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Research Article

Use of remifentanil in comparison with sodium nitroprusside for controlled hypotension during rhinoplasty: Randomized controlled trail

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KEYWORDS

Remifentanil;
Sodium nitroprusside;
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Abstract *Objective:* To evaluate the clinical efficacy of remifentanil infusion in comparison with sodium nitroprusside regarding controlled hypotension during rhinoplasty.
Background: Controlled hypotension is a well-known technique used in many operations to reduce blood loss and need for blood transfusion and to provide satisfactory bloodless surgical field. Many pharmacological agents are used to perform controlled hypotension intraoperatively.
Patients and methods: A total of 130 adult consented patients of both sexes undergoing rhinoplasty aged 20–45 years with ASA I or II, were randomized to receive remifentanil infusion 0.25–0.5 μg/kg/min (group I = 65 patients) or sodium nitroprusside 0.5 μ/kg/min intraoperatively with adjusting dose till reaching target MAP around 80 mmHg. Anesthetic technique was standard for both groups. Time to onset of induced hypotension and time to target MAP were recorded in addition to heart rate during induced hypotension, PaO_2, PCO_2 and PH together with the total infusion dose of the hypotensive agents in both groups.
Results: Remifentanil infusion intraoperatively induces adequate hypotension with no statistical significant difference to that induced by sodium nitroprusside ($P < 0.05$).
Conclusion: This study confirmed that remifentanil infusion with dose of 0.25–0.5 μg/kg/min. induced desired controlled hypotension intraoperatively during rhinoplasty with no complications occurred either intra- or postoperative with advantage of rapid recovery from anesthesia.

1. Introduction

Controlled hypotension has been used to reduce bleeding and the need for blood transfusion, and also to provide a satisfactory bloodless surgical field in many operations as in oromaxillofacial surgery, endoscopic sinus surgery, rhinoplasty, middle ear surgery, major orthopedic surgery (as hip or knee

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replacement, spinal) cardiovascular, neurosurgery and liver transplant surgery [1].

Controlled hypotension is defined as a reduction of the systolic blood pressure to 80–90 mmHg, a reduction of mean arterial pressure (MAP) to 50–65 mmHg or a 30% reduction of baseline MAP [2]. Many pharmacological agents used for controlled hypotension include those that can be used successfully alone or in combination with others to limit dosage requirements and the adverse effects of each agent [3]. The common agents that had been used are inhalational anesthetics, sodium nitroprusside, nitroglycerin, adenosine, prostaglandin E, beta blockers (especially esmolol), calcium channel blockers and nacrcotics (especially remifentanil [4] (see Figs. 1–6).

Other agents may be used mainly as adjunctive as ACE inhibitors and α_2 agonists (e.g. clonidine) [5]. The main goal of any hypotensive drug is to achieve the desired level of controlled hypotension without affecting the perfusion of vital organs and should have a rapid onset, which is easy to be administered and disappears quickly when administration is discontinued without toxic metabolites [6]. The new ultrashort acting μ-opioid receptor agonist (Remifentanil) hydrochloride is known to have a hypotensive effect during a propofol total intravenous anesthesia = TIVA, and this is used effectively for controlled hypotension and providing a clear dry surgical field [7].

Sodium nitroprusside is a well-known direct vasodilator (acting on both arterioles and venules) commonly used to induce controlled hypotension with its high potency and short duration of action but it has many side effects and disadvantages making it is not suitable for many patients. Rebound hypertension and increased potentials for cyanide toxicity, and tachyarrhythmia are the common side effects [8].

