

COMPARISON BETWEEN PROSTAGLANDIN E1, AND ESMOLOL INFUSIONS IN CONTROLLED HYPOTENSION DURING SCOLIOSIS CORRECTION SURGERY A CLINICAL TRIAL

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Abstract

Background: scoliosis correction surgery is common in children, and adolescents. Deliberate hypotension is indicated in scoliosis correction procedures, because bloodless field is needed for exposure of the nerve roots, and to decrease the need for blood transfusion. Protection of the kidneys during deliberate hypotension is essential. The ideal hypotensive drug maintains the renal function and the urine output during the period of hypotension. Aim of this study is to compare Prostaglandin E1, and Esmolol hypotensive effects, bleeding score, and their effects on the serum creatinine, and urine output.

Patients and methods: Twenty patients under went hypotensive anesthesia during scoliosis correction procedure, were enrolled in this clinical trial. In group 1 (n = 10) (Esmolol infusion), group 2 (n = 10) (prostaglandin E1 infusion), Parameters were measured: Mean arterial blood pressure, Heart rate, (preoperative, just after induction, 15 minutes, 30 minutes, 60 minutes after starting the infusions, and 15 minutes after discontinuation of infusions). The bleeding score was assessed at (15 minutes, 30 minutes, 60 minutes after starting the infusions).

Results: heart rate was significantly higher in prostaglandin E1 group than Esmolol group at 15, 30, 45, and 60 minutes. There was significant difference in the bleeding score only after 30 minutes, The target mean blood pressure (50 mmHg) was achieved at 30 minutes in group 2 (prostaglandin E1), while it was achieved at 60 minutes in group 1 (Esmolol group). There were significant differences in Mean blood pressure between both groups at 15, 30, 45, 60 minutes after starting the infusions. Creatinine level was significantly lower in prostaglandin E1 group, while the intraoperative urine output was significantly higher in prostaglandin E1 group.

Conclusions: Prostaglandin E1 hypotensive effects started earlier than Esmolol and its bleeding score is better than esmolol especially at thirty minutes after initiation of the infusion. Prostaglandin E1 can maintain renal function and urine output more than Esmolol. This study recommended using Prostaglandin E1 to induce hypotensive anesthesia in scoliosis correction surgery.

Key words: Prostaglandin E1, Esmolol, hypotensive anesthesia, Scoliosis.

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Introduction

Deliberate hypotension (Induced hypotension) is decreasing of blood pressure by 30% or the mean blood pressure (50-70 mmHg) or systolic blood pressure (80-90 mmHg) pharmacologically. Deliberate hypotension is indicated in microsurgical procedures, when bloodless field is needed such as ear surgery, or to decrease the need for blood transfusion as in scoliosis correction procedure (Thomas et al, 1974).

Scoliosis correction is one of the major operations, the main problem is the blood loss, blood loss in this operation may be 3-4 units, also the patients are usually adolescents and young age, and there is increased risk of blood transfusion complications specially infection. Another advantage of induced hypotension during scoliosis correction surgery is exposure of the roots and nerves (Degoute, 2007).

There are many drugs used to induce hypotension, may be intravenous drugs, as Na nitroprusside, nitrates, Ca channels blockers, beta blockers, Remifentanyl, ACE inhibitors and clonidine, Adenosine, these drugs have many complications as bradycardia, depression of myocardial contractility. Volatile anesthetics are halothane, isoflurane and sevoflurane in which high dose is needed to produce hypotension; it can be harmful for the kidney and liver (Longnecke, 1984).

The success of such technique is to keep the perfusion for vital organs; the major complications of deliberate hypotension are renal, hepatic, and cerebral blood flow impairment and alteration of the auto regulation of the organs.

Esmolol is a selective ultra short β_1 blocker lowers blood pressure by decreasing cardiac output and heart rate. It has rapid onset of action within 1 minute of starting infusion. Many studies investigated the effects of Esmolol on auto regulation of the liver, kidney and brain. Many studies demonstrated its effect on cerebral auto regulation (Masuda R, Takeda S, 2008 and Wiest, 1995).

Prostaglandin E1 (PGE1) is a vasodilator by its

direct effect on the smooth muscles fibers, it has also direct bronchodilator, and PGE1 is an agonist at the PGE2-sensitive receptor (subtype EP2) that activates adenylate cyclase to increase intracellular cyclic adenosine. Monophosphate (cAMP), induces smooth muscle relaxation. Therefore, increased intracellular cAMP may contribute to the spasmolytic effects observed, other studies demonstrated that PGE1 can maintain the renal and hepatic blood flow, doesn't disturb their auto regulation. It is usually used in cardiac patient as patent ductus, coarctation of the aorta, (Lam, 1990 and Tobias, 2002).

Aim of this study: is to compare Prostaglandin E1 and Esmolol hypotensive effects, the bleeding score, and renal function in controlled hypotension for scoliosis correction surgery.

