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ANALYSIS OF THE EFFECT OF LOW DOSE DOPAMINE IN TREATMENT OF PRERENAL AZOTEMIA IN ADULT PATIENTS ATTENDING NEPHROLOGY UNIT IN NAUTH, NNEWI, NIGERIA

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ABSTRACT: Background: This was a conventional comparative treatment-controlled study designed to analyze the effect of dopamine infusion in the treatment of prerenal azotemia (PRA). **Material and Methods:** thirty randomized consecutive adult patients (group A= 15, B=15) aged 18 and 58 years with PRA were recruited. Group a received conventional treatment only (fluid replacement and frusemide), while group B received conventional treatment and dopamine. 24 hours urine volume, hemodynamic changes (pulse and blood pressure), serum electrolyte, urea, and creatinine were measured for the first 5 days of hospitalization. Duration of oliguria and hospitalization, mortality, number of patients who developed acute tubular necrosis (ATN), and or required dialysis was computed. **Results:** Duration of oliguria and hospitalization were shorter in group B than in group A patients (P = 0.025). The daily and hourly urine output was more in group B than in group A patients (P = 0.025). However, from the second day, patients in group B excreted more sodium than patients in group A (P = 0.001). 5 patients in group A (33.30 %) and 3 (20 %) in group B developed ATN; while 6 (40%) in group A and 4 (26.7 %) in group B developed uremic syndrome and needed dialysis (P > 0.05). 2 (13.3 %) died in group A and 1 (6.7%) in group B from uremia. **Conclusion:** Although dopamine infusion added to conventional treatment increased the urinary output, shortened the duration of oliguria and hospitalization in patients with PRA, Renal function, development of ATN, uremic syndrome, need for dialysis and mortality were not influenced. Hence, routine prescription of dopamine infusion in the treatment of PRA is not recommended by this study.

INTRODUCTION: Prerenal Azotemia (PRA) represents a rapidly reversible decrease in glomerular filtration rate (GFR) as a result of renal hypoperfusion leading to increasing levels of urea and creatinine with Oliguria [1].

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Insufficient renal perfusion normally results from inadequate cardiac output, hypovolemia, or vascular disease, thereby limiting the flow of blood to the kidneys.

The abrupt impairment of renal function can be reversed by the treatment of the primary cause [1]. The resulting systemic hypotension stimulates the rennin angiolensin aldostcrone axis, antidiuretic hormone release, and the sympathetic nervous system, which results in redistribution of blood flow away from the renal cortex, avid tubular reabsorption of Na^+, urine and sodium output

decline and osmolality increases [2]. The blood urea nitrogen increases before changes in serum creatinine become apparent [1, 2]. The Oliguria and azotemia in PRA are, therefore, essentially a functional disorder. The usual treatment of prerenal azotemia is the correction of the underlying hypotension using crystalloids, or colloids, and diuretics. Currently, ionotropic agents such as dopamine are increasingly being used to reverse PRA [3]. If the renal hypoperfusion is not promptly and effectively treated and becomes sustained or severe, acute tubular necrosis may ensue [4]. The hallmark of acute tubular necrosis (ATN) is an abrupt decrease in GFR and acute onset or worsening of azotemia which is not immediately reversible after withdrawal of the causative agent or fluid replacement [5].

This is because the Ischemia sets off a sequence of tubular epithelial cell pathophysiologic processes that, once initiated, perpetuate the tissue damage and functional defects independent of total renal blood flow [4, 5] Prerenal azotemia is the most common type of acute renal failure (ARF) and is responsible for 40% of the cases of ARF seen in hospitalized patients [3]. Dopamine (DA), an endogenous catecholamine, is the immediate precursor of norepinephrine and epinephrine in catecholmate synthesis. It acts on specific dopaminergic (DA-1 and DA-2) receptors which are widely distributed on vascular smooth muscle cells of renal, mesenteric, coronary, cerebral, and other organ beds. Stimulation of DA-1 receptors causes vasodilation [6].

