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RESEARCH ARTICLE

Nephrolithotripsy Surgery Using Spinal Anesthesia Method: a Comparison in Hemodynamic Changes between the Patients Injected Atropine and Ephedrine

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Coordinates: 28°30'00"N; 53°33'38"E

Key words: Systolic and diastolic blood pressures, Mean arterial pressure, heart beat, Pulse rate

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Abstract

As the acute hypotension developed from sympathetic blockage resulting due to spinal anesthesia after surgical operations such as PCNL is always remain a controversial issue. This study was conducted with the aim of comparing the hemodynamic changes after injecting atropine and ephedrine before prone position in patients undergoing nephrolithotripsy surgical operation through spinal anesthesia. A total of 90 subjects (patients) for PCNL through spinal anesthesia with ASA Class I and II, no migraine and chronic headaches, no cardiovascular disease, no coagulation disorder, having an age range in between 20-60 years old were chosen and categorized into three groups. The first and second groups were injected 5 mg of atropine and 5 mg of ephedrine immediately before the prone position, while the third group received no medication. Systolic blood pressure, diastolic blood pressure, respiration, venous oxygen saturation, and the patient's pulse were recorded at every five minutes gaps after surgery. Statistical results revealed a significant difference between the three groups of atropine, ephedrine, and control in terms of systolic blood pressure before the prone position, immediately after the prone position, 5, 15, and 25 min after it. The changes in the diastolic blood pressure across the three groups of atropine, ephedrine, and control immediately after the prone position and 25 min after it was statistically significant. The variations of the heart rate were also significant between the three groups before the prone position, immediately after the prone position, 5, 10, 15, and 25 min after it. The results obtained from this study indicate that to prevent hypotension resulting from spinal anesthesia following PCNL surgery, in which the patient adopts a prone position, prophylactic prescription of atropine and ephedrine immediately before the prone position can reduce the extent of hypotension.

Introduction:

Urinary stones form through pathological biomineralization processes in the urinary system (Giannossi *et al.*, 2012). Indeed, kidney stone disease is a chronic medical condition having a 50% chances of relapse, significantly affecting the quality of life (Ferakis & Stavropoulos, 2015; Nalbant *et al.*, 2012). Various methods have been suggested for management of kidney stones. Currently, PCNL (NephroLithotomy) is known as the golden standard for treating large kidney stones (Agarwal *et al.*, 2011). Percutaneous PCNL should be performed under general or spinal anesthesia. For this operation, a small skin incision is created and a nephroscope is then transported into the kidneys to assess the stones. Further, the stones are crushed through laser, ultrasonic, or electrohydraulic via the nephroscope and are then removed. Eventually, a nephrostomy tube is incorporated inside kidneys for

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removal of secretions (Matlaga & Lingeman, 2011). PCNL must be operated under local, general or regional anesthesia. Evidence suggests that general anesthesia are more advantageous than regional anesthesia including better hemodynamic control, air tract control, and greater satisfaction of the patient and surgeon (Ganvir *et al.*, 2016). It must be taken into an account that the spinal anesthesia also required more attention than general anesthesia especially for better pain control after the operation, diminishing the use of analgesic drugs, and preventing the various side effects of the drugs used in general anesthesia. Further, the extent of complications in PCNL surgery towards spinal anesthesia has been reported to be less (Aravantinos *et al.*, 2007). Among researchers, use of spinal anesthesia in PCNL is highly controversial due to the crucial issue of acute hypotension developed following sympathetic block (Urwin *et al.*, 2000; Indelli *et al.*, 2005; Sakura, 2007; Ditzler *et al.*, 1959). Thus, in treating hypotension resulting from spinal anesthesia, given its physiological cause, the two essential methods of increasing the resistance of systemic vessels and raising the volume of intravascular fluid are crucial (Macarthur & Riley, 2007). The acceptable and physiologic level of hypotension which is an issue, dependent on various factors and no precise definition available for it. Various methods have been used including intravenous administration of crystalloid and different vasopressors to prevent hypotension resulting from spinal anesthesia. Unfortunately, the interpretation of these studies is not easy due to different definitions employed and the different types of evaluated populations. Thus, in the present study, the effects of intravenous atropine and ephedrine have been examined and compared before prone position in preventing the hemodynamic complications during the nephrolithotripsy surgery.

