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Baroreflex Integrity: A Comparative Study between Propofol and Propofol with Sevoflurane Anesthesia

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Abstract

Background: The baroreceptor reflex is the main mechanism for short-term regulation of blood pressure and a major determinant of the blood pressure responses associated with various behaviors. Baroreflex Sensitivity (BRS) is the amount of change in beat-to-beat interval (RR) against a 1mmHg systolic blood pressure deviation. BRS is traditionally measured by bolus injection of vasoactive drugs such as phenylephrine which causes increase in Systolic Blood Pressure (SBP) or Na Nitroprusside (NTP) which causes decrease in systolic blood pressure.

Methods: This comparative study included 40 patients who were scheduled for laparoscopic gynecological surgery. Patients were divided into two groups (propofol-group) and (combined propofol & sevo group) with 20 patient in each group. Pressor and depressor tests were done pre, intra and postoperative with recording systolic blood pressure and R-R interval as well as the diastolic overshoot in the awake state, under anesthesia and postoperatively.

Results: There were no significant differences in patient population demographic data, awake pretest SBP and HR. The results of our study suggest that there was no significant depression of baroreceptors except for the depressor slopes in the propofol group after induction of anesthesia with full recovery of baroreceptors in the postoperative results.

Conclusion: Data obtained from this study showed that use of propofol alone may lead to depression of baroreceptors as compared to combined use of sevoflurane and propofol. On the other hand, there was no difference in haemodynamics among both groups.

Key Words: *Anesthesia – Propofol – Sevoflurane – Baroreflex.*

Introduction

THE baroreceptor reflex is the main mechanism for short-term regulation of blood pressure and a major determinant of the blood pressure responses associated with various behaviors [1]. The cardiac branch of the baroreflex that relates blood pressure to Inter-Beat Interval (IBI) is one relevant source of vagal influences and cardiac autonomic regulation, being the main generator of autonomic measures such as respiratory sinus arrhythmia and heart rate variability [2].

Baroreflex Sensitivity (BRS) is the amount of change in beat-to-beat interval (RR) against a 1mmHg systolic blood pressure deviation. BRS is traditionally measured by bolus injection of vasoactive drugs such as phenylephrine which causes increase in Systolic Blood Pressure (SBP) or Na Nitroprusside (NTP) which causes decrease in systolic blood pressure. The increase/decrease in SBP tempts a decrease/increase in the corresponding RR interval (milliseconds) [3,4].

Propofol, an intravenous anaesthetic, is now widely used in clinical practice because of its favorable recovery profile and low incidence of side effects [5].

The effects of contemporary available general anesthetics, such as propofol or sevoflurane on baroreflex control of Heart Rate (HR) have been extensively investigated in humans [6]. More importantly, how long volatile and intravenous anesthetics exert depressive effects on the baroreflex function after general anesthesia and, thus, how full recovery of baroreflex function actually takes place [7].

Patients and Methods

The study was held at Kasr El-Ainy Hospital in Gynecology and Obstetrics Department in the period from April 2012 - December 2012. This comparative study included 40 patients who were scheduled for laparoscopic gynecological surgery.

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The study was done after approval of Departmental Ethics and Research Committee and obtaining written informed consent from all patients enrolled in the study; held at Kasr El-Ainy Hospital, Faculty of Medicine.

Sample size measurement:

Our study was the first to discuss the effect of combined propofol and sevoflurane anesthesia on baroreflex integrity, so, we couldn't calculate sample size for this article.

Inclusion criteria:

- Adult female patients 20-40 years.
- (American Society of Anesthesiologists physical status I).
- Undergoing laparoscopic gynecological surgery lasting for 1-2 hours.

Exclusion criteria:

Major organ dysfunction (as hepatic, renal and respiratory dysfunction).

- Patients on steroid therapy.
- Patients with systemic illness known to affect inflammatory response as rheumatoid arthritis.
- Women with Body Mass Index (BMI) >30.
- Patients receiving cardiovascular drugs.
- Age less than 20 and above 40 years.
- Patients with dysautonomia.
- Diabetics.

