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Comparative use of Oral Rehydration Solution and Intravenous Hydration in the Prevention of Contrast-Induced Nephropathy following Coronary Angiography and Percutaneous Coronary Intervention - Ayman Amer El-Sherif Ahmad - MD HB Heart and Vascular Institute

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Contrast-induced nephropathy (CIN) is a widely recognized and clinically significant problem in patients undergoing minimally invasive procedures that require contrast administration. CIN is defined as an increase in baseline serum creatinine (S.Cr) by 0.5 mg/dl or a rise of 25% from the baseline level prior to contrast administration, and the nephropathy cannot be attributed to any other known cause of deranged kidney functional.For renal insufficiency to be attributed to contrast there must be no other identifiable cause of renal insufficiency and it has to occur within 7 days of administration with most cases occurring within 48-72 hours after administration of contrast. The markers used to determine renal insufficiency are serum creatinine levels, estimates glomerular filtration rate (eGFR) and estimated creatinine clearance (CrCl). CIN is considered a well-known complication of coronary angiography (CA) and percutaneous coronary intervention (PCI) due to the use of iodinated contrast media. The overall incidence of CIN in the general population has been reported from 2% in the general population without risk factors to more than 40% in high-risk patients .The incident rate of CIN is approximately 150,000 patients each year in the world, and at least 1% requires renal replacement therapy (RRT). CIN is mostly a self-limited condition. The level of S.Cr typically increases over 1 to 3 days, peaks at 4 to 5 days, and returns to baseline in 7 to 14 days. Only less than a third of the patients retain residual renal dysfunction. Dialysis due to CIN is required in only 3% of patients undergoing PCI .

Although there are many complex pathways involved in the development of CIN, the end result is thought to be ischemic injury to the renal medulla. Under normal conditions, the renal medulla is poorly oxygenated and operates in a near hypoxic environment. After administration of contrast, renal blood flood temporarily increases, then decreases over a prolonged period. These changes are mediated by a complex interplay of many factors. Renal vasoconstriction plays a major role and is mediated by vasoactive substances such as endothelin, adenosine, nitric oxide, and prostaglandins. Direct cytotoxic and osmotic effects of contrast on renal tubules also play a role and may be partly mediated by free radical formation. Increased intratubular pressure, increased urine viscosity, and tubular obstruction further contribute to renal injury.A study involving 936 patients scheduled for PCI involved randomizing the patients into two groups of normal and abnormal serum creatinine levels, then hydration and non-hydration groups. All the patients were monitored using creatinine levels 24 hours, 3 days and 7 days after administration of contrast. The results showed that CIN was more prevalent among the abnormal group (37.68%) than the normal group (6.52%) and that hydration was more effective among the abnormal group more so among those with diabetes mellitus.

Randomized trials have found IV hydration with normal saline to be consistently effective in the prevention of CIN in patients of all risk categories. Although the exact mechanism is unclear, it is theorized that the administration of IV fluids increases intravascular volume, promotes diuresis, dilutes the overall intravascular contrast load, induces vasodilation, suppresses the renin–angiotensin–aldosterone axis, and suppresses the release of antidiuretic hormone. The efficacy of oral hydration for the prevention of CIN in patients who receive contrast as outpatients or elective radiological procedures is still conflicting. A randomized controlled trial (RCT) study found a higher rate of CIN in patients undergoing elective cardiac catheterization who received oral fluid regimen than those who received IV normal saline. Conversely, a few studies demonstrated no

difference in the incidence of CIN between oral fluid hydration group and IV fluid regimen group. Because providing water alone does not increase the sodium content of body fluids, increasing the water intake of patients might not expand the intravascular volume or promote renal blood flow effectively. In contrast, supplementation with an oral hydration solution (ORS) might be effective as a CIN prophylactic.Low-osmolar ORSformula is 2.6 grams sodium chloride (NaCl), 2.9 grams trisodium citrate dehydrate, 1.5 grams potassium chloride (KCl), 13.5 grams anhydrous glucoseperliter of fluid.ORS contains moderately high concentrations of sodium (Na) and glucose which promotes water absorptionby a process of facilitated diffusion where the Na ion combines simultaneously with the glucoseby a sodium–glucose cotransporter 1 (SGLT1) protein, and then both the Na ion and glucose moleculesare transported together to the interior of the cell and thereby increased renal blood flow could be expected. One study compared intravenous saline infusion with oral supplementation of ORS in the prevention of CIN in a rat model, and concluded that hydration with ORS was comparable to IV saline infusion in preventing CIN, and recommended further evaluation in the clinical setting.