Methodology:

The present piece of work is a double-blind random clinical trial study. Total 90 patients from PCNL surgery were chosen as subject and written permission was granted from them. The inclusion criteria were patient preference of performing spinal anesthesia, ASA Class I and II, no migraine and chronic headache, no cardiovascular disease, no coagulation disorder and being within the age range of 20-60 years old. Failure of spinal anesthesia in the first place, any respiratory problem, and any PCNL operation which caused open surgery or hospitalization in ICU wards were considered as the exclusion criteria. Before entering the study, all of the studied patients were checked-up and evaluated by a certain surgeon and randomly assigned (using random numbers table) into one of the three groups of atropine, ephedrine, and control. Across all of the patients before doing the spinal anesthesia after positioning on the surgical bed, a suitable venous pathway was considered and after installing electrocardiography leads on the patient's chest and installing pulse oximetry and wrapping the blood pressure monitor cuff around the patient's arm, vital signs including systolic blood pressure, diastolic blood pressure, respiration, venous oxygen saturation, and patient's pulse rate were measured and recorded. For each patient, 5 cc of crystalloid liquid (Ringer) was prescribed against each kilogram of their respective body weights via a peripheral vein, 15 min before the operation. All patients sit in the proper position and underwent spinal anesthesia through middle line technique. For this purpose, the patients sit on the bed, their head and neck were flexed and after specifying the site of needle insertion, which was the fourth or third lumbar intervertebral space, the region was disinfected by betadine and then dried. Special needle of spinal anesthesia (G23) was inserted from the topmost lower spinous process margin of the intervertebral space of interest and after sensing a pop sound, which suggested penetration of the needle into the dura layer, the needle was adjusted such that it was placed in the subarachnoid space. After ejection of the clear CSF which showed entrance of the needle to the desired space, anesthetic agent (3 cc of Marcaine 0.5%) was injected. The time of initiation of anesthesia was considered as the patient's inability in sensing pain with a painful stimulus such as pinch in the lower limbs, and its level was considered T10 vertebra. After concluding the preliminary stages, the patient was helped by the surgical team to sit in the prone position and 0.6 mg of atropine and 10 mg of ephedrine were injected immediately by a technician who was not aware of this drug. The systolic blood pressure, diastolic blood pressure, respiration, venous oxygen saturation, and pulse rate of the patient were remeasured and recorded again at minutes 5, 10, 15, and 25 of the operation. Eventually, the data were analyzed by SPSS 16 using chi-square, repeated erusaem, ANOVA, T-Test, Fischer, and correlation tests. For all the analysis, $p<0.05$ was considered as statistically significant.

Results:

The patients' records in terms of age, gender, history of operation and blood pressure were almost similar across the three studied groups (Table-1)..

Table-1: Demographic factors of three group
mean ±SD; count (percent)

Factor	Control	Atropine	Ephedrine
Age (p=0.125)	43.83 ± 7.17	47.30± 7.57	44.03 ± 7.18
Sex (p= 0.727)			
Male	16(53.3)	19(63.3)	17(56.7)
Female	14(46.7)	11(36.7)	13(43.3)
Surgical history (p≥0.093)			
No	6(20.0)	13(43.3)	13(43.3)
Yes	24(80.0)	17(56.7)	17(56.7)
History of blood pressure (p≥0.189)			
No	16(53.3)	16(53.3)	22(73.3)
Yes	14(46.7)	14(46.7)	8(26.7)

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The results of systolic and diastolic blood pressure revealed from the three groups are tabulated in Table-2. As per the results, the systolic blood pressure immediately after the prone position and at 5, 15, and 25 minutes after it was reported to be higher in the ephedrine group than in atropine and control groups. The systolic blood pressure before the prone position was observed to be higher in the atropine group when compared with ephedrine and control groups.

Table-2: Comparison in blood pressure among three group

Status	Control	Atropine	Ephedrine	p values
BP.S.3 bP*	115.80±6.13	145.13±19.63	130.93±15.36	<0.001
BP.S.IaP**	113.97±10.65	122.80±17.95	123.23±16.00	<0.033
BP.S5	114.93±6.25	122.47±13.60	124.13±12.88	<0.005
BP.S.10	113.60±10.38	114.50±14.52	118.70±12.16	≥0.245
BP.S.15	113.87±8.32	120.30±11.20	125.33±10.89	<0.001
BP.S.25	108.87±8.75	119.53±8.75	122.10±9.66	<0.001
trend "p"	**0.045**	**0.001**	**0.037**	
BP.D.3 bP*	82.50±6.90	83.83±6.48	85.77±6.41	≥0.162
BP.D. IaP**	69.87±18.16	79.37±11.85	79.07±10.01	<0.013
BP.D5	76.40±5.14	79.03±9.51	78.27±8.20	≥0.412
BP.D.10	71.27±13.78	74.63±10.60	77.63±8.09	≥0.089
BP.D.15	74.43±5.10	78.30±8.96	78.53±7.39	≥0.057
BP.D.25	71.43±8.57	78.37±6.91	77.77±7.23	<0.001
trend "p"	**0.020**	**0.010**	**0.006**	