Dopamine exerts a wide range of cardiovascular effects in a dose-dependent fashion. At low intravenous infusion rates of 0.5 - 2.5 μg/kg/min (the so-called Renal dose), dopamine acts predominantly on the dopaminergic receptors, resulting in renal vasodilatation and increases in renal blood flow, urinary sodium excretion, GFR, and dieresis [7]. Because of these unique properties, dopamine has become widely used to increase urine output in an attempt to prevent the development of ATN in patients with PRA. This improves mortality and reduces the duration of hospitalization [8]. However, the ability of dopamine to achieve these goals is poorly documented and largely anecdotal [8]. Mas-Font *et al.* [9] examined the protective effect of low dose dopamine in patients undergoing coronary artery bypass surgery. These researchers found that dopamine neither improved renal function nor prevented ARF when compared with a control group [7, 9]. In early and established ARF, the results have been mixed. In a prospective study, Fakhari *et al.* [10] found that once serum creatinine (Scr) reached 6 mg% in patients with malaria-related ARF, dopamine (1 μg/kg/min) given with frusemide (200 mg 6 hrly) was of no value. However, when Scr had increased to only 2-4 mg/dl this combination of dopamine and frusemide was more effective than frusemide alone in reversing ARF [10].

Some reports in their in-depth review concluded that in an early phase of ARF, dopamine coupled with frusemide might be of benefit in improving azotemia and shortening the duration of ARF [11]. All these studies have been done abroad and largely on Caucasians. There is, therefore, the need to carry out a similar study locally so as to gain an insight into the place of dopamine in the management of ARF in our environment.

MATERIALS AND METHODS:

Study Design: The study was a comparative, conventional treatment controlled clinical study designed to quantify and analyze the effect of dopamine infusion in the treatment of prerenal azotemia. Thirty (30) consecutive patients with prerenal azotemia (PRA) were studied. Using computer-generated random numbers; the study population was divided into 2 groups (A and B). Group a received conventional treatment consisting of fluid replacement and parenteral frusemide; while group B received dopamine infusion in addition to conventional treatment. The clinical course of the PRA in the 2 groups was monitored and compared with each other utilizing hemo-dynamic changes, duration of Oliguria, and hospitalization primarily from PRA, urinary sodium, Urea, and creatinine excretion in the first 72 h and changes in serum urea and creatinine.

Study Area: This is a hospital-based prospective study which was conducted at Nnamdi Azikiwe University Teaching Hospital, Nnewi, Anambra State, Nigeria, between February, 2018 and December, 2019. The Renal Unit of this hospital serves Anambra State and the neighboring Imo and Abia State and the environs.

Study Population: The first consecutive 30 patients with prerenal azotemia (PRA) were recruited into the study. Using computer-generated random numbers (graph pad prism), the study population was divided into 2 groups; A and B. Those that received conventional treatment only [fluid replacement and intravenous frusemide A (n=15)] and those on conventional treatment and renal dose dopamine infusion B (n=15). In both groups, there were equal numbers of males and females, namely 7 males (46.7%) and 8 females (53.3%), respectively. Their ages ranged from 18 to 58 years for group A with a mean age of 37 ± 12 years, while the ages for group B ranged from 22 to 50 years with a mean age of 36.5 ± l0 years.

Ethical Approval and Informed Consent: The protocol was approved by the Board of Ethics Committee of NAUTH, Nnewi, Nigeria, with Ref: NAUTH/CH/66/VOL/10/58/2018/030. The entire adult patient with prerenal azotemia (PRA) gave their informed consent for the study.

Inclusion and Exclusion Criteria: Adult patients between 18 and 58 years were included in the study; patients with an identifiable clinical syndrome which may have led to PRA; namely. Hypovolemia: *e.g.,* Hemorrhage, Gastrointestinal loss (Diarrhoea, vomiting), Loss to extravascular space (burns, peritonitis, diuretic abuse, severe nephrotic syndrome). Hypotension: *e.g*., diminished cardiac output (cardiogenic shock, congestive cardiac failure, pericardial tamponade), Systemic vasodilation (septicemia, anaphylactic shock). Systemic or renal vasoconstriction: *e.g.* Anaes-thesia, surgery, hepatorenal syndrome.

Patients belonging to group B (above) who developed oliguria (urine volume <400 ml/24 h) and serum creatinine > 132 μmol/litre [13]. Patients with previous history of renal disease as judged by serum creatinine > 132 μmol/1 (1.5 mg %) or serum urea > 7.5 mmol/l (45 mg/dl) were excluded. Patients with intrinsic ARF *e.g.*, glomerulonephritis, vascular or interstitial disease, were excluded. Patients who had been on dialysis were also excluded. Patients with Acute Tubular Necrosis (ATM) were similarly excluded from the study. The following exclusion criteria were used to differentiate [14] the two conditions base on labora-tory tests.