Patients and Methods

After receiving ethical approval, and Parental written informed consents, twenty patients under went hypotensive anesthesia for scoliosis correction in Kasr EL Ani hospital, were enrolled in this clinical trial. Patients were divided into 2 groups, group 1 (n = 10), received Esmolol infusion, and group 2 (n = 10) received Prostaglandin E1 infusion as hypotensive drugs. The patients were ASAII-II; the age ranged 13-18 years old, they were with accepted pulmonary function tests.

Setting

The study was done in Kasr El Ini Teaching Hospital Cairo University.

Study design: clinical trial.

The sample size was a convenient sample.

Exclusion criteria: Were Cardiac disease, Diabetes mellitus, Gross anemia, hemoglobinopathies, polycythemia, Hepatic disease, Ischemic cerebrovascular disease, renal disease, Respiratory insufficiency, severe systemic hypertension.

Each patient received 500 ml of lactated Ringers solution, 30 minute before induction of anesthesia.

For premedication midazolam 0.1 mg/kg IV was given 15 minute before induction.

Induction of anesthesia was achieved by 2.5-3 mg/kg propofol injected intravenously on 3-5 minute to prevent sudden drop of blood pressure, fentanyl 1 µg/kg iv. Tracheal intubation was facilitated with 0.1 mg/kg vecuronium Maintenance of anesthesia:

Anesthesia was maintained with 50% O2 in air with 1.3 MAC of isoflurane, and then 0.05 mg/kg vecuronium.

Ventilation was adjusted to maintain end tidal Co2 between 30-35mmHg

6 ml/kg/hour IV crystalloid solution was given, and arterial canula was inserted for invasive blood pressure monitoring.

The patients were placed in prone position.

Monitoring included invasive blood pressure measurement, SO2 (O2 saturation), end tidal CO2 and ECG.

Target mean arterial pressure was 50 mmHg.

In group 1 (Esmolol) was initially given by a bolus of 500 µg/kg, and the infusion of Esmolol was started at a rate of 100 µg/kg/min, then increased gradually (300-500 µg/kg/min) every 5 minutes until the target mean blood pressure was achieved.

In group 2 (PGE1) was started at an infusion rate of 0.5 µg/kg/min, and increased gradually every 5 minutes (the maximum dose is 2 µg/kg/min) to reach the target mean blood pressure.

Parameters measured

Mean arterial blood pressure, Heart rate, (preoperative, just after induction, 15 minutes, 30 minutes, 60 minutes after starting the infusions, and 15 minutes after discontinuation of infusions), surgical field estimated by using bleeding score (2), the target was the score 2-3 (15 minutes, 30 minutes, 60 minutes after starting the infusions), intraoperative urine output (liters), creatinine mg/dl (preoperative, and just post operative).

Bleeding score

0	No bleeding
1	Slight bleeding no suction is required
2	Slight bleeding occasional suction is required
3	Moderate bleeding, frequent suction is required
4	Moderate bleeding, frequent suction is required, bleeding threaten surgical field directly after suction removed.
5	Severe bleeding, constant suction is required, bleeding appears faster than can be removed by suction surgical field severely threatened and surgery is impossible.

Statistical analysis

Sample was convenient sample.

Statistical analysis: Data were presented as mean and standard deviation (SD). Comparison of quantitative variables between the study groups using Mann Whitney U test for independent samples. Within group comparisons base line and after application were done using Wilcoxon signed rank test for paired samples. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculation were done using computer programs Microsoft Excel version 7 (Microsoft Corporation, Ny, USA) and (statistical Package for the social Science; SPSS Inc, Chicago, IL, USA) statistical program.

Results

There was no significant difference between both groups in age, sex and weight (Table 1).

Table 1
Demographic data of both groups mean ± SD

	Group 1 (Esmolol) (n = 10)	Group 2 (PGE1) (n = 10)
Age (yr)	14.7 ± 1.9	14.6 ± 1.9
Sex (m/f)	2/8	1/9
Weight (kg)	40.5 ± 11.1	39 ± 10.7
ASA I/II	4/6	5/5

Heart rate was significantly higher in Group

2 (PGE1) than group 1 at 15,30,45,60, but it was insignificant at 15 minute after discontinuation of the infusions (Table 2).

Table 2
Heart rate changes during hypotensive anesthesia mean ± SD

	Group 1 (Esmolol) (n = 10)	Group 2 (PGE1) (n = 10)
Preoperative heart (HR) Beat/min	83.6 ± 2.7	83.4 ± 2.3
Just After induction (HR) Beat/min	81 ± 2.6	79.7 ± 3.1
15 min (HR) after starting of infusion. Beat/min	64.7 ± 1.7	77.5 ± 3.9*
30 min (HR) after starting of infusion. Beat/min	63.5 ± 1.7	75.5 ± 3.7*
45 min (HR) Beat/min	62.2 ± 1.2	73.6 ± 3.0*
60 min (HR) Beat/min	60.1 ± 1.6	70.9 ± 2.9*
15 min (HR) after discontinuation of infusion.	81 ± 2.4	79.9 ± 4

* p ≤ 0.05

There was significant difference in the bleeding score only after 30 minutes, p was (0.005), and it was insignificant at 15, 45, 60 minutes after initiation of infusions (Table 3). The target mean blood pressure (50 mmHg) was achieved at 30 minutes in group 2 (prostaglandin E1), while it was achieved at 60 minutes in group 1 (Esmolol group). There were significant differences in Mean blood pressure between both groups at 15, 30, 45, 60 minutes after starting the infusions (Table 4).