BP.S.- Blood Pressure Systolic, BP.D.- Blood pressure Diastolic; bP*- before Peron; IaP**- Immediately after Peron

Thus, based on the results of one-way ANOVA, there was a significant relationship between the three groups of atropine, ephedrine, and control groups in terms of systolic blood pressure before the prone position, immediately after it as well as 5, 15, and 25 min after adopting this position ($p<0.05$). Also, Fig.- 1 indicates that in the ephedrine and atropine groups, the trend of systolic blood pressure before the prone position, immediately after the position unit 10 min after 10 had a descending trend, while after it up to 25 min, it increased, where there was a significant difference between them ($p<0.05$). On the other hand, in the control group, the systolic blood pressure had diminished after the prone position up to 25 min after it.

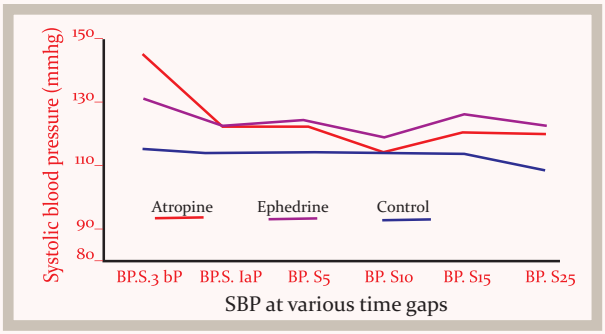

Figure-1: Comparative chart of systolic blood pressure

Diastolic blood pressure immediately after the prone positon and 25 min after it, was found higher in the atropine group as compared to ephedrine and control groups. A significant relationship was observed between the three groups in terms of diastolic blood pressure immediately after the prone position and 25 min after it ($p<0.05$). However, before the prone position and at 5, 10, and 15 min after the prone position, no significant difference was observed between the three groups ($p>0.05$). Moreover, Fig.-2 revealed that in the atropine group, the diastolic blood pressure had a descending trend before the prone position, immediately after up to 10 min after it, while thereafter up to 25 min, it found an ascending trend, where a significant difference was observed between them ($p<0.05$). However, in the ephedrine group, diastolic blood pressure had grown from immediately after the prone position up to 25 min after it.

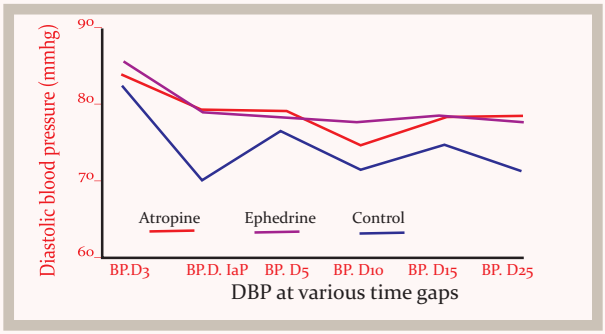

Figure-2: Comparative chart of diastolic blood pressure

The results of pulse rates, 02 sat, and respiratory rates are reported in Table-3.

Table-3: Comparison in hemodynamic changes in three group

Status	Control	Atropine	Ephedrine	p values
HR.3 bP*	69.40±5.22	69.47±12.39	76.23±7.42	<0.004
HR. IaP**	75.20±5.59	78.37±6.96	88.70±12.19	<0.001
HR.5	78.37±4.92	77.53±9.37	88.00±12.32	<0.001
HR.10	78.63±4.43	81.83±9.88	88.07±12.09	<0.001
HR.15	79.33±5.73	84.53±10.62	88.63±11.06	<0.001
HR.25	79.10±5.96	85.03±10.16	86.27±11.17	<0.009
Trend "p"	**0.001**	**0.001**	**0.001**	
O2.3 bP*	96.33±2.06	96.63±1.19	96.27±1.66	≥0.781
O2.IaP**	96.33±1.83	96.77±1.17	96.20±1.63	≥0.439
O2.5	96.47±1.78	96.60±1.45	96.27±1.66	≥0.723
O2.10	96.47±1.59	96.60±1.45	96.27±1.66	≥0.697
O2.15	96.53±1.61	96.83±1.23	96.27±1.66	≥0.432
O2.25	96.60±1.57	96.83±1.23	96.27±1.66	>0.432
trend "p"	**0.588**	**0.319**	**0.416**	
Breathing.3 bP*	18.53±1.17	18.33±1.24	18.70±1.18	≥0.453
Breathing. IaP**	18.57±1.17	18.33±1.24	18.67±1.18	≥0.520
Breathing.5	18.57±1.17	18.33±1.24	18.67±1.18	≥0.520
Breathing.10	18.57±1.17	18.33±1.24	18.67±1.18	≥0.520
Breathing.15	18.57±1.17	18.33±1.24	18.67±1.18	≥0.520
Breathing.25	18.57±1.17	18.33±1.24	18.67±1.18	≥0.520
trend "p"	**0.419**	**0.999**	**0.419**	