For PRA: Urine protein-No proteinuria, Urine sediment analysis - normal or a few hyaline cast, Urine sodium (mmol/l) < 20, Urine creatinine (μmol/l > 8840, Urine/plasma creatinine > 40, Urine/plasma urea > 8, fractional excretion of filtered sodium ($FENa^+$ %) < 1, Renal failure index (RFI) < 1.

For ATN: Urine protein mild to moderate proteinuria, Urine sediment analysis – pigmented granular cast, Urine sodium (mmol/l) > 40, Urine creatinine (μmol/l) > 3500, Urine/plasma creatinine < 20, Urine/plasma urea < 3, fractional excretion of filtered sodium ($FENa^+$ %) > 2, Renal failure index (RFI) > 2.

Sample Technique: All clinical departments of the hospital, including accident and emergency, were notified of the study, and active findings were undertaken. Complete randomization using computer-generated random numbers was employed to divide the study population into two groups A and B. All p-patients in group a received conventional treatment only, and patients in group B received conventional treatment plus dopamine infusion. (conventional treatment comprised blood transfusion and 0.9% saline at 100-200 ml/h to correct the deficit (3-6 litres) within 48 h and to maintain the systolic blood pressure above 110 mm Hg [12], I.V Frusamide 3 mg/kg body weight 12 hrlyx 48 hrs was also part of the conventional therapy [15]. The water deficit was derived from the formula: ideal body water (litres) = observed body water x observed serum Na^+/Normal serum Na^+ (140 mmol/l).

The deficit (in litres) is the difference between the ideal body water and observed body water levels [12]. This formula was only applicable to patients with hypernatremic hypovolemia. For those patients with eunatremic or hyponatremic hypovolemia, the total fluid deficit in both groups was approximated, utilizing clinical parameters such as degree of dehydration, pulse rate, and magnitude of hypotension on presentation in line with recommendation [12]. The renal dose dopamine for group B was I.V. Dopamine 2 (μg/kg/min in 0.9 % saline to run for 48 h [13]. The total dose of dopamine for each patient for 48 hrs duration was calculated and added into 1000ml of 0.9% saline and delivered in a separate intravenous line at the rate

of five drops per minute (5 DPM). There was a standing order that this line must not be interrupted. The only major problem was that of getting reliable vascular access. There was no significant side effect referable to dopamine administration in all the patients; the following data were obtained: hourly Blood pressure pulse rate, hourly urine output, daily weighing, daily serum electrolyte/urea/creatinine, fasting blood sugar on day 1, daily estimation of urine sodium, urea, creatinine and potassium excretion and calculation of urinary indices. Morbidity in two groups was compared using the following as endpoint therapy: Duration of hospitalization primarily from prerenal azotemia. Development of Acute Tubular necrosis (ATN). Development of uremic syndrome and the need for dialysis. Mortality in the two groups was computed using death from a complication of ARF as endpoint.

Sample Collection: Fasting venous blood was drawn from the antecubital vein and transported in fluoride specimen bottles for fasting blood sugar estimation. Venous blood was also preserved in plain bottles for serum electrolyte, urea, and creatinine estimation. This was allowed to clot and centrifuged for 5 min at 3000 rounds per minute, and the supernatant serum extracted by means of pipette. After obtaining informed consent, a Urine sample was collected from each patient in a sterile plain bottle for dip tick as well as urine sediment analysis. The patient was also given a 4-litre plastic container with 10 ml of concentrated hydrochloric acid as a preservative, this enabled daily urine output to be accurately measured and urinary sodium, potassium, urea, and creatinine excretion to be measured.

The patient was instructed to empty his or her bladder by say 8 o'clock the following morning and then to collect all subsequent urine output in the container for the next 24 h having to void the last specimen by 8 o'clock the following day. The patient was instructed to avoid wasting any urine specimen during this 24 h period of collection. The importance of urination before delectation was emphasized to avoid accidental loss of urine. This process was repeated daily for the next five days. For the patients who were catheterized, the catheter was spigoted and then released hourly to empty the bladder into the plastic container. Blood pressure was taken in the supine position from the right arm using standard fourteen centimeters (14 cm) cuff width with a length of 25 cm and standard mercury sphygmomanometer (accoson brand). The systolic and diastolic blood pressures were taken as the Korotkoff sound, phases first and fifth [14,] respectively. All samples were assayed at the chemical pathology and microbiology laboratories of NAUTH, Nnewi, Nigeria

Methods:

Serum and Urine Parameters were determined by the Following Methods: 24 h urine output was quantified in milliliters and volumes hourly and 1 kg. Bodyweight/minute computed. Urinalysis to detect albumin, sugar, hemoglobin *etc*., was by means of dip strip (Combur 9, Boehringer and Ingelheim Ltd) urine sediment analysis by means of microscopy at the microbiology laboratory. Serum osmolality was calculated from the formula:

Serum osmolality = $2(Na^+)$ + Glucose + Urea/2 [15] (Mosmol / kg water) mmol / l mmol / l mmol / l.