Table 3
Bleeding score of both hypotensive drugs mean ± SD

Timing of bleeding scores assessment.	Group 1 bleeding score	Group 2 bleeding score.
15 min	2.5 ± 0.5	2.3 ± 0.6
30 min	2.2 ± 0.4	1.7 ± 0.4*
45 min	1.6 ± 0.4	1.5 ± 0.5
60 min	1.3 ± 0.3	1.2(0.4

* p ≤ 0.05

Table 4
blood pressure changes of both groups mean ± SD

	Group 1 (Esmolol) (n = 10)	Group 2 (PGE1) (n = 10)
Preoperative mean blood pressure (MBP) (mmHg)	72.6 ± 3.7	73.8 ± 3.3
15 min (MBP) mmHg. After initiation of the infusion	60.8 ± 3.5	55.2 ± 2.6*
30 min (MBP) mmHg	60.7 ± 1.5	52.9 ± 1.7*
45 min (MBP) mmHg	59.6 ± 2.3	51.9 ± 1.9*
60 min (MBP) mmHg	55.4 ± 2.1	50.1 ± 1.1*
15 min after the discontinuation of infusion (MBP) mmHg	72.7 ± 3.8	72.7 ± 3.8

* p ≤ 0.05

Post operative creatinine was significantly higher in Esmolol group than in prostaglandin E1 group, P was <0.001. Intraoperative urine out was significantly higher in prostaglandin E1 than in Esmolol group (Table 5, 6).

Table 5
preoperative, and postoperative mean ± SD of creatinine (mg/dl)

creatinine mg/dl	Group 1 (Esmolol)	Group 2 (PGE1)
preoperative	0.4 ± 0.2	0.5 ± 0.3
postoperative	1.8 ± 0.3	0.7 ± 0.1*

* p ≤ 0.05

Table 6
Mean ± SD of intraoperative urine output.

Intraoperative urine output (liter)	Group 1 (Esmolol)	Group 2 (PGE1)
	800 ± 200)	1200 ± 200*

* p ≤ 0.05

Discussion

There are many considerations about the drugs used to induce hypotensive anesthesia in scoliosis correction surgery, as maintenance of organ blood flow, organ auto regulation which in turn determines the organ functions, and the presence of respiratory, or

cardiac lesions (Tobias, 2002).

This study was planned to compare the hypotensive effects of Esmolol, and Prostaglandin E1 and their effects on the renal function. This study found that both drugs could induce hypotension, and good bleeding score, however Prostaglandin E1 hypotensive effect started earlier than Esmolol and its bleeding score is better than esmolol especially at thirty minutes after initiation of the infusion. Post operative creatinine was significantly lower in Prostaglandin E1 group than in Esmolol group, and the urine output was significantly higher in PGE1 group. The explanation is PGE can maintain renal blood flow and renal autoregulation more than Esmolol. Some studies found that PGE1 can maintain the mesenteric blood flow, so it can maintain hepatic, renal blood flow, and organs auto regulation. PGE1 is an agonist at the PGE2-sensitive receptor (subtype EP2) that activates adenylate cyclase to increase intracellular cyclic adenosine monophosphate (cAMP) induces smooth muscle relaxation that maintains blood flow in the small venules and arterioles of the different organs (Takeda et al, 2000 and Hoka et al, 1993).

Other studies found that Prostaglandin E1 has many advantages over Esmolol, as it does not decrease

heart rate, depress myocardium, it has antiarrhythmic effects, and decrease Oxygen consumption. So it can be used in border line cardiac patients, another benefit of this drug is its action through the direct smooth muscle fibers relaxation, it has a bronchodilator effects, so it can be used in respiratory impairment patients (Kubota et al, 2004 and Gibson, 2004).

Other studies demonstrated that esmolol when combined with inhalational anesthesia it will impair the cerebral auto regulation (Mackenzie et al, 1993).

The mechanism of action of Esmolol depends on decreasing heart rate, and cardiac output that leads to decrease the renal blood flow which stimulates the reninangiotensin system. So the glomerular filtration rate falls (Andel et al, 2001).

Conclusions: Prostaglandin E1 can induce hypotensive anesthesia in scoliosis surgery as Esmolol, Prostaglandin E1 hypotensive effects started earlier than Esmolol and its bleeding score is better than esmolol especially at thirty minutes after initiation of the infusion. Prostaglandin E1 can maintain renal function and urine output more than Esmolol. This study recommended using Prostaglandin E1 to induce hypotensive anesthesia in scoliosis correction surgery.

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