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Prophylaxis of Contrast-Induced Nephropathy in Intravascular Contrast Computed Tomography Procedures by Use of Low Osmolality Contrast Media and Good Hydration

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ABSTRACT

Consequent to the extended use of intravenous iodinated contrast media, increased adverse effects have been recognized, with Contrast-Induced Nephropathy (CIN) constituting one of the most serious of these adverse effects. The purpose of the current study was to investigate a prophylaxis strategy for reducing the effect of intravenous contrast on the development of CIN. Data were collected from 120 patients who received intravenous iodinated contrast agents during CT procedures. CIN was defined as a relative increase of more than 25% or an absolute increase of ≥ 0.5 mg/dL (44 µmol/L) in serum creatinine levels within 48-72 hours post-CT. Our prophylaxis strategy involved intravenous administration of 500 ml normal saline within one hour before the CT procedure and 3 liters of oral hydration within 12 hours post-CT. Additionally, the volume of administered low osmolality contrast media was based on the weight of the patient. A paired t-test revealed no statistically significant differences in creatinine (t = 0.07, P = 0.942) or urea (t = 0.52, P = 0.608) pre-CT vs. post intravenous iodinated contrast media-enhanced CT. Use of low osmolality contrast media and good hydration pre and post intravenous iodinated contrast administration are effective approaches to the prevention of CIN.

Keywords: contrast-enhanced computed tomography, contrast-induced nephropathy, hydration, low osmolality contrast media

INTRODUCTION

Contrast-Induced Nephropathy (CIN) is defined as a deterioration of renal function as measured by an increase in serum creatinine of more than 25% or 44 µmol/L within three days of intravascular administration of contrast media (CM) in the absence of other etiology such as nephrotoxins, hypotension, urinary obstruction, or atheromatous emboli [1,2]. Several different definitions are used in the literature, most relying on the measurement of serum creatinine concentrations. Contrast-induced acute kidney injury (CI-AKI) has also been described in which injury or damage to the kidney has taken place, but is subclinical in that no measurable reduction in renal filtration is apparent [3]. The American College of Radiology suggests using the term postcontrast acute kidney injury (PC-AKI) rather than CIN as the literature points to an association but not causality [4].

Standardization of evidence-based best practices in nursing care may reduce the incidence of acute kidney injury due to contrast material by standardized fluid orders, patient education about oral hydration, and by limiting the volume of contrast material [5]. Several studies recommended that hydration is the intervention best supported by evidence for a preventive effect on CIN, though no randomized controlled trials directly compared hydration versus no hydration. Furthermore, intravenous hydration seems to be more effective than unlimited oral hydration [6-9]. An experimental study suggested that non-ionic contrast agents are less nephrotoxic than ionic alternatives. Consequently, the type and volume of contrast used correlate with the risk of CIN [10].

Comprehensive literature searches for randomized controlled trials of outpatient oral hydration treatment suggested that the oral fluid regimen might be regarded as a possible outpatient treatment option for CIN prevention in patients with normal to moderately reduced kidney function [11]. CIN is associated with adverse outcomes such as hospitalization, mortality, and dialysis. Unfortunately, there are no published reports from the Gaza Strip showed the incidence of CIN or the side effects of intravenous contrast injection during CT examinations.

The purpose of our study was to investigate a preventive approach to control the incidence of CIN among patients undergoing CT procedures involving intravenous contrast.

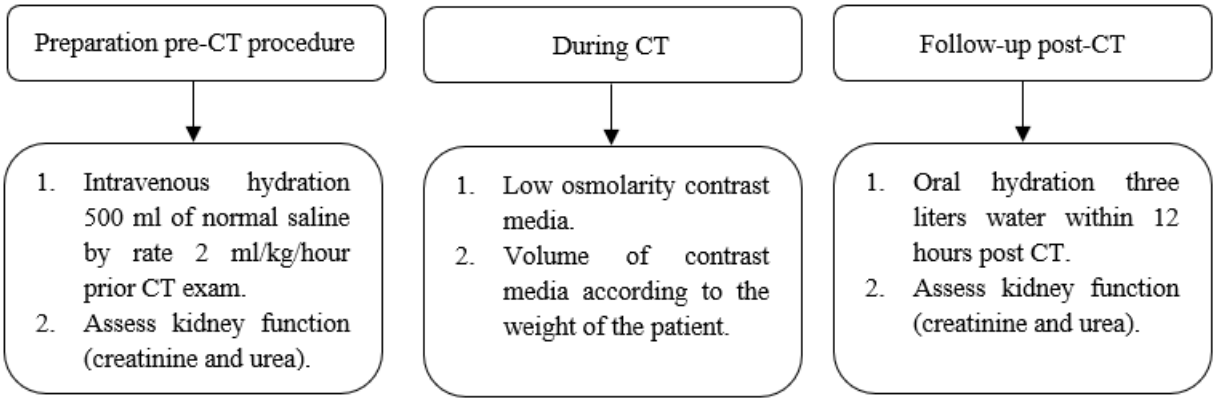

Figure 1. Flowchart of the prophylaxis strategy

MATERIALS AND METHODS

The present work was designed as a pre-experimental study design with prospective data collection aiming to study the deterioration of renal function as a side effect of iodinated contrast administration. This study was conducted in the Gaza Strip-Palestine hospitals for three months and included 120 hospitalized patients who underwent contrast-enhanced CT. The sample size determined by consecutive sampling in which every patient meets the criteria of inclusion is selected during the study period. The ethical approval was obtained from the human resource development general directorate in the Ministry of Health. Patients were evaluated by following their medical files. Pre and post-procedure urea and serum creatinine levels were recorded from the patients' files.

The study included the non-urgent admitted patients who documented with normal kidney function. We excluded the patients at risks such as patients with a history of severing allergy CM, congestive heart failure (CHF), preexisting chronic kidney disease (CKD), patients with a renal transplant, oncology patients and patients with anemia.

The flow diagram of the study is illustrated in **Figure 1**, which identifies the patient flow and the prevention strategy. The patients were given intravenous hydration of 500 ml normal saline (0.9%) by rate 2 ml/kg/hour before the CT procedure [12] prescribed by a consultant physician as hospitals policy for hospitalized patients. Pre-CT procedure serum creatinine and urea levels were obtained. During the procedure, the particular contrast material used, the dose of the contrast material, and the route of administration were documented. The volume of contrast media was administrated concerning a body weight-tailored CM dose of 1.0 ml/kg. During the 12 hours immediately following the CT exam, patients were instructed