The efficacy of ORS on outpatient for the prevention of CIN in patients who receive contrast worth further exploration and research because it has a clinical implication, and would be cost-effective in terms of health service offered to such a category of patients. The main objective of this research is to determine if oral hydration with ORS is non-inferior to IV hydration in the prevention of CIN following CA or PCI in patients with moderate risk of developing CIN at Suez Canal University (SCU) hospital.

Objectives: Some studies demonstrated the superiority of saline infusion over oral fluids in decreasing CIN and the severity of kidney dysfunction. In their RCT, experiment included 53 patients and randomized them on the day prior to the scheduled catheterization to one of two groups – group 1 received normal saline for 24 h (at a rate of 1 ml/kg/h) beginning 12 h prior to scheduled catheterization, and group 2 were allowed unrestricted oral fluids. Ten subjects (18.9%) developed acute renal insufficiency. The incidence of acute renal insufficiency was significantly lower in group 1 (1 out of 27) as compared to group 2 (9 out of 26; p = 0.005 for comparison between groups; relative risk 0.11, 95% confidence interval 0.015 to 0.79). However, it was a small sized trial and its findings cannot be effectively generalized. There are plenty of studies that compared the efficacy of variable protocols of oral hydration as a prophylactic measure against CIN, in comparison with IV hydration, that showed that the oral hydration is not inferior to the intravenous hydration. Kong et al. (2017) reported that there was no statistically significant difference in the mean S.Cr or urea nitrogen at 12 hours, 2 and 3 days after the coronary procedures among the groups of oral and IV hydration (P > 0.05). Two different oral hydration protocols were used: Patients in group B (oral hydration group 1) consumed 500 ml of tap water 2 hours before the procedures, and another 2000 ml of tap water within the 24 hours following the procedures. Patients in group C (oral hydration group 2) consumed 2000 ml of tap water only within the first 24 hours after the procedure. In all three groups, patients were allowed to drink additional tap water or other fluids freely before and after the procedures.

Results: In this study, both groups were well-matched as there was no statistical significant difference between ORS group and IV group regarding age, gender, chronic illnesses, and BMI (p= 0.48, 0.79, 0.28, 0.133, and 0.26, respectively). Additionally, no statistically significant difference regarding the baseline LVEF (p=0.98), contrast volume (p=0.07) and the mean Mehran score (p=0.66) was found. There was no significant difference between CIN positive and CIN negative patients regarding procedure type or the contrast media volume. SimilarlyDussolet al. (2006) showed that the volume of contrast medium, the type of

radiological procedures and heart failure were not risk predictors. The mean age of our sample was 57.7 ± 8.61 years and about three-fourths of them were males (74%). About 63.7% were hypertensive and about half of the sample was diabetics. Additionally, 22.7% of our sample reported being active smokers. Similarly, a study was conducted to compare between oral and IV hydration in CIN prevention, the mean age was 64±14 years, 217 (70%) patients were men, 99 (32%) had diabetes mellitus. In another study, Cho et al. (2010) reported a mean age of 78±8 years in their study. About 17.5% of their sample was men and 36.2% of them were active smokers. Diabetes was present in 36.2% of the sample while 95.5 complained of HTN. A research experiment included 53 participants in their study, 52 of whom were males. Diabetic patients represented 18.85% of their sample. Another study by Akyuzet al. (2014) showed that 68.8%, 60.8%, and 70.6% of their sample were males, diabetics, and hypertensive, respectively.

Conclusions: In conclusion, ORS hydration is not inferior to IV hydration with respect to CIN prevention and offers an equivalent and practical approach in preventing a decline in renal function after contrast exposure without additional delay in hospital days. Thus, prophylactic hydration against CIN on outpatient basis can be effectively used. Further studies are suggested for more support of this modality. Our study has the strength of being the first RCT demonstrating that ORS is not inferior to IV hydration in regarding CIN prevention with perfect matching of the baseline characteristics of the two comparison groups. Additionally, we provided several time points of measurement of S.Cr and eGFR (72h, 1 week, and 2 weeks) to help not to overlook the delayed onset CIN. Our study faced some limitations. First, this is a single-center study whose results could not be effectively generalized before further confirmatory multi-centric trials. Second, these results may also not be valid for radiological procedures using the IV route (computerized tomography, etc.) rather than the intra-arterial route. Third, this study was unblinded; however, blinding at the patient level is not methodologically feasible and furthermore, lack of blinding was not expected to affect study outcomes which were objective and dependent on robust laboratory data (S.Cr and eGFR). Lastly, as a proof of concept study, patient included in ORS arm required hospitalization to confirm receiving the planned ORS protocol, however, future reallife trials assessing home-based ORS ingestion are required, as the value of the regimen is highly dependent on simplicity of the regimen so as not to require hospitalization to receive it.