Serum and urine urea and creatinine were determined by diacetyl monoxime method [16]. Serum and urine Sodium and potassium concentrations were measured with a (Jallenkamp flame photometer (FGA 33) [16]. 24 h sodium excretion and FeNa, were calculated using blood and urine measurements with formula [16]:

FeNa = Na urine mmol / l x Creat serum µmo l/ l / Na urine mmol / l x Creat urine mmol / l x 1000 X 100%

Fasting blood sugar was determined using glucose oxidase test (reaction) [17].

Statistical Analysis: All data collected were examined and summarized as means and standard deviation of means. Standard tables, bar diagrams, and bar charts were employed for vivid display of data.

The student t-test for comparison of the independent means was utilized to test the significance of the differences between the groups. This analysis using unpaired t-tests was with the assistance of graph pad prism 7.04. All reported P values are two-sided, and P values less than 0.05 were considered to be statistically significant. Chi-square (x^2) and fisher's exact test were also used in the analysis.

RESULTS:

Combined Precipitating Factors Causing Pre-renal Azotemia: Table 1 shows the analysis of the precipitating factors in the causation of PRA in this series revealed gastroenteritis to be commonest (26.7%). This was followed by post laparotomy and post cesaerian section (each 10%), while postpartum hemorrhage, road traffic accident, congestive cardiac failure, hepatorenal syndrome, incomplete abortion and post-hysterectomy each represented 6.67% of the cases. On the other hand, PRA from anaphylaxis, thermal burns, lobar pneumonia and acute pelvic inflammatory disease (PID), were the least common causes with each contributing only 3.3% of the cases.

TABLE 1: ANALYSIS OF COMBINED PRECIPITATING FACTORS IN PRA

Causes	No. of Patients	Males	Females	% of Total	Died
Gastroenteritis	8	3	5	26.67	1
Post partum hemorrhage	2	0	2	6.67	0
Road traffic accident (RTA)	2	2	0	667.	0
Congestive cardiac failure (CCF)	2	2	0	6.67	0
Post laparotomy	3	3	0	10.0	1
Hepatorenal syndrome	2	2	0	6.67	0
Incomplete abortion	2	0	2	6.67	0
Anaphylaxis	1	1	0	3.33	0
Post cesaerian section	3	0	3	10.0	0
Post hystrectomy	2	0	2	6.67	0
Thermal burns	1	0	1	3.33	0
Lobar pneumonia	1	1	0	3.33	0
Acute pelvic disease	1	0	1	3.33	0
Total	30	14 (46.7%)	16 (53.3%)	100%	1

Conditions Causing Prerenal Azotemia: Table 2 shows a grouping of the conditions causing PRA in this study. Medical conditions were the commonest, contributing 14(46.7%); followed by obstetrics and gynaecological; 10(33.3%) and lastly surgical, 6(20%) cases.

TABLE 2: GROUPING OF CONDITIONS CAUSING PRA

Conditions	Surgical	Medical	Obstetrics & Gynecological
Road traffic accident	2	0	0
Post laparotomy	3	0	0
Thermal burns	1	0	0
Gastroenteritis	0	8	0
Congestive cardiac failure	0	2	0
Hepatorenal syndrome	0	2	0
Lobar pneumonia	0	1	0
Anaphylaxis	0	1	0
Post partum hemorrhage	0	0	2
Incomplete abortion	0	0	2
Post caesarian section	0	0	3
Post hysterectomy	0	0	2
Total	0	0	1
% of Total	6	14	10
	20	46.7	33.3

Fluid Deficit in Patients in Group A and B: The comparison of fluid deficit replaced in the 2 groups revealed that the mean fluid deficit (in litres) in group A was 3.6 ± 0.55 litres not significantly different when compared with group 3.83 0 ± 59 litres (P > 0.05) **Fig. 1.**

Duration of Oliguria and Hospitalization in Patients in Group A and B: The patients treated with conventional treatment and dopamine infusion (Group B) had a shorter duration of oliguria and hospitalization.