Study design:

- Before induction of anesthesia; patients were randomly assigned to one of two equal groups each containing 20 patients. Randomization was achieved by permuted-block randomization, ensuring allocation concealment include Sequentially-Numbered, Opaque, Sealed Envelopes (SNOSE).
- Group A (n=20): This group received general anaesthesia in the form of TIVA using propofol.
- Group B (n=20): This group received general anaesthesia using both propofol and sevoflurane.

Anesthetic management:

Awake control study:

Upon arrival to the pre-induction room, the patient will receive supplementary oxygen via a nasal cannula, and will be monitored with ECG and pulse oximeter. Under local infiltration anesthesia (lidocaine 2%) a peripheral venous (20 gauge) cannula was inserted, and a 20 gauge arterial cannula was inserted in the radial artery of the non dominant hand after performance of modified Allen's test. Each patient received 10ml/kg Hartmann's solution before initiation of the study.

To assess baroreflex control of HR, pressor and depressor tests were performed using i.v. bolus injections of phenylephrine (1µg/kg) and sodium nitroprusside (1 µg/kg) to increase and decrease Systolic Pressure (SP) by 15-30mmHg, respectively and the first component of baroreflex was measured as the R-R interval changes secondary to BP changes (msec/mmHg).

The second component namely baroreflex control of arteriolar constriction was assessed by measuring the overshoot in diastolic arterial pressure during the recovery phase of the cardiovascular response to the Valsalva maneuver (peak diastolic blood pressure within 30 seconds). The over-shoot during this phase is associated with the increase in blood pressure above the level at rest caused by the return of cardiac output after release of the raised airway pressure, coupled with an increased systemic vascular resistance reflecting the continuing baroreceptor reflex arteriolar constriction. Patients were trained to perform Valsalva maneuvers in the form of forced expiration against closed glottis and maintaining straining for 10 seconds in the supine position while recording HR and BP changes.

Induction of anesthesia:

All patients received 100% oxygen via face mask for 2 to 3min prior to induction of general anesthesia and they received analgesia in the form of fentanyl 3µg/kg 5 minutes before planned intubation.

In Group A, anaesthesia was induced with propofol at dose 2mg/kg.

In Group B, anesthesia was induced with propofol (dose 1mg/kg) and end tidal concentration of 2.5% sevoflurane.

Maintenance:

In Group A anesthesia was maintained with propofol infusion at a rate of 150µg/kg/min.

In Group B anesthesia was maintained with end tidal concentration 1.5% sevoflurane and propofol infusion at a rate 75µg/kg/min.

Analgesia was supplemented in the form of Paracetamol intravenously over 20 minutes after induction (15mg/kg) in addition to diclofenac by intravenous infusion over 20 minutes (2mg/kg).

Baroreflex control of heart rate was again assessed with the pressor and depressor tests using i.v. bolus injections of phenylephrine (1 µg/kg) and sodium nitroprusside (1 µg/kg) to increase and decrease Systolic Pressure (SP) by 15-30mmHg, respectively. Baroreflex control of vasoconstriction was assessed by the application of Positive End Expiratory Pressure (PEEP) of 30cm H_2O then the expiratory valve is released and the peak diastolic blood pressure overshoot in the early phase (within 30 seconds of release) was recorded.

Postoperative management:

After discontinuation of propofol infusion or sevoflurane anesthesia and after the return of adequate spontaneous respiration and responses to verbal commands was confirmed, extubation was done and patients were transferred to the recovery room where they were left undisturbed with supplemental oxygen 2L/min.

After 20 minutes of recovery, Baroreflex control of heart rate was again assessed with the pressor and depressor tests using i.v. bolus injections of phenylephrine (1 µg/kg) and sodium nitroprusside (1 µg/kg) to increase and decrease Systolic Pressure (SP) by 15-30mmHg, respectively, also, Baroreflex control of arteriolar constriction was assessed again by valsalva maneuver the same way as in the awake preoperative state.

Results

There were no significant differences in patient population demographic data, awake pretest Systolic Blood Pressure (SBP) and Heart Rate (HR).

In the present study, simultaneous recordings of haemodynamic variables including systolic blood pressure, heart rate variability and diastolic overshoot were comparatively analyzed between patients receieving propofol and combined propofol and sevoflurane with using pressor, depressor tests and Valsalva maneuver for baroreflex integrity.

In the propofol group, systolic blood pressure was significantly decreasaed intraoperatively after the depressor test while significant difference in heart rate variability between the pressor and depressor tests that was recorded preoperatively and postoperatively was abolished intraoperatively.