The purpose of this study was to evaluate the effectiveness of remifentanil to induce controlled hypotension as primary

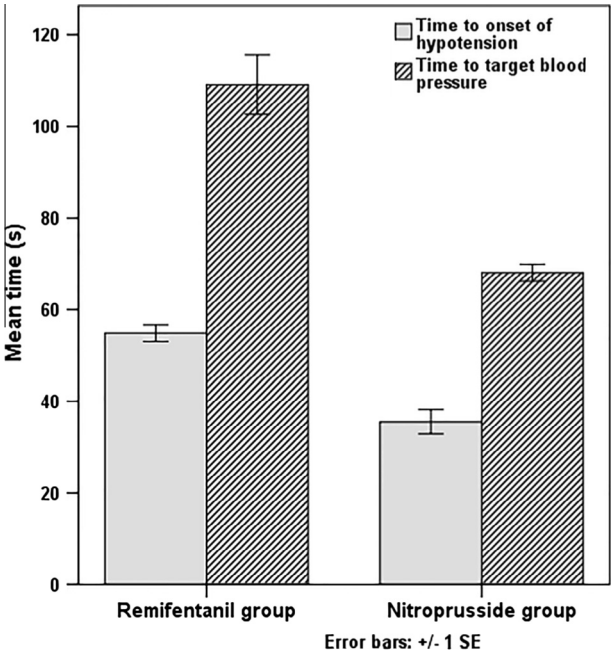

Figure 1 Mean time to onset of induced hypotension and time to target blood pressure in both study groups.

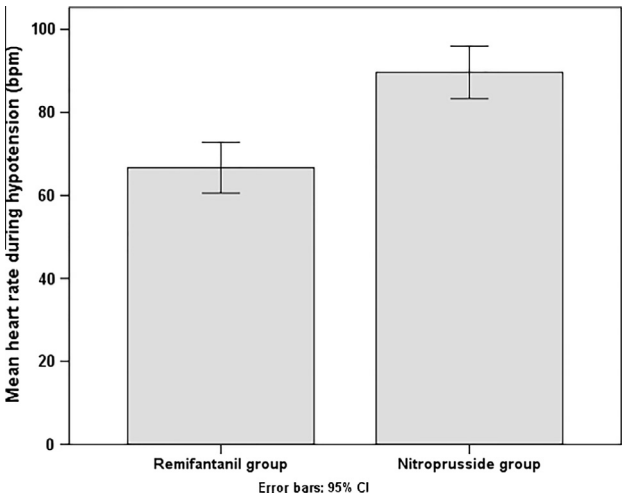

Figure 2 Mean heart rate during induced hypotension in both study groups.

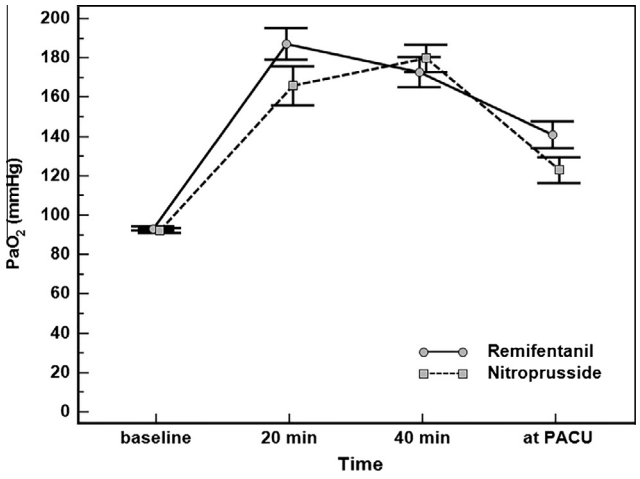

Figure 3 Change in PaO_2 in both study groups. Error bars represent 95% CI.