Mean 3.0 ± 1.11 days and 6.0 ± 1.11 days) respectively, compared with patients treated with conventional treatment only (mean 4.0 ± 1.44 days and 7.0 ±1.44 days) (P = 0.025) **Fig. 2.**

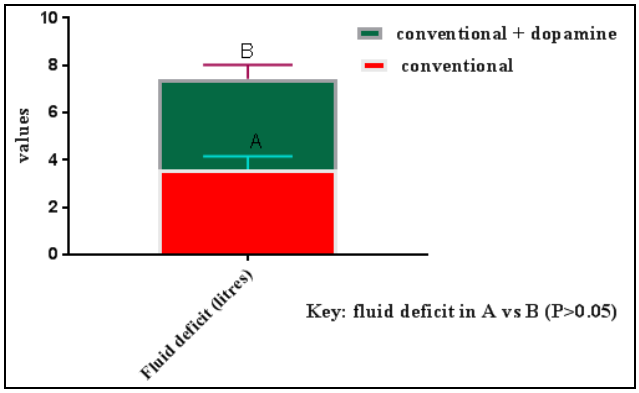

FIG. 1: COMPARISION OF FLUID IN GROUP A AND B

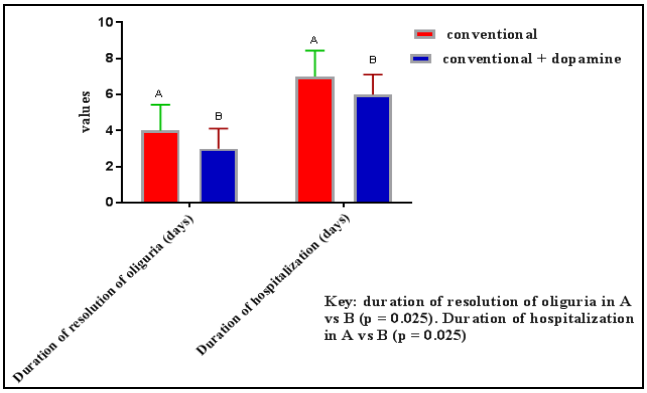

FIG. 2: COMPARISION OF DURATION OF RES-OLUTION OF OLIGURIA AND HOSPI-TALIZATION IN GROUP A AND B

Hemodynamic, Urine Output, and Osmolality in Patients in Group A and B: The mean pulse and blood pressure for Group A patients were 101 ± 11.2/min and 84/56 ± 1 l/9 mmHg, respectively, while those for group B were 106 ± 10.3 and 82/54 ± 13/10 mmHg. Comparison of the average pulse and blood pressure changes in the 2 groups did not reveal any statistical significance at (P > 0.05). On the other hand, the urine output both hourly and at 24 h was significantly more in group B patients (mean 17.3 ± 3.1ml and 415 ± 74 ml respectively); compared with group A (mean 14.6 ± 3.0 ml and 349 ± 70 ml respectively) (P = 0.025). However, this difference disappeared when one looked at the urine output in mls/kg body weight/hour. The mean plasma osmolality in the two groups when compared are not statistically different, being 298 ± 9.0 mosmol/kg H_20 and 298 ± 8.0 mosmol/kg H_20 for group A and B respectively (P > 0.05) **Table 3.**

TABLE 3: COMPARISON OF HEMODYNAMICS, URINE OUTPUT AND OSMOLALITY IN GROUP A AND B

Parameters	Age	Pulse(min)	BP (in mmHg)	UO (ml/24hrs)	UO/hr (ml/hr)	UO (ml/kg/hr)	Osmolality (mosmol/kg H_2O)
Group A Conventional (n = 15)	37.00±12.0	101±11.23	84/56±11/90	349±70	14.6±3.04	0.24±0.07	298±9.0
Group B Conventional + dopamine (n=15)	36.50±10.0	106±1 0.34	82/54±13/10	415±74	17.3±3.13	0.27±0.07	298±8.0
T- value	0.2032	1.26	0.3367	2.534	2.518	1.17	0.162
P-value	0.059	0.065	0.162	0.025	0.025	0.076	0.651

BP = Blood pressure, UO = Urinary output, hr-hour

Serum Urea, Cr and Urinary Urea, Cr, Na and Fractional Na Excretion in Patients in Group A and B: The mean serum urea on the first and fifth day in group A (19.0 ± 5.0 and 11.0 ± 13.0 mmol/l) were not significantly different compared with group B were (18.0 ± 5.0 mmol/l and 6.0 ± 4.0 mmol/l) (P > 0.05 respectively).

