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# EVALUATION OF EFFECTS OF ORAL CLONIDINE AS PRE-MEDICATIVE DRUG ON THE FUNCTIONS OF KIDNEY

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**Abstract:**

***Objective:*** *The purpose of this research work was to evaluate the impacts of oral clonidine as a pre-medicative drug on 24-hour urine output, specific gravity of urine, renin activity of plasma as well as electrolytes levels of serum & urine.*

***Methodology:*** *This research work was carried out on 50 females from 20 to 40 years of age who were undergoing the cystocoele-rectocoele perineorraphy repair under GA (General Anesthesia) in Benazir Bhutto Hospital Rawalpindi in the year of 2019. We randomly separated the patients into groups with 25 patients in each group. Group-1 and Group-2 took tablets of clonidine at the dose of 5.0 µg/kg and tablet of placebo, respectively, 90 minutes before the application of General Anesthesia. In this research work, we obtained the samples of urine and blood for measuring laboratory parameters before and after six hours of receiving the tablets. The comparison of the differences between the patients of both groups was carried out with the help of Mann-Whitney test, and student T test. We considered the P value of less than 0.050 as significant statistically.*

***Results:*** *We found no important alterations prior and after taking the tablets in the level of blood K and Na as well as the specific gravity of urine in Group-2 (P >0.050). There was high level of urine Na & K in the patients of Group-1 (P=0.0010), however, there were no significant differences in the levels of blood's K & Na (P>0.050). Specific gravity of urine was much low in the patients of Group-1 after taking the tablets (P<0.0090). An important rise in 24 output of urine (P=0.0010) and a significant reduction in the renin activity of plasma was visible in the patients of Group-1 (P=0.0010).*

***Conclusion:*** *The findings of this research work confirmed that clonidine is a secure pre-medicative medicine in General Anesthesia and it is not the factor behind the alterations in levels of serum electrolytes.*

***KEYWORDS****: General Anesthesia, Alterations, Gravity, Renin, Electrolyte, Statistically, Urine, Clonidine.*

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## INTRODUCTION:

Clonidine is an imidazoline compound and it is selective Alpha-2 adrenoceptor agonist [1]. Clonidine is normally used for pre-medicative purposes and valued adjunct in anesthesia in modern era. There are some desirable influences of clonidine in anesthesia as analgesia, sedation, peri-operative stabilization of hemodynamics and weakening the need of other medicines for anesthesia [2]. There is also other utilization of the clonidine for the decrease of the hypertension of supine [3], nocturnal natriuresis, and removal of syndrome from dependence on opiate, alcohol, nicotine (cigarette smoking, narcotics, panic anomaly, diarrhea in the diabetics and liver cirrhosis [4].

There are many effects of clonidine on various organs of human body but its impacts on the kidney function like diuresis, are of much significance. The proper mechanism of this issue in completely not understood. However, there is presence of many clinical theories for the description of the effects of this drug on the kidney function of human body [5-6]. This research work was carried out to assess the influences of clonidine as a pre-medicative medicine on the renin activity of plasma, 24-hours output of urine, specific gravity of urine and serum and levels of urine electrolytes.

## METHODOLOGY:

This research work was a randomized controlled study. This research work included 50 female patients having age from 20 to 40 years fulfilling the ASA (American Society of Anesthesiologists) (ASA) physical status-1, 2 who underwent cystocoele-rectocoele perineorraphy under impact of General Anesthesia in Benazir Bhutto Hospital Rawalpindi in the year of 2019. All the patients who were suffering from HTN (Hypertension), cardiovascular complications, renal abnormalities and psychotic diseases were not included in this current research work. Ethical committee of the institute gave the permission to conduct this research work. We obtained the written consent from all the patients after describing them the purpose of this research work. We separated all the patients into two different groups with 25 patients in each group.

Patients of Group-1 & Group-2 obtained tablet of clonidine with a dose of 5.0 µg/kg and tablet of placebo, correspondingly with 30.0cc water ninety minutes prior to the application of anesthesia. We then inserted the Foleys catheter. We inducted the General Anesthesia with sufentanil (2.0 µg/kg) & thiopental (5.0 mg/kg); and then facilitated the tracheal intubation with the use of atracurium (0.30 mg/kg), followed by 30.0% oxygen and 70.0% nitrogen combined with the halothane with a variation from 0.50% to 1.50%. We also monitored the patients for their BP (Blood Pressure), PR (Pulse Rate), ECG (Electrocardiogram) as well as pulse oximetry. At the completion of surgery, atropine & neostigmine were used for the reversing the neuromuscular block's residual. We used the crystalloid solution (NaCl 0.30 with 3.33 dextrose) in duration of course of anesthesia through injection. On the very 1st day of the operation, patients obtained 2.0 ml/kg/hour dose of dextrose 5.0%-Nacl 0.90% serum.