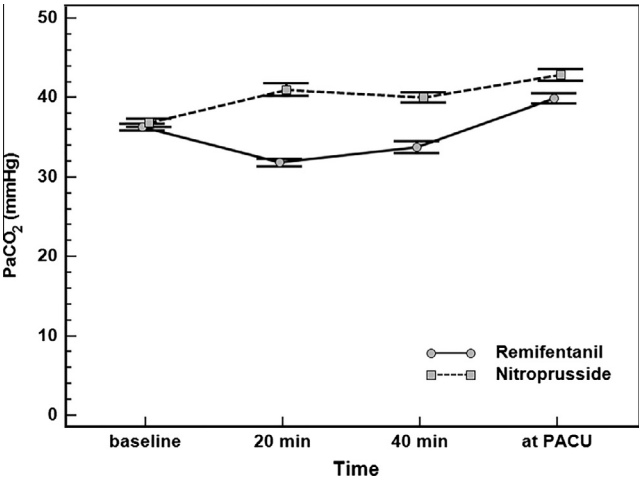

Figure 4 Change in $PaCO_2$ in both study groups. Error bars represent 95% CI.

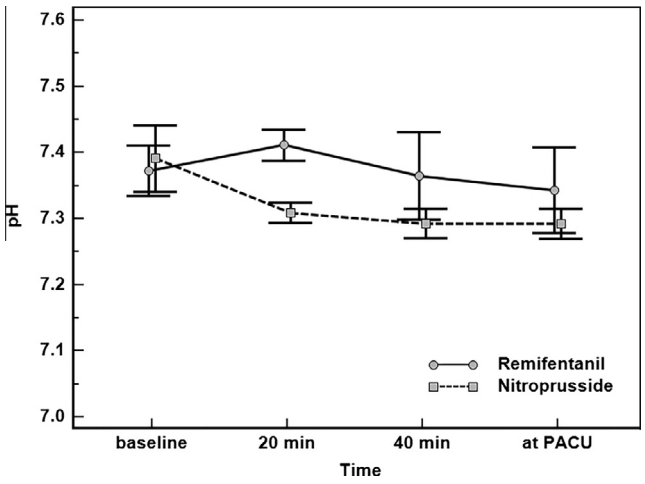

Figure 5 Change in pH in both study groups. Error bars represent 95% CI.

goal and to reduce the disadvantage of traditional methods used to induce controlled hypotension as the secondary goal.

2. Patients and methods

After approval of the local ethical committee, a total of 130 patients ASA I or II of both sexes with ages ranging from 20 to 45 years undergoing rhinoplasty were randomly divided using closed sealed envelope method of randomization into two groups remifentanil group (group I, $n = 65$ patients) or sodium nitroprusside group (group II, $n = 65$ patients).

Exclusion criteria were, patients with uncontrolled hypertension, severe renal or hepatic diseases, anemia age < 20 and > 45 years, patients who refused to participate in this study and patients with severe ischemic heart disease or cardiac failure.

All patients were admitted on the day before surgery and fasted for at least 8 h before surgery. All patients received preoperative sedation in the form of midazolam (0.5 mg/kg) two hours before surgery.

In all patients, a 20-gauge catheter was inserted into the left radial artery for direct determination of arterial blood pressure (systolic, mean, diastolic). Heart rate was continually recorded by 5-lead ECG, also other routines were monitored in the form of pulse oximetry, and end tidal CO_2 was connected. Serial arterial blood gas analysis was done to detect any changes in PH or in the partial pressures of Oxygen (PaO2) and carbon dioxide ($PaCO_2$). Samples were taken every 30 min after the induction of general anesthesia until 20 min in the recovery room.

An 18-gauge cannula was inserted into a suitable vein for fluid and drug administration: Ringer's solution was administered continuously at a rate of 5 ml/kg/h.

3. Anesthetic technique

- In all cases, induction was done by 2 mg kg^{-1} propofol followed by rocurorium 0.6 mg/kg to facilitate orotracheal intubation by cuffed tubes, then the patients were connected to the mechanical ventilator to maintain an end tidal CO_2 ranging from 30 to 35 mmHg and to ensure $SpO_2 \geqslant 97\%$ with 50% N_2O in oxygen. Anesthesia was maintained by Sevoflurane with MAC 1.5–2% and with increments of the muscle relaxant (rocurorium) every 40 min ($= 0.15$ mg/kg).
- After induction of anesthesia, patients received intraoperative infusion according to their groups either remifentanil (group I) or sodium nitroprusside (group II).