The mean serum creatinine in group A on the first and fifth day (329 ± 67.0 µmol/l and 198 ± 262 umol/l respectively), were not significantly different compared with group B (313 ± 68.0 µmol/l and 127 ± 81.0 µmol/l respectively) (P > 0.05). Although on the whole, the rate of decline of serum urea and creatinine were greater in group B than in group A. The differences were not found to be statistically significant (P > 0.05, respectively). The urine microscopy was essentially benign, urinary sodium excretion less than 20 mmol/l, fractional sodium excretion < 1%, and the ratio of urine urea (U) and plasma urea (P) greater than 8 in keeping with the diagnosis of prerenal azotemia.

The rate of urinary urea excretion by the 3rd day of admission was greater in patients with conventional treatment and dopamine than in patients treated with the conventional method alone. The mean urinary urea excretion for day 1 and day 3 was not significantly different between group A (164 ± 48 and 159 ± 39 mmol/l) and group B (158 ± 39 and

193 ± 61 mmol/l respectively) (P > 0.05). Furthermore, Patients in group B excreted more sodium in their urine from the second day than patients in group A. The Urinary sodium excretion in group A (30.3 ± 6.5, 47.5 ± 6.7 mmol/l) for days 2 and 3 respectively were significantly decreased than in group B for the corresponding days (40.1 ± 7.3 mmol/l, 83.2 ± 23.2 mmol/l) (P = 0.001, 0.001 respectively). However, although fractional sodium excretion was more in group B patients than in group A from the second day, this was not found to be statistically significant (P > 0.05) **Table 4.**

TABLE 4: COMPARISON OF CR, UREA, URINARY UREA, CR AND NA EXCRETION AND FRACTIONAL NA EXCRETION IN GROUP A & B PATIENTS

Parameter (days)	Duration	Conventional Treatment (A)	Conventional Treatment + Dopamine (B)	T- value	P- value
Urea(mmo/l)	1	19.0 ± 5.0	18 ± 5.0	0.441	0.168
	2	19.0 ± 6.0	18 ± 7.0	0.560	0.202
	3	16.0 ± 9.0	16.0 ± 11.0	0.271	0.912
	4	13.0 ± 11.0	11.0 ± 9.0	1.000	0.567
	5	11.0 ± 13.0	6.0 ± 4.0	1.170	0.057
Cretinine (µmol/l)	1	329 ± 67	313 ± 68	0.641	0.090
	2	318 ± 96	297 ± 96	0.083	0.059
	3	270 ± 14	264 ± 149	0.110	0.056
	4	238 ± 21	213 ± 160	0.372	0.086
	5	198 ± 262	127± 81	1.000	0.614
Urinary urea excretion (mmo/l)	1	164 ± 48	158 ± 39	0.403	0.057
	2	182 ± 43	193 ± 32	2.261	0.164
	3	159 ± 39	193 ± 61	1.803	0.066
Urinary Cr excretion (µmol/l)	1	13527 ± 2529	12970 ± 2304	0.6897	0.218
	2	12907 ± 2289	13253 ± 2518	0.6465	0.173
	3	10293 ± 1778	11553 ± 1948	0.6749	0.059
Urinary Na excretion (mmol/l)	1	7.5 ± 4.24	7.40 ± 4.14	0.0871	0.679
	2	30.3 ± 6.50	40.1 ± 7.32	3.877	0.019
	3	47.5 ± 6.70	83.2 ± 23.2	5.730	0.001
Fractional sodium Excretion (%)	1	0.13 ± 0.08	0.13 ± 0.07	0.1428	0.062
	2	0.67 ± 0.04	0.71 ± 0.07	0.2431	0.222
	3	1.22 ± 1.04	1.39 ± 0.56	0.5537	0.658

Combined Mortality and Morbidity Characteristics in Patients in group A and B: The survival, morbidity and mortality characteristics of the group a patients and group B patients. In group A, 10 patients (67%) survived, while 5 patients (33%) died; whereas in group B, 11 patients (73%) survived, and 4 patients (27%) died. While 5 patients in group A developed ATM, only 3 patients in group B developed ATM (P = 0.341). Also, the number of patients in groups A and B who developed the uremic syndrome and needed dialysis were 6 and 4, respectively (P= 0.439). 5(33 %) patients died in group A while 4 (27%) patients died in group B (P= 0.5) **Table 5.**