In the combined group, SBP was significantly decreasaed intraoperatively after the pressor and depressor tests while significant decrease in heart rate variability between the pressor and depressor tests that was recorded preoperatively and intraoperatively was abolished postoperatively.

Our study revealed that in patients randomized to the two groups there was a positive significant correlation between changes in systolic blood pressure (SBP mmHg) and R-R interval (msec) following phenylephrine administration preoperatively, intra-operatively and postoperatively (T1-T3). Also there was a negative significant correlation between systolic blood pressure (SBP mmHg) and R-R interval (msec) following Sodium Nitroprusside administration preoperatively, intraoperatively and postoperatively (T1-T3).

In Group A the slope following sodium Nitroprusside infusion was significantly less steep compared to intraoperative slope following phenyl ephrine infusion and postoperative slope following sodium Nitroprusside infusion (p=0.007 and <0.0001).

However, in Group B under all circumstances the slope was comparable in the preoperative, intraoperative and postoperative period irrespective of agent used (phenyl-ephrine and sodium nitroprusside).

In the preoperative, intraoperative and postoperative period the slope was comparable between both groups (Groups A & B) irrespective of anesthetic technique and/or agent used (phenylephrine and sodium nitroprusside).

Diastolic overshoot:

Diastolic overshoot (mmHg) was comparable (p=0.067), irrespective of anesthetic technique (Groups A & B) and timings (preoperative, intraoperative and postoperative.

Table (1): Mean ± SD. For slope during preoperative, intraoperative and postoperative among the two groups.

	Group A (n=20)		Group B (n=20)	
	PH	Na	PH	Na
Preoperative	9.41±1.24	8.51±1.37	8.46±1.48	8.44±0.99
Intraoperative	9.19±1.26	7.27±1.47*	8.24±1.5	8.31±1.07
Postoperative	8.95±1.94	9.51±2.24	8.79±0.98	7.93±1.44

PH : Phenyl-Ephrine.
Na : Sodium Nitroprusside.

Table (2): Mean ± SD. For diastolic overshoot (mmHg) among all groups.

	Preoperative	Intraoperative	Postoperative
- Group A (TIVA n=20)	8.0±0.7	7.6±0.6	7.8±0.6
- Group B (Combined n=20)	8.0±0.6	8.0±1.0	8.1±0.8

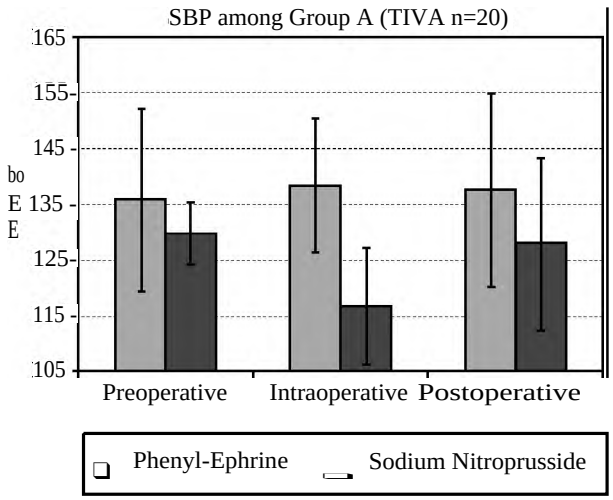

Fig. (1): Systolic Blood Pressure (SBP) among Group A patients. *Denotes significantly lower compared to intraoperative phenyl-ephrine administration $p<$ 0.0001.

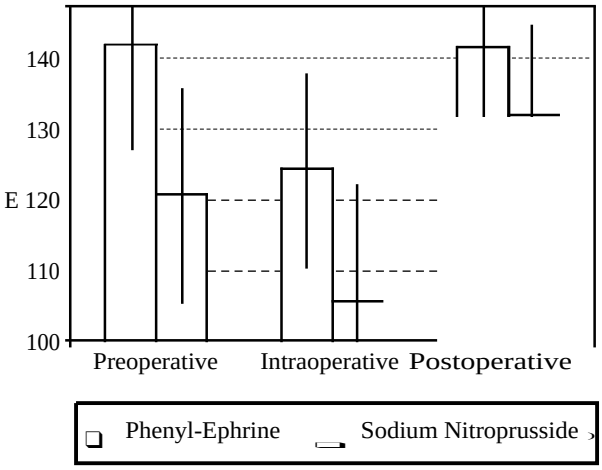

Fig. (2): Systolic Blood Pressure (SBP) among Group B. *significantly lower compared to preoperative and postoperative values (p=0.011, 0.012 for phenyl ephrine and p=0.039 and <0.0001 for sodium Nitroprusside) respectively. B= Combined anesthesia (Propofol + Sevoflurane).