We evaluated the samples of urine and blood before as well as six hours after receiving the tablets for the determination of K, Na and specific gravity of urine and renin activity of plasma. We also noted down the 24 hours output of urine. We used the Mann Whitney test and student T test for the statistical analysis of the collected information. P value of less than 0.050 was considered as significant statistically.

## RESULTS:

There were similar baseline background & demographic traits between Group-1 & Group-2. We did not find significant differences between the patients of both groups regarding pulse oximetry, blood pressure, PR and ECG. We found no significant alteration prior and after taking the tablets in the levels of blood & urine K & Na as well as specific gravity of urine in the patients of Group-2 (P >0.050) (Table-I).

**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**

| Parameters | | Mean±SD | Placebo group | | T | Mean±SD | Clonidine group | | T |
|---|---|---|---|---|---|---|---|---|---|
| | | | P value | Free degree | | | P value | Free degree | |
| Serum Na level meq/l | before | 137.87± 5.10 | -5.524 | 29 | 0.06 | 138.4±6 | 1.053 | 29 | 0.3 |
| | 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 | 0.14 |
| | after | 4.243±0.438 | -1.555 | 29 | 0.13 | 3.763±1.117 | | | |
| Urine Na level meq/l | before | 188.37±40.21 | | | | 175.53±28.69 | -6.408 | 29 | 0 |
| | after | 192.77±34.24 | -0.926 | 29 | 0.36 | 199.60±19.21 | | | |
| Urine k level meq/l | before | 33.993±1.986 | | | | 34.383±2.257 | -6.976 | 29 | 0 |
| | after | 34.183± 2.047 | -0.935 | 29 | 0.36 | 36.240±2.103 | | | |
| Urine specific gravity | before | 1021.43±5.33 | | | | 1023.03±0.08 | 2.793 | 29 | 0.01 |
| | after | 1021.43±5.11 | -1.015 | 29 | 0.32 | 1021.13±3.96 | | | |

There was high level of urine K & Na in the patients of Group-1 (P=0.0010), but there were no differences in the levels of blood K & Na (P>0.00) (Table-I & Table-II).

Specific gravity of urine was low in the patients of Group-1 after taking the tablets (P<0.0090) (Table-I). This alteration was much significant as compared to the patients of Group-2 (Table-II).

**Table-2: Comparison of Mean of Serum and Urine Laboratory Tests Prior and After Receiving Clonidine**

| | t-test | Free | 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 |

A noteworthy increase in 24 hours output of urine was present in the patients of Group-1 as compared to the patients of Group-2 (Table-III). We also observed the reduction in the renin activity of plasma in the patients of Group-1 (P=0.0010) (Table-III).

**Table-3: Comparison of Mean and SD of Plasma Renin Activity And 24 Hours Urine Volume In 2 Groups**

| | Group | Mean | SD | T | Free Degree | p- Value |
|---|---|---|---|---|---|---|
| Plasma renin activity (Nano gram/milliliter /hours) | Clonidine group | 0.247 | 0.2432 | 9.91 | 58 | 0.001 |
| | 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 | | | |

## DISCUSSION:

A study conducted by Laisalmi in the year of 2001, he compared the influence of 4.5 μg/kg dose of clonidine & placebo on the hemodynamics, neuroendocrine parameters & response in 25 patients who underwent cholecystectomy through laparoscopy [7]. The findings of that research work stated no differences in the output of urine, oxygen tension of urine and anti-diuretic hormone between the patients of both groups [8]. In other research work conducted by Buchman stated that transdermal clonidine among the patients present with proximal

jejunostomy enhanced weekly volume of urine though it was not much significant [9,10,11]. This finding is consistent with our results about the increase of the output of urine with the use of clonidine.

Lenaert in his study conducted in 2006, discovered that additional clonidine's administration to diuretics in the patients of ascitic induced the diuresis [12], this finding is also compatible with the results of this current research study. Poliak declared after examination that tablet of clonidine can cause the reduction in the levels of noradrenaline & dopamine as well as renin activity of plasma, but he discovered no change in the level of epinephrine [13]. One other research study performed by Mase in year of 1996 concluded that intravenous clonidine administration in awake dogs resulted in enhancement of renal prostaglandins and reduce the renin activity of plasma that also caused the induction of hypo-osmotic diuresis [14]. This current research work also observed the similar findings.