TABLE 5: COMPARISON OF COMBINED MORTALITY AND MORBIDITY IN GROUP (A AND B)

S. no.	Aetiology	Group A	Group B	Total	P-value
1	Thermal burns	1	0	1	
2	Hepatorenal syndrome	1	1	2	
3	Post C/S 2° to obstructed labour	1	0	1	
4	Acute PID with bacteremia	1	0	1	
5	Gastroenteritis	1	0	1	
6	Hemorrhage 2° to RTA	0	1	1	
7	Incomplete abortion, sepsis	0	1	1	
8	Post laparotomy 2° to intestinal obstruction	0	1	1	Fisher exact test I tailed: P-value =0.5
	Total (%)	5(33)	4(27)	9(30)	
	Morbidity				
1	Patients who developed acute tubular necrosis (ATN)	5	3	8	Fisher exact test: p=0.341
2	Patients with uremic syndrome and needed dialysis.	6	4	10	χ^2 =0.6 p=0.439
	Total	11	7	18	

DISCUSSION: Prerenal azotemia is a rapidly reversible decrease in glomerular filtration rate due to renal hypoperfusion and resulting in rising levels of urea and creatinine with oliguria. Dopamine, especially at low doses, has virtually become a standard of care even in established ARF, on the basis of some favourable experimental evidence and theoretical effects that might augment renal recovery *in-vivo*. Unfortunately, there are few studies that have prospectively tested low-dose dopamine, either in prerenal azotemia or in the prevention of ARF in high-risk patients. A significant reduction in the mean serum creatinine and time to recovery of ARF in the dopamine-treated group [10, 18]. While these findings are of substantial import, the small sample size and specific clinical scenario limit its generalizability.

In this study, 30 consecutive patients with prerenal azotemia were recruited and randomized into 2 groups: A and B. Patients in group A were treated with the conventional method only, while those in group B were treated with the conventional method and dopamine. The effect of dopamine in the treatment of prerenal azotemia was determined by comparison and analysis of different outcome parameters between these 2 groups. The result of the study has shown that the commonest cause of PRA is volume depletion secondary to gastro-enteritis, post laparotomy, and post-cesarean section. The least common causes are thermal burns, sepsis (lobar pneumonia and acute pelvic inflammatory disease) [19].

The result also showed that medical conditions are the commonest causes of PRA in this series, followed by obstetrics and gynaecological, and lastly surgical conditions. This finding is in keeping with previous report [20]. In this study, the mean duration of oliguria was significantly decreased in group B patients than in group A patients. Similarly, the mean daily and hourly urine output was significantly increased in group B patients than in group patients. This finding agrees with the well-documented accounts of the ability of dopamine to cause renal vasodilation, increases in renal blood flow and glomerular filtration rate, and hence natriuresis and dieresis [11]. Some previous researchers in their series found that low dose dopamine alone consistently increases urine output in resuscitated, oliguric patients and that the time course to maximal effect on urine flow is variable [21, 22]. The actions of dopamine on the kidney are complex, and many factors are responsible for the increased urine output seen with this agent in various disease states [22]. Increases in renal blood flow observed with low dosages of dopamine result from renal vasodilation and decreased renal vascular resistance by stimulation of the DA-1 adrenergic receptor. This increased blood flow appears to be preferentially directed towards the renal cortex [22]. However, in recent years, many researchers have questioned the reliability of urine flow rate as a measure of the effectiveness of pharmacologic intervention in ARF [17]. Some studies have shown that an imposed increase in urine flow rate correlates poorly with changes in renal function, the course of azotemia or patient survival [18].

The result of the study has shown that patients in group B spent less number of days in hospital than patients in group A. This may have resulted from a shortening of the duration of oliguria in group B patients as well as a more rapid fall in the level of azotemia. As would be expected, the cost of inpatient care would be more in group A than in group B patients. The actions of dopamine on the kidney at low infusion rates, coupled with minimal toxicity, have contributed to the popularity of prescribing dopamine in critical care units in an attempt to reverse oliguria [21]. The phrase "renal dose dopamine" is sometimes used when referring to the use of dopamine in oliguria.