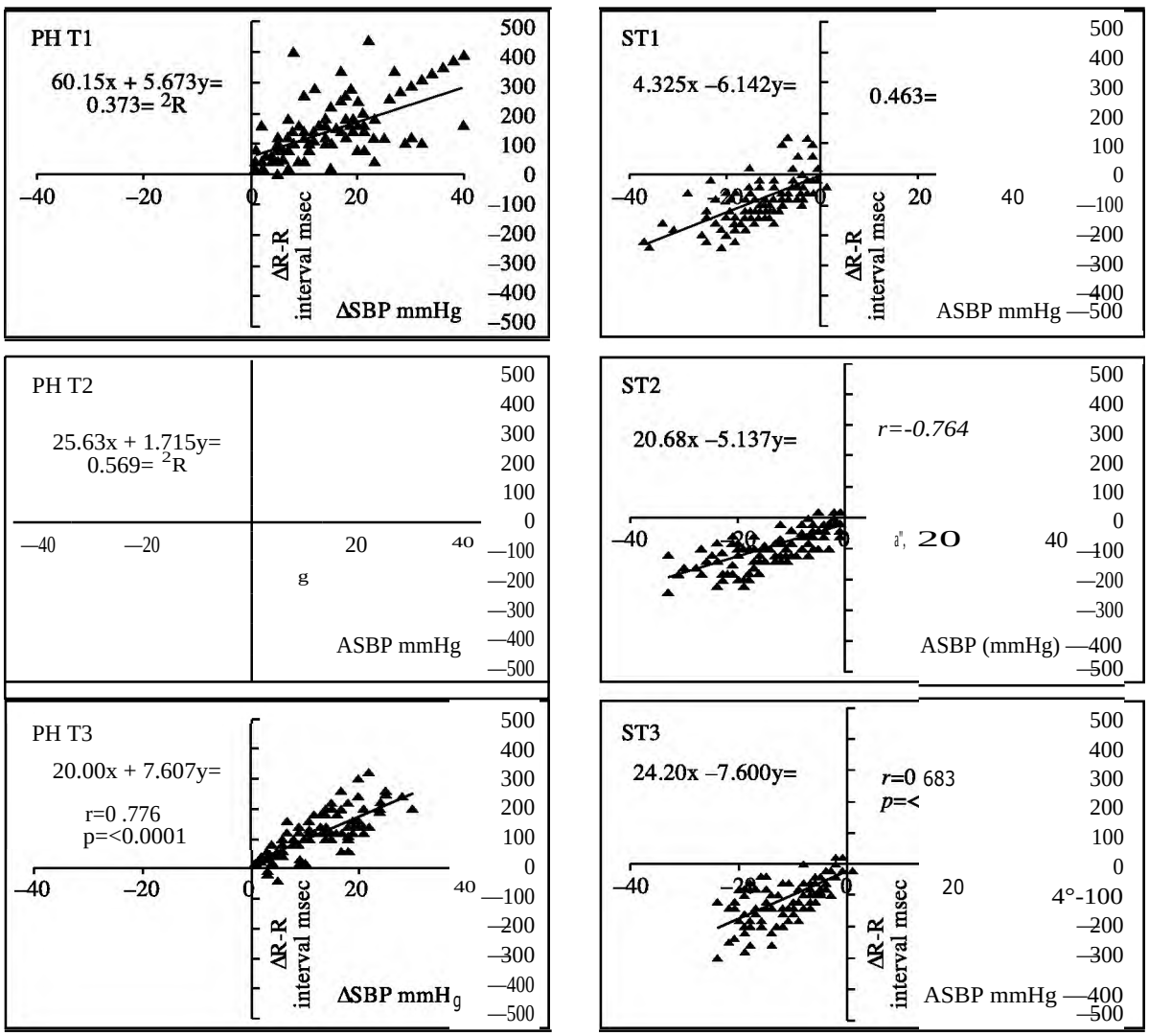

Fig. (3): Illustrates correlation between changes in SBP AmmHg and R-R interval Amsec among Group A patients (TIVA n=20).

