Original Article

Assessment of clonidine effect as premedicative drug on kidney function

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Abstract

Objective: To assess the effect of oral clonidine as a premedicative drug on 24-hour urine output, urine specific gravity, plasma renin activity as well as serum and urine electrolytes levels.

Methods: This prospective study was carried out on 60 women aged 20-40 years old undergoing repair of cystocoele - rectocoele perineorraphy under general anaesthesia in Asali Hospital in 2004 in Khorramabad, Iran. Subjects were randomly divided into two equal groups of 30 each. Group I and group II received clonidine tablet at the dose of 5μg/kg and placebo tablet, respectively, 90 minutes before induction of general anesthesia. In this study, blood and urine samples were taken for laboratory measurements prior as well as 6 hours after taking the tablets. Differences between the two groups were compared through Mann-Whitney u-test, χ^2 test and t-student test. P-value<0.05 was considered statistically significant.

Results: There were no significant changes before and after receiving tablets in urine and blood Na and K as well as urine specific gravity in group II (P >0.05). Group I had higher urine Na and K level (P=0.001), however, no differences had been shown in blood Na and K level (P>0.05). Urine specific gravity was lower in group I after receiving tablet (P<0.009). A significant increase in 24-hour urine output (P=0.001) and a marked decrease in plasma renin activity was seen in group I (P=0.001).

Conclusion: This study suggests that clonidine is a safe premedicative drug in anaesthesia and does not change the serum electrolytes levels (JPMA 60:570; 2010).

Introduction

Clonidine, an imidazoline compound,[1] is a selective alpha-2 adrenoceptor agonist[2-4] that is used as a premedicant and valuable adjunct in anaesthesia in recent years. Desirable effects of clonidine in anaesthesia include sedation, analgesia, perioperative haemodynamic stabilization, and diminishing the requirement of other anaesthetic drugs.[5] Clonidine may also be used to reduce supine hypertension,[4] nocturnal natriuresis,[4] withdrawal syndrome from dependence on narcotics, opiate, alcohol and nicotine (smoking), panic disorder, emesis in cancer chemotherapeutic regiment, diabetic diarrhoea[5] and cirrhosis.[3] Although clonidine affects different organs, its effect on renal system as diuresis is significant. The exact mechanism is not fully understood. However, there are theories on how this drug acts on the renal system.[6-12]

This study was designed to evaluate the effect of clonidine as a premedicative drug on plasma renin activity, 24-hour urine output, urine specific gravity as well as serum and urine electrolytes levels.

Methods

This prospective, randomized, double-blind and placebo-controlled study was carried out on 60 women aged 20-40 years in American Society of Anaesthesiologists (ASA) physical status I, II undergoing repair of cystocoele - rectocoele perineorraphy under general anaesthesia in Asali Hospital Khoramabad, Iran in 2004. Patients with hypertension, cardiovascular, renal and psychotic diseases were excluded from this study. After obtaining the approval from the hospital ethics committee and written informed consents from the patients, they were randomly divided into two equal groups of 30 cases each. Group I and group II received Clonidine tablet at the dose of 5μg/kg and placebo tablet, respectively, with 30cc water 90 minutes before induction of anaesthesia. Foleys catheter was then inserted. General Anaesthesia was induced with sufentanil (2μg/kg) and thiopental (5mg/kg); and tracheal intubation was facilitated with atracurium (0.3mg/kg), followed by oxygen and nitrous oxide (30%, 70%, respectively) in combination with halothane which varied from 0.5% to 1.5%. Patients were monitored for blood pressure (BP), pulse rate (PR), electrocardiogram (ECG) and pulse oximetry. At the end of the operation, residual of neuromuscular block was reversed by neostigmine and atropine. The injected fluid used during the anaesthesia course was crystalloid solution (Nacl 0.3% plus dextrose 3.33%) based on the following formula: Replacement of insensible loss (2 ml/kg/h) plus moderate surgical trauma loss (5 ml/kg/h) plus blood loss (every 1 ml of blood loss with 3 ml of serum) plus urine loss (every 1 ml urine loss with 1 ml of serum). On the first day of the surgery, patients received 2 ml /kg/hour of

dextrose 5% - Nacl 0.9% serum. Blood and urine samples were assessed prior as well as 6 hours after taking the tablets for determining Na, K, urine specific gravity and plasma renin activity. Besides, the 24-hour urine output was charted. Data were analyzed by Mann-Whitney u-test, χ^2 test and t-student test. P-value<0.05 was considered statistically significant.