However, this phrase implies a local effect on the kidneys for a drug that is administered systemically. Dopamine, at I.V. infusion rates of 3 μg/kg/min; possesses effect beyond the kidneys. For example, cardiac output increased an average of 17% to 37% in a group of hypertensive patients receiving dopamine at infusion rates of 1 and 2 μg/kg/min respectively [8, 22]. Some studies have even reported increases in systemic vascular resistance with low infusion rates [23, 24]. Data from this study indicate that there is no significant difference between the pulse rate and blood pressure changes in patients with PRA treated with conventional method alone and those treated with conventional method and low dose dopamine. Although some studies have shown that low dose dopamine can provoke distal ischemia and gan-

grene with extravasation adjacent to an artery [25] trigger tachyarrhythmias and myocardial ischemia and hasten the onset of gut ischemia [25, 26] there was no such deleterious effect observed in this study. This agrees with previous finding [17]. Patients in this study were oliguric for less than 24 h before intervention was initiated, and findings reflect early use of low dose dopamine in oliguria. Meanwhile, previous studies showed that the cardiac index did not change with low dose dopamine therapy; they concluded that the effects on urine output do not appear to be mediated by improvements in cardiac function [25, 27].

The trend in serum urea and creatinine changes seen in this study is in conformity with that seen in a number of other studies [28]. Although the rate and magnitude of fall of serum urea and creatinine by day 5 were more in group B than in group A patients, this change was not significantly different. Theoretically, dopamine-induced diuresis would be expected to result in increased urinary excretion of urea and creatinine and a parallel fall in their serum levels; a previous report showed that this is not so in practice. An imposed increase in urine flow rate correlates poorly with changes in renal function and the course of azotemia [29].

However, a study has noted that dopamine coupled with frusemide may be of benefit in improving azotemia and shortening the duration of ARF [30]. It has been documented that the renal vasodilatory effects of dopamine may enhance the delivery of residual frusemide to a critical area of the nephron, thus augmenting the action of this drug [13]. Studies also showed that no vasoactive agent had been shown to be beneficial in reducing the course of azotemia when GFR is profoundly reduced (Ccr < 5 ml/min) [30, 31]. It has already been noted that the mean duration of hospitalization primarily due to prerenal azotemia as morbidity defining entity is shorter for group B than for group patients. The study showed that 5 patients in group A and 3 patients in group B respectively developed ATN; while 6 patients in group A and 4 patients in group B developed uremic syndrome and needed dialysis. Comparing these morbidity characteristics statistically, the difference is not significant. This finding is in consonance with the previous report where the percentage of patients with ARF requiring dialysis was found to range from 20-60% [32]. Among the subgroup of patients who survive initial dialysis, less than 25% required further dialysis, demonstrating the potential reversibility of the syndrome [32]. However, it was unable to demonstrate that low dose dopamine significantly reduces progression of PRA to ATN or obviates the need for dialysis [33]. In this study, 2 patients died in group A while 1 patient died in group B for uremia. This gives combined mortality of 10%, which is in agreement with the rates observed in other studies [30, 33].

Like in this study, low-dose dopamine does not appear to improve patient survival in several other studies [8, 30]. However, slight trends toward reduced mortality among patients treated with low dose dopamine compared with an untreated group [34]. It is likely that failure to detect any change in morbidity and mortality in this study may reflect either a true lack of efficacy of dopamine or may be due to failure to demonstrate improved outcome as a result of the difficulty in satisfactorily adjusting for differences in case-mix as well as small sample size.

CONCLUSION: This study has looked at the effect of dopamine in the treatment of prerenal azotemia (PRA) at the nephrology clinic, NAUTH, Nnewi, Nigeria. Medical conditions are the commonest cause of PRA in this environment, with gastroenteritis leading. There is compelling evidence that diuretics and low dose dopamine augment renal blood flow, glomerular filtration rate, and natriuresis and limit ATP utilization and oxygen requirements in nephron segments at high risk for ischemic injury, actions that could potentially limit renal injury and accelerate recovery in PRA. As with this study, most clinical studies, however, have failed to demonstrate convincingly that low-dose dopamine improves renal function or outcome in patients with PRA. Although the duration of oliguria and hospitalization was shortened with dopamine in this study, other more clinically relevant outcome parameters such as improvement in renal function, development of ATN, need for dialysis, and mortality were not influenced. Although no adverse effect directly referable to dopamine was noted in this series, low dose dopamine can precipitate serious cardiovascular and metabolic complications in critically ill patients.

It is therefore apparent that low-dose dopamine has limited value in reversing or speeding recovery from ARF. Accordingly, the routine use of low-dose dopamine in the treatment of PRA should be discouraged until a multicentre, prospective, randomized and placebo-controlled trial establishes its safety and efficacy.

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