PH: Phenyl-Ephrine. Tl: Preoperative. T3: Postoperative
S : Sodium nitroprusside. T2: Intraoperative.

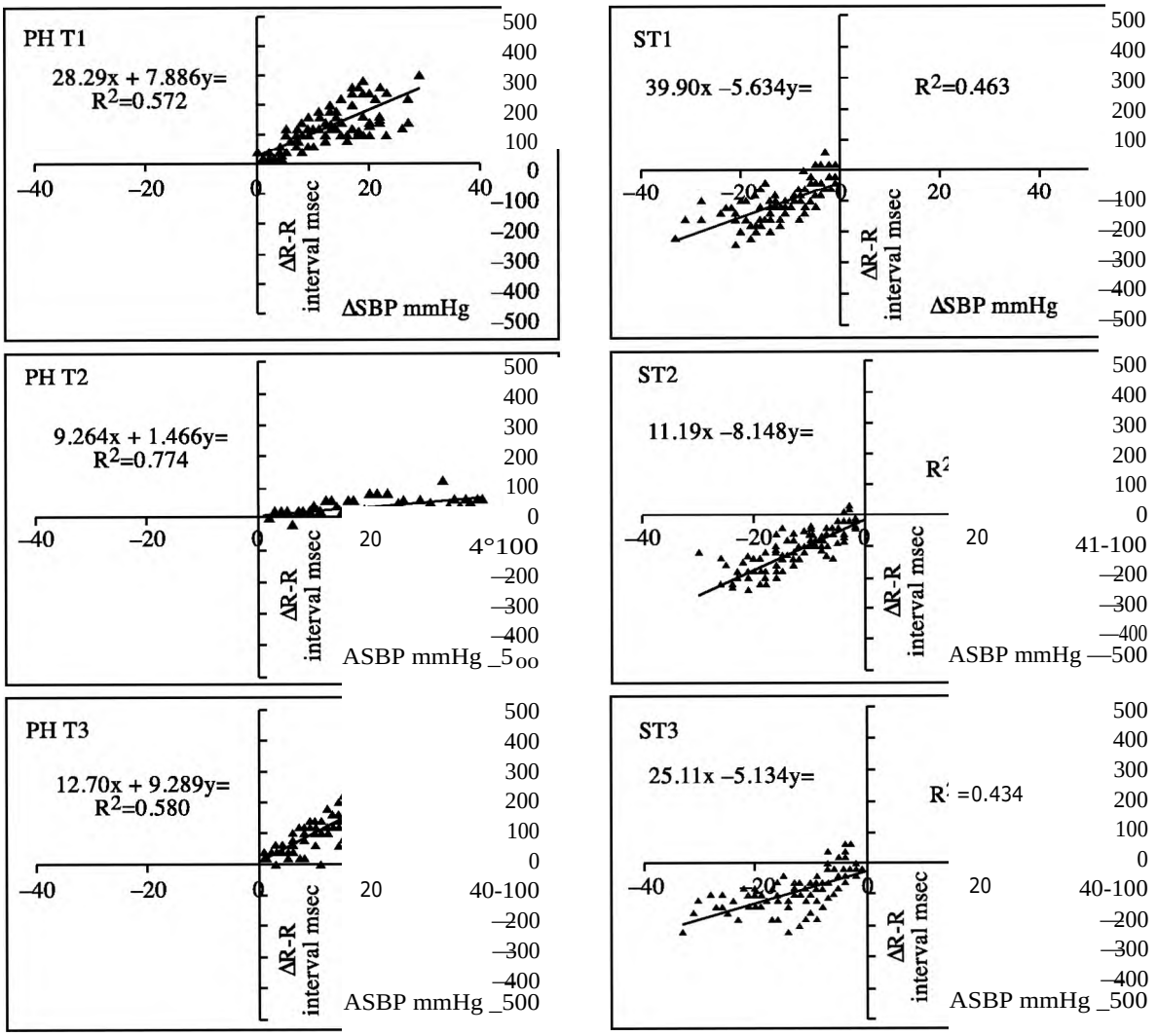

Fig. (4): Illustrates correlation between changes in SBP \mmHg and R-R interval 1msec among Group B patients (combined n=20).