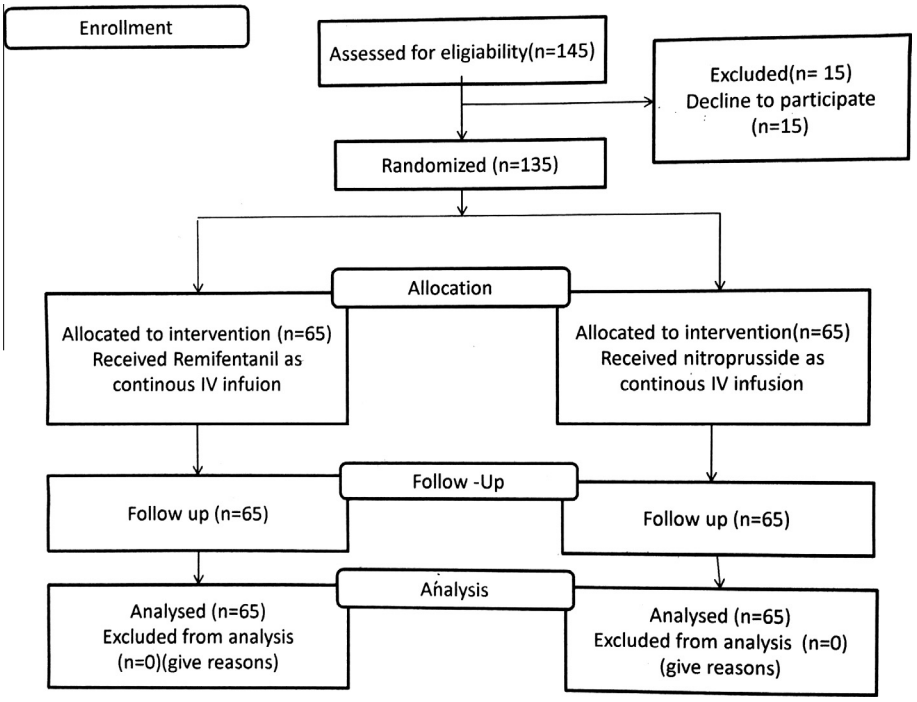

Figure 6 Method done for the flowchart to assess eligibility and randomization.

3.1. In group I

Patients received 1 μg/kg remifentanil I.V. over 30–60 s., followed by a continuous infusion of 0.25–0.50 μg/kg/min until systolic blood pressure was brought within 80 mmHg, then infusion rate was adapted to maintain hypotension at this level.

3.2. In group II

Patients received sodium nitroprusside as a continuous I.V. infusion at a rate of 0.5 μg/kg/min until systolic blood pressure was brought within 80 mmHg, then infusion rate was adapted to maintain hypotension at this level.

Direct visual analysis of the surgical field was performed from starting surgery until the end of the surgery using the six point scale.

In all cases, the surgeon infiltrated the submucosal tissue of the nose with 1:100.000 epinephrine to minimize blood loss. The surgeon was blinded to the hypotensive agent used, as well as to the monitor recording the hemodynamic variables. After the surgery, patients were recovered and were transferred to the recovery area (PACU) for a continuous monitoring.

3.3. Statistical analysis

The required sample size has been calculated using the G*Power software version 3.1.7 (Universität Düsseldorf, Germany). The primary outcome measures were the time to onset of induced hypotension, time to target hypotension, and heart rate during hypotension. Secondary outcome measures were the PaO_2, $PaCo_2$, and pH. It was estimated that a sample of 65 patients in either study group would have a power of 81% (type II error, 0.19) to detect a statistically significant difference between the two study groups for a medium effect size of Cohen's $d = 0.5$, which is equivalent to a difference of 0.5 SD in the outcome measures. This difference was chosen as it could be regarded as a clinically relevant difference to seek in this pilot study. This calculation used a two-sided unpaired t test and assumed a two-tailed type I error of 0.05.