Results

Baseline demographic and background characteristics were similar between groups I and II. There were no significant differences between the two groups regarding BP, PR, ECG and pulse oximetry. There were no significant changes before and after receiving tablets in urine and blood Na and K as well as urine specific gravity in group II (P >0.05) (Table-1). Group I had higher urine Na and K level (P=0.001), however, no differences had been shown in blood Na and K level (P>0.05) (Table-1 and 2). Urine specific gravity was lower in group I after receiving the tablet (P<0.009) (Table-1). This change was significant compared to group II (Table-2). Significant increase in 24-hour urine output (P=0.001) was seen in group I compared to group II (Table-3). Significant decrease in plasma renin activity was seen in group I (P=0.001) (Table-3).

Discussion

In a study by Laisalmi et al in 2001, the effect of clonidine with dose of 4.5 μg/kg and placebo on haemodynamics, neuroendocrine response and parameters were compared in 30 patients undergoing laparoscopic cholecystectomy. Results showed no differences in urine output, urine oxygen tension and anti-diuretic hormone between the groups.[13] In another study done by Buchman et al, transdermal clonidine in patients with proximal jejunostomy increased weekly urine volume although it was not significant.[14] This is in line with our findings on the increased urine output by clonidine.

Lenaert et al in 2006, concluded that additional administration of clonidine to diuretics in ascitic patients induced diuresis[3] which is also compatible with our study.

Poliak et al concluded that clonidine tablet causes decrease in noradrenaline and dopamine level as well as plasma renin activity, but no change in epinephrine level was seen.[15]

Table-1: Comparison of the blood and urine Na and K (meq/lit), and urine specific gravity before and after receiving tablet in placebo and clonidine groups.

		Placebo group				Clonidine group			
		Mean±SD	P value	Free degree	T	Mean±SD	P value	Free degree	T
Serum Na level meq/l	before	137.87± 5.10	-5.524	29	0.06	138.4±6	1.053	29	0.301
	after	140.83±4.65				137.67±4.88			
Serum k level meq/l	before	4.143±0.564				4.11±0.464	1.53	29	0.137
	after	4.243±o.438	-1.555	29	0.131	3.763±1.117			
Urine Na level meq/l	before	188.37±40.21				175.53±28.69	-6.408	29	0.001
	after	192.77±34.24	-0.926	29	0.362	199.60±19.21			
Urine k level meq/l	before	33.993±1.986				34.383±2.257	-6.976	29	0.001
	after	34.183± 2.047	-0.935	29	0.358	36.240±2.103			
Urine specific gravity	before	1021.43±5.33				1023.03±0.08	2.793	29	0.009
	after	1021.43±5.11	-1.015	29	0.319	1021.13±3.96			

Table-2: Comparison of mean of serum and urine laboratory tests prior and after receiving clonidine.

	t-test	Free degree	P-Value
Serum Na	-4.126	28	0.057
Serum K	-1.897	28	0.053
Urine Na	3.246	28	0.002
Urine K	4.372	28	0.001
Urine specific gravity	-2.925	28	0.005

In a study carried out by Mase et al in 1996, intravenous administration of clonidine in awake dogs led to increase in renal prostaglandins and decrease in plasma renin activity that induced hypo-osmotic diuresis.[16] Similar findings were observed in our study.

El-Mas and colleagues in 2007 demonstrated that clonidine with dose of 150 microgram/kg per day for 12 weeks in rats increased urine output during 8-hour treatment

Table-3: Comparison of mean and S.D of plasma renin activity and 24 hours urine volume in 2 groups.

	group	Mean	SD	T	Free degree	p- value
Plasma renin activity	Clonidine group	0.247	0.2432	9.91	58	0.001
(nanogram/milliliter /hours)	Placebo group	0.7793	0.4824			
24 hours urine volume(ml)	Clonidine group	2884.666	384.05	7.24	58	0.001
	Placebo group	2161.333	422.29			

period. Plasma and urine osmolality and electrolytes were not altered by clonidine[17] while in our study, group I had higher urine electrolytes level and lower urine osmolality. This difference may be due to a different dosage of clonidine used in our study (5 microgram /kg).

Conclusion

This study showed that clonidine as a premedicative drug does not decrease blood electrolytes and increases 24-hour urine output and urine Na and K level as well. Moreover, it decreased plasma renin activity and urine specific gravity, thereby requiring appropriate fluid therapy in perioperative period.

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