El-Mas & his colleagues in the year of 2007 stated that a dose of clonidine of 150.0 microgram/kg every day for complete twelve weeks in rats enhanced the output of urine in the duration of 8-hours treatment. There was no alteration in the osmolality & electrolytes of plasma and urine by the use of clonidine [15] whereas in this current research work, there was higher level of urine electrolytes in the patients of Group-1 and low osmolality of urine. This difference was the outcome of the different clonidine dose of 5 microgram per kg for the patients of this study.

## CONCLUSION:

This current research work stated that clonidine is a good pre-medicative drug and it does not reduce the level of serum electrolytes and enhances the 24 hours output of urine and level of K & Na of urine. It is also responsible for the decrease in the renin activity of plasma and specific gravity of urine, thereby demanding proper fluid treatment in perioperative duration.

## REFERENCES:


1. Naruse T, Ishida T, Ishii R, Tagawa T. Preclinical assessment of a new transdermal delivery system for clonidine (M-5041T). Fundam Clin Pharmacol 1996; 10: 47-55.
2. Kulka PJ, Tryba M, Zenz M. Preoperative alpha2-adrenergic receptor agonists prevent the deterioration of renal function after cardiac surgery: results of a randomized, controlled trial. Crit Care Med 1996; 24: 947-52.
3. Intengan HD, Smyth DD. Clonidine-induced increase in osmolar clearance and free water clearance via activation of two distinct alpha 2-adrenoceptor sites. Br J Pharmacol 1996; 119: 663-70.
4. Ohara-Imaizumi M, Kumakura K. Effects of imidazole compounds on catecholamine release in adrenal chromaffin cells. Cell Mol Neurobiol 1992; 12: 273-83.
5. Lenaerts A, Codden T, Meunier JC, Henry JP, Ligny G. Effects of clonidine on diuretic response in ascitic patients with cirrhosis and activation of sympathetic nervous system. Hepatology 2006; 44: 844-9.
6. Shibao C, Gamboa A, Abraham R, Raj SR, Diedrich A, Black B, et al. Clonidine for the treatment of supine hypertension and pressure natriuresis in autonomic failure. Hypertension 2006; 47: 522-6.
7. Atlas D, Diamant S, Zonnenschein R. Is imidazoline site a unique receptor? A correlation with clonidine-displacing substance activity. Am J Hypertens 1992; 5: 83S-90S.
8. Maze M, Tranquilli W. Alpha-2 adrenoceptor agonists: defining the role in clinical anaesthesia. Anesthesiology 1991; 74: 581-605.
9. El-Mas MM, Abdel-Rahman AA. Intermittent clonidine regimen abolishes tolerance to its antihypertensive effect: a spectral study. J Cardiovasc Pharmacol 2007; 49: 174-81.
10. Lenaerts A, Codden T, Van Cauter J, Meunier JC, Henry JP, Ligny G. Interest of the association clonidine-spironolactone in cirrhotic patients with ascites and activation of sympathetic nervous system. Acta Gastroenterol Belg 2002; 65: 1-5.
11. Penner SB, Mueller HA, Smyth DD. Alpha 2-adrenoceptor stimulation in the periventricular nucleus increases urine flow rate with minimal effects on blood pressure. Proc West Pharmacol Soc 2002; 45: 13-4.
12. B.E M, D.E L. General anesthetics. In: Brunton LL, John L, Keith LP, eds. Goodman & Gilman's the pharmacological basis of therapeutics 9th ed. New York: McGraw-Hill, Health Professions Division, 1996: III (14).
13. Laisalmi M, Koivusalo AM, Valta P, Tikkanen I, Lindgren L. Clonidine provides opioid-sparing effect, stable hemodynamics, and renal integrity during laparoscopic cholecystectomy. Surg Endosc 2001; 15: 1331-5.
14. Buchman AL, Fryer J, Wallin A, Ahn CW, Polensky S, Zaremba K. Clonidine reduces diarrhea and sodium loss in patients with proximal jejunostomy: a controlled study. J Parenter Enteral Nutr 2006; 30: 487-91.
15. Poliak M, Horky K, Kopecka J, Gregorova I, Dvorakova J. The effect of clonidine on humoral factors in patients with arterial hypertension. Cas Lek Cesk 1990; 129: 301-5.