Data were analyzed using IBM© SPSS© Statistics version 22 (IBM© Corp., Armonk, NY, USA) and MedCalc© version 13 (MedCalc© Software bvba, Ostend, Belgium). Continuous numerical variables were presented as mean and SD, and intergroup differences were compared using the independent-samples (unpaired) t test. The Welch test was used in place of the t test whenever equality of variance could not be assumed. Categorical data were presented as number and percentage and differences were compared using the Pearson chi-squared test.

A two-sided p-value < 0.05 was considered statistically significant.

Our study is a non-equivalence study. So you are supposed to use usual two-sided tests (see Table 1).

Table 1 Category scale of intraoperative surgical field assessment.

0	No bleeding.
1	Slight bleeding – no suctioning required.
2	Slight bleeding – occasional suctioning required.
3	Slight bleeding – frequent suctioning required.
4	Moderate bleeding – frequent suctioning required. Bleeding threatens the surgical field directly after suctioning removed.
5	Severe bleeding – constant suctioning required. Bleeding appears faster than can be removed by suction. Surgical field severely threatened and surgery is not possible.

4. Results

Demographic data, duration of hypotension, duration of anesthesia and baseline hemodynamic data did not show any statistically significant difference among groups (Table 2). Infusion rate and the total dose of remifentanil and nitroprusside are shown in Table 3. There were no statistically significant differences between both groups regarding PaO_2, $PaCO_2$ and PH data (Table 4).

Measurements of systolic, diastolic and mean arterial pressure during the period of hypotension showed no significant differences between both groups. Heart rate during the periods of hypotension was significantly lower in group (I) = remifentanil group compared to group (2) = sodium nitroprusside group ($p < 0.05$).

Time to reach target systolic arterial blood pressure of 80 mmHg was significantly more in remifentanil group than in nitroprusside group ($P < 0.05$) (Table 3). There were no postoperative complications in any group and all patients were discharged in the same day of operation (after 6 h of operation end).

Table 2 Patients' characteristics in both study groups.

Variable	Remifentanil group ($n = 65$)	Nitroprusside group ($n = 65$)	p-value
Age (years)	30.0 (8.6)	29.0 (10.9)	0.580[a]
Weight (kg)	70.9 (24.5)	68.2 (26.3)	0.555[a]
Gender (M/F)	39/16	46/19	0.853[b]
Baseline SBP (mmHg)	114 (19)	115 (22)	0.797[a]
Baseline MAP (mmHg)	84 (9)	82 (12)	0.308[c]
Baseline DBP (mmHg	69 (18)	65 (19)	0.300[a]
Baseline heart rate (bpm)	73 (20)	75 (20)	0.569[a]
Duration of anesthesia (min)	79 (32)	82 (22)	0.557[c]

Data are presented as mean (SD).
[a] Unpaired t test.
[b] Pearson chi-squared test.
[c] Welch test.

Table 3 Details of the induced hypotension in both study groups.

Variable	Remifentanil group (n = 65)	Nitroprusside group (n = 65)	p-value
Time to onset of induced hypotension (s)	36 (21)	55 (15)	<0.0001[a]
Time to target blood pressure (s)	68 (15)	109 (52)	<0.0001[a]
Duration of induced hypotension (min)	47 (13)	48 (19)	0.948[a]
SBP during induced hypotension (mmHg)	81 (10)	80 (10)	0.585[b]
MAP during induced hypotension (mmHg)	57 (4)	56 (4)	0.174[b]
DBP during induced hypotension (mmHg)	48 (6)	48 (6)	0.864[b]
Heart rate during induced hypotension (bpm)	67 (25)	90 (25)	<0.0001[b]
Total dose of hypotensive agent (mg)	1.6 (0.6)	5.4 (2.8)	<0.0001[a]
Infusion rate of hypotensive agent (μg/kg/min)	0.31 (0.13)	0.98 (0.61)	<0.0001[a]

Data are presented as mean (SD).
[a] Welch test.
[b] Unpaired t test.