PH: Phenyl-Ephrine.
S : Sodium nitroprusside.
Ti: Preoperative.
T2: Intraoperative.
T3: Postoperative

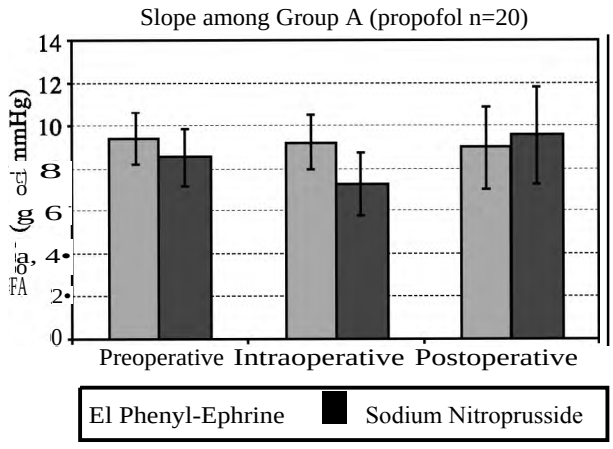

Fig. (5): Mean ± SD for slope among Group A (Propofol n=20) patients. * denotes significantly lower compared to intraoperative phenyl-ephrine,p=0.007 and postoperative sodium nitroprusside.

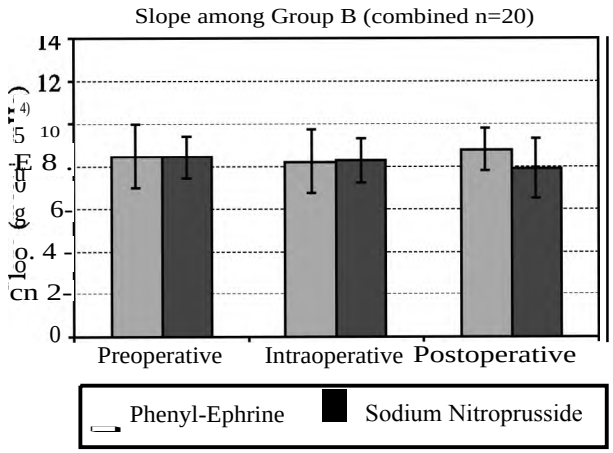

Fig. (6): Mean ± SD for slope among Group B (Combined n=20) patients.

Discussion

The term 'arterial baroreceptor reflex' is used to refer to a variety of physiological responses elicited by changes in baroreceptor afferent activity. While the baroreceptor reflex is often used in specific reference to the reflexive change in ABP and heart rate brought about by changing autonomic outflow to the heart and vasculature, there are a large number of physiological responses resulting from changes in baroreceptor afferent input, and they would each appropriately be termed a baroreceptor reflex [8].

The results of our study suggest that there was no significant depression of baroreceptors except for the depressor slopes in the propofol group after induction of anesthesia with full recovery of baroreceptors in the postoperative results.

The effects of propofol on baroreflex function have shown controversial results previously, but appear to be dose-related. Cullen et al., studied propofol infusion rates of 54 and 108ug/kg/min supplementing 66% nitrous oxide in oxygen in spontaneously breathing healthy patients, and found that phenylephrine pressor and nitroprusside depressor tests were unaffected, this study was similar to our study in using pressor and depressor tests as well as valsalva maneuver for the assessment of baroreflex integrity. The different findings of this study from ours may be as a result of applying it on only 12 patients (divided on two groups) undergoing a variety of general surgical procedures. More over the patients received morphine sulfate 0.15mg/kg IM 1hr before arrival in the induction room and despite the patients were breathing spontaneously, their end tidal CO_2 was not monitored [9].

Similarly, Samain et al., showed in spontaneously breathing patients that propofol infusions of 100 and 200u/kg/min, which resulted in blood propofol concentrations of 3mg/ml and 4.5mg/ml, respectively, did not affect phenylephrine pressor test gain [10].

