	Esmolol group (n=10)
Early recovery (minutes)		
Eye opening	6±5	9±10
Spontaneous breathing	6±6	4±5
Extubation	6±7	7±5
Stating name and date of birth	8±10	15±20
Late recovery		
PACU stay (minutes)	37±35	43±36
Oral intake <3 hours	11±37	4±13
Ambulation <3 hours	7±4	2±7
Hospital stay (hours)	4±5	3±4

PACU - post anesthesia care unit

Table 4 - Post operative medications in both groups (values are number of patients).

Post operative medications	Remifentanil group (n=10)	Esmolol group (n=10)
0-4 hours		
Analgesics	None	10 (all)
Anti-emetics	10 (all)	5
Anti-shivering	None	10 (all)
Cardiovascular	None	None
4-48 hours		
Analgesics	10 (all)	10 (all)
Antiemetics	7	6
Cardiovascular	None	None

Discussion. Our study compares the hypotensive effect of remifentanil with the hypotensive effect of esmolol, and we postulated that the hypotensive effect of remifentanil was comparable to that of esmolol, and this result allowed us to use remifentanil as a hypotensive drug as a prophylaxis against emergence hypertension, especially in cases where a betablocker may be contraindicated

The factors in emergence hypertension after craniotomy are different from those common after surgical procedures. Pain does not appear to be an

important factor in development of hypertension. Neurosurgical patients experience less pain than other postoperative patients, it is not clear whether they perceive a lesser nociceptive stimulus with surgical incision, or they have an altered ability to experience pain (in effect auto-analgesia). One factor contributing to the reduced nociception may be the site of the surgery. The common neurosurgical incisions are in areas of reduced nerve fiber density compared with incisions in the lumbar spine or maxillofacial region. Moreover, the dura, in contrast to the sinuses, is not richly innervated with pain receptors,[4] and the brain itself is insensible to cranial operation. Only patients with frontal craniotomy reported a pain score more than 4 and required more than 10 mg morphine equivalent in the PACU.[5]

Quinton et al[6] questioned whether propofol and remifentanil sedate patients post cardiac surgery. The result showed that the addition of remifentanil reduced propofol requirement by 61% during a 2 hour period. The authors concluded that this could lead to more rapid weaning and extubation. In a study in a general ICU by Kessler et al,[7] patients received either remifentanil or morphine. A sedation score of 4 was aimed for, and midazolam was added if needed to achieve this score. Results showed that remifentanil alone achieved the desired sedation level in most patients, while morphine alone was sufficient in 73% of the patients. When remifentanil is used in the ICU, initially 0.1-0.15 mic/kg/min is given; this dose can then be increased in increments of 0.025 mic/kg/min to achieve the desired level of sedation and analgesia. If the infusion rate reaches 0.2 mic/kg/min and the desired level of sedation is not reached, then a sedative agent such as propofol should be added. The licensed dose is 0.006-0.74 mic/kg/min.[8]

The current study compared remifentanil infusion and esmolol infusion in controlling blood pressure during emergence hypertension after craniotomy. This study found both remifentanil and esmolol can equally control blood pressure during emergence and there was no significant difference between both groups, but there was earlier recovery in the remifentanil than esmolol group, and there was less need for analgesics. Both groups needed antiemetics equally. Group one (remifentanil group) did not need anti shivering drugs, while group 2 did. From these findings, remifentanil can be used safely for controlling blood pressure during emergence. It has the following advantages over esmolol; it can be used where esmolol is contraindicated, such as in cardiac patients, asthmatics, and chronic obstructive pulmonary diseases. Also, some disadvantages have been reported after the use of b-blockers, such as prolonged anesthetics recovery of volatile anesthetics,[8] tachyphylaxis or myocardial depression.[9] Also remifentanil has faster recovery than esmolol, so it is better for postoperative neurosurgical assessment after craniotomy operation.[10]

In a study of Guy et al,[2] comparing intraoperative blood pressure control by remifentanil infusion versus fentanyl as repeated incremental doses, they demonstrated that remifentanil was appropriate to control blood pressure and produce hemodynamic stability for use during craniotomy. Also in a study of Loop & Priebe,[11] they studied the hypotensive effect and the recovery after anesthesia when the remifentanil was combined with propofol, desflurane, or sevoflurane to induce controlled hypotension during otorhinolaryngology surgery. They concluded that, remifentanil had better rapid recovery from anesthesia and the hypotensive effect and could be used in controlled hypotension during otorhinolaryngology surgery. In a study of Balakrishnan et al,[12] they compared remifentanil and fentanyl in patients undergoing surgery for intracranial mass lesions. They concluded that remifentanil-based anesthesia was found to provide stable hemodynamics during the induction, maintenance, and emergence phases of anesthesia when compared with fentanyl. Second, the frequency of adverse event rates for the 2 opioids were similar. Third, they also found that remifentanil affected the rate of emergence for at least 50% of the patients in their study. Fourth, remifentanil use significantly decreased the amount of concomitant anesthetics (isoflurane) use. All the previous studies support our findings regarding the hypotensive effect of remifentanil.[13,14]

One limitation of this study is that the hypotensive effects of the drugs may be covered by the residual effects of inhalational anesthetics and the narcotics used in anesthesia; also the testing recovery effect of both drugs may be affected by postoperative edema induced by the surgical procedure.

In conclusion, remifentanil infusion allows hemodynamic stability during emergence of anesthesia and can be used to control emergence hypertension. Also, it can be continued for sedation in the ICU postoperatively as it allows good sedation, analgesia, and hemodynamic stability. Other studies are needed to evaluate the hypotensive effects of remifentanil, and whether it can also be used for hypotensive anesthesia in surgical procedures other than neurosurgical operations such as during scoliosis operations in children, or ear microsurgery.

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