Table 4 Change in arterial blood gas variables in both study groups.

ABG variable	Time	Remifentanil group (n = 65)	Nitroprusside group (n = 65)	p-value
PaO_2	Baseline	93 (4)	92 (5)	0.171[b]
	20 min	187 (33)	166 (40)	0.001[a]
	40 min	173 (31)	180 (28)	0.187[a]
	At PACU	141 (27)	123 (26)	<0.0002[a]
$PaCO_2$	Baseline	36 (2)	37 (2)	0.130[a]
	20 min	32 (2)	41 (3)	<0.0001[b]
	40 min	34 (3)	40 (3)	<0.0001[a]
	At PACU	40 (3)	43 (3)	<0.0001[a]
pH	Baseline	7.37 (0.16)	7.39 (0.20)	0.552[b]
	20 min	7.41 (0.10)	7.31 (0.06)	<0.0001[b]
	40 min	7.36 (0.27)	7.29 (0.09)	0.045[b]
	At PACU	7.34 (0.26)	7.29 (0.09)	0.142[b]

Data are presented as mean (SD).
[a] Welch test.
[b] Unpaired t test.

5. Discussion

In the present study, controlled hypotension is a well established technique to decrease blood loss and improve surgical visibility during rhinoplasty and also many other operations. Many techniques have been successfully used in healthy patients. In this study, we traced the advantage of using Remifentanil to induce controlled hypotension rather than the traditional use of sodium nitroprusside. The remifentanil group showed statistically significant decrease time to reach target systolic arterial blood pressure (86 ± 15) after (36 ± 12) versus sodium nitroprusside group (109 ± 55) after (55 ± 15).

These results were also reported by other studies such as Philip [4] who used remifentanil to induce hypotensive in total intravenous anesthesia and also Schuttler et al. [9] who used remifentanil in comparison with alfentanil in patients undergoing major abdominal surgery.

Sodium nitroprusside also provided controlled hypotension in the second group of patients in this study with advantages of short duration of action, potency, and short time to reach the target hypotension, and this result was also reported by Boezzart and his colleagues [10], who also used nitroprusside for inducing controlled hypotension for functional endoscopic sinus surgery in comparison with esmolol and reported that nitroprusside is a very effective drug in inducing controlled hypotension.

In the current study, we reported disadvantages of sodium nitroprusside as reflex tachycardia which is not suitable in patients with ischemic heart diseases, arrhythmia, tachyphylaxis, and also rebound hypertension which is not suitable for already hypertensive patients. These disadvantages were also reported by Pinaud and his colleagues [11] who used nitroprusside to induce hypotension in patients undergoing craniotomies. Nitroprusside also involved in inducing light but significant hypercapnia and acidosis as previously shown in this study, and this was also reported by Tinker and Michenfelder [12] who did a full study on nitroprusside in 1976.

Nitroprusside is a direct vasodilator acting directly on the vascular smooth muscle causing generalized vasodilatation and increase cardiac output, so increasing the blood flow to the mucous membranes and to the capillaries these may lead to increasing bleeding during surgery. This disadvantage of nitroprusside was not reported in this study but, it is reported by Chan et al. [13] who used nitroprusside to induce hypotension in patients undergoing anterior maxillary osteotomy who revealed disadvantages of nitroprusside in the form of

degradation by light, cyanide toxicity and the need for invasive blood pressure measurement.

6. Conclusion and recommendations

The present study showed that remifentanil infusion was interesting in providing controlled hypotension as well as dry surgical field in patients undergoing rhinoplasty with no need for additional use of a potent hypotensive agent. Further studies on large scale are recommended to confirm these results.

Conflict of interest

We have no conflict of interest to declare.

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