On the other hand, the results of our study were in agreement with another study by Ebert et al., who explored potential mechanisms contributing to hypotension by recording cardiovascular responses including sympathetic neural activity from patients during induction of anesthesia with propofol (2.5mg/kg plus 200 micrograms/kg/min) or, for comparison, etomidate (0.3mg.kg-1 plus 15 micrograms.kg-1.min-1). Etomidate induction preserved blood pressure, whereas propofol produced significant hypotension. Both cardiac and sympathetic baroslopes were maintained with etomidate but were significantly reduced with propofol, especially in response to hypotension. These findings suggest that propofol-induced hypotension is mediated by an inhibition of the sympathetic nervous system and impairment of baroreflex regulatory mechanisms. Etomidate, conversely, maintains hemodynamic stability through preservation of both sympathetic outflow and autonomic reflexes [11].

Similarly, the results of our study agrees with M. Sato et al., where his study was designed to determine cardiovagal baroreflex gain during propofol infusion and to characterize its recovery profile using the pharmacological and spontaneous sequence methods in 13 healthy volunteers without cardiovascular or autonomic disorders, he concluded that cardiac baroreflex responses assessed by pharmacological and spontaneous sequence techniques were depressed during propofol anaesthesia at a calculated blood concentration of 5ug/ml in healthy humans [12].

Diastolic overshoot was comparable irrespective of anesthetic technique (Groups A & B) and timings (preoperative, intraoperative and postoperative). These results do not agree with a study by Turtle who observed a consistent and significant decrease of the diastolic overshoot after a Valsalva maneuver (or equivalent sustained lung inflation) during propofol infusion anesthesia, the effect being more marked in patients receiving the higher infusion rate [13].

Conclusion:

Data obtained from this study showed that use of propofol alone may lead to depression of baroreceptors as compared to combined use of propofol and sevoflurane.

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الملخص العربى

يستخدم مصطلح "منعكس مستقبلة الضغط الشريانى" للإشارة إلى مجموعة متنوعة من الاستجابات الفسيولوجية التى تسببها التغيرات فى وارد النشاط لمستقبلة الضغط. بينما غالباً ما يستخدم منعكس مستقبلة الضغط فى إشارة محددة إلى تغيرات انعكاسية فى ضغط الدم الشريانى ومعدل ضربات القلب الناجمة عن تغيرالتدفق اللاإرادى إلى القلب والأوعية الدموية. يتم قياس منعكس مستقبلة الضغط الشريانى باستخدام الادوية الفعالة فى الاوعية مثل الفينيل افرين الذى يسبب ارتفاع فى ضغط الدم الشريانى والصوديوم نيتروبروسيد الذى يسبب انخفاض فى ضغط الدم الشريانى.

\الأسالیب: وشملت هذه الدراسة المقارنة ٤٠ من المرضى الذين كان من المقررلهم اجراء عملية جراحية بالمنظار لأمراض النساء. تم تقسيم المرضى إلى مجموعتين (مجموعة البروبوفول) و (مجموعه المجمعه البروبوفول والسيفوفلوران) مع ٢٠ مريض فى كل مجموعة. لتقييم مراقبة منعكس مستقبلة الضغط لمعدل ضربات القلب، أجريت الاختبارات قبل، داخل وبعد العملية الجراحية مع تسجيل ضغط الدم الانقباضى والفاصل الزمنى RR فضلا عن التجاوز الانبساطى فى حالة اليقظة، وبعد العمل الجراحى تحت التخدير.

\النتائج: لم تكن هناك فروق ذات دلالة إحصائية فى البيانات الديموغرافية السكانية للمرضى، ضغط الدم الانقباضى ومعدل ضربات القلب فى اختبارات ما قبل التخدير. وتشير نتائج دراستنا أنه لا يوجد انخفاض كبير فى منعكس مستقبلة الضغط الشريانى باستثناء خافضة المنحدرات فى المجموعة البروبوفول بعد التخدير مع الاسترجاع التام لمنعكس مستقبلة الضغط الشريانى فى نتائج ما بعد الجراحة.

\الاستنتاج: البروبوفول وحده قد يؤدى إلى خفض مستقبلة الضغط بالمقارنة مع الاستخدام المشترك باستخدامه مع السيفوفلوران. من ناحية أخرى، لم يكن هناك اختلاف فى ضغط الدم الشريانى بين المجموعتين.