A significant relationship was reported between the three groups in terms of pulse rate before the prone

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position, immediately after the prone position, as well as 5, 10, 15, and 25 min after it ($p<0.05$). No significant difference was observed between the three groups in terms of 02 sat and respiratory rate ($p>0.05$).

In addition, Fig.- 3 shows that across the three groups, the heart rate had revealed an increasing trend from before the prone position up to 15 min after it ($p<0.05$). However, after that, no significant difference was observed between atropine and ephedrine ($p>0.05$).

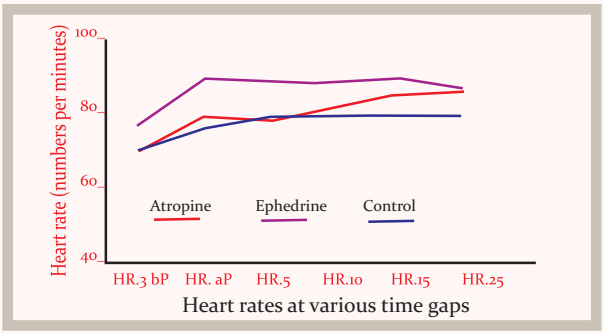

Figure-3: Comparative chart of Heart rate

Based on the results shown in Table-4, the extent of bleeding before the prone position, immediately after as well as 5, 10, and 15 min after the position was evidenced as significant ($p<0.05$). According to Diagram 5, after 5 min, the extent of bleeding was observed to be higher in the atropine group than in the ephedrine group.

Table-4: Comparison in Bleeding among three group

Status	Control	Atropine	Ephedrine	p values
Bleeding. bP*00		.00	.00	
BLE. IaP**	.00	.00	.00	.
Bleeding.5	.00	2.50±5.37	6.50±9.39	<0.001
Bleeding.10	106.67±25.91	113.67±107.72	74.67±20.30	<0.001
Bleeding.15	160.67±34.03	137.67±45.99	140.00±39.57	<0.018
Bleeding.25	178.00±28.58	171.00±48.31	158.33±42.43	≥0.300
trend "p"	**0.001**	**0.001**	**0.001**	

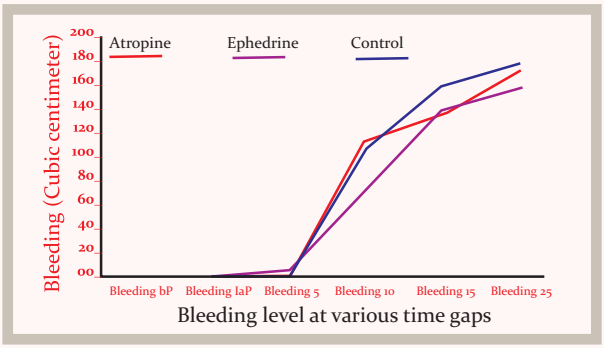

Figure-4: Comparative chart of bleeding

Discussion:

The hypotension that is developed during surgical operations through spinal anesthesia is very common, and if remain uncontrolled then it could be said as the most common complication (50-90%) (Bjornestad & Rosseland, 2010; Cyna *et al.*, 2006; Mercier *et al.*, 2007). This study compared the hemodynamic changes and heart rate resulting from atropine and ephedrine injection before prone position in patients undergoing nephrolithotripsy surgery though spinal anesthesia. The results of the present study suggest that the variations of systolic blood pressure before and immediately after the prone position and at 5, 15, and 25 min after it revealed a significant difference between the three groups of atropine, ephedrine, and control. Also, in terms of diastolic blood pressure changes, the results suggest that immediately after the prone position as well as 25 min after it, there was a significant relationship between the three groups. Atropine is indeed a mixed acid aromatic-ester with an organic base which competitively blocks acetylcholine attachment to its receptor, thus preventing its activation, whereby the cellular effects of acetylcholine are inhibited. Generally, atropine reduces the parasympathetic activity of all muscles and glands which are regulated by the parasympathetic nervous system. It, on the other hand, raises the heart rate through deactivating the vagal tone in M2 receptor in the heart (Katzung & Trevor, 2015; Stoelting & Hiller, 2006). However, ephedrine is indeed a sympathomimetic amine, whose main mechanism of action involves enhancing the indirect mobility of the adrenergic receptor system through increasing the noradrenaline activity in post-synaptic a and ß receptors. Accordingly, ephedrine is typically used for treating hypotension resulting from spinal anesthesia (Katzung & Trevor, 2006; Stoelting & Hiller, 2006). Sigdel *et al.* (2015)compared the prophylactic effect of atropine and ephedrine in preventing hypotension in elderly patients with spinal anesthesia. They indicated that administering 6 mg of atropine or 12 mg of ephedrine one minute before the spinal anesthesia in elderly patients mitigates hypotension and bradycardia resulting from it. In the present study, the results also showed that administering 6 mg of atropine and 10 mg of ephedrine immediately before the prone position in PCNL patients had diminished the extent of hypotension and bradycardia. Comparison of ephedrine group with the two other groups in terms of blood pressure changes indicated that systolic blood pressure from immediately after the prone position and at 5, 15, and 25 min after it has been higher in the ephedrine group compared to the two other groups. Desalu & Kushimo (2005) compared the prophylactic effect of ephedrine infusion and pre-hydrating 60 pregnant women undergoing C-section through spinal anesthesia, where they found that the mean systolic pressure was greater in the ephedrine group when compared to the saline group. Alday Muñoz *et al.* (2011) compared the effect of ephedrine and phenylephrine on preventing hypotension resulting from spinal anesthesia. They reported that the ability of ephedrine and phenylephrine in preventing hypotension during the C-section surgery was the same. In the present study, in the

ephedrine and atropine group, although changes in systolic blood pressure before the prone position, immediately after the position, and up to 10 minutes after that have had a descending trend, thereafter up to 25 min, we have experienced increased blood pressure. However, in the ephedrine and atropine group during 25 min, systolic and diastolic blood pressures were reported to be higher than those of the control group. The changes in the diastolic blood pressure of the atropine group in immediately after the prone position and 25 min after that were reported to be higher when compared to the ephedrine and control groups. Hirabayashi *et al.* (1994) investigated muscular administration of atropine in spinal anesthesia and concluded that in the patients whose anesthesia level has reached T4 level, no difference was found in terms of hypotension. However, in the present study, as anesthesia level reached T6 level, to perform PCNL, the blood pressure in the atropine group was reported to be higher than that of the control group at all minutes of the study.

Nevertheless, although at minutes of this study, atropine was able to develop an acceptable blood pressure in patients to prevent hypertension, thus it can be concluded that the variations and fluctuations of blood pressure were milder against the ephedrine group while compared to the two other groups. In the study by Jain et al. (2016) it was found that in C-section surgery, maternal HR after ephedrine administration was reported to be significantly higher, while the extent of maternal bradycardia was reported to be greater after injecting phenylephrine. In the present study, again ephedrine had increased heart rate significantly. Aragão *et al.* (2014) performed a study in which the preventive effect of metaraminol, phenylephrine, and ephedrine was investigated to prevent and treat hypertension in C-section surgery through spinal anesthesia. They found that the rate of incidence of hypotension, heart rate, and need to atropine was not different across the groups. In the present study, across the three studied groups, the extent of heart rate elevation was significantly different across the three groups, where the heart rate found an ascending trend in all groups before the prone position up to 15 minutes after it. However, this increase in heart rate in the atropine group was observed at all minutes up to 25 except for 10. Shahriari & Khooshideh (2017) investigated ephedrine and atropine in preventing bradycardia in elderly patients undergoing skin tumor resection, whereby the effect of ephedrine was reported to be greater than atropine in managing symptomatic bradycardia. In the present study, again ephedrine had developed a balanced heart rate without fluctuation in most minutes in patients. However eventually, by comparing the three groups in terms of the extent of bleeding, it was found that a significant difference existed between the three groups in terms of the extent of bleeding from immediately after the prone position and at the minutes of 5, 10, and 15 min.

Conclusively, the results obtained from this study indicate that to prevent hypotension resulting from spinal anesthesia following PCNL surgery, in which the patient adopts a prone position, prophylactic prescription of atropine and ephedrine immediately before the prone position can reduce the extent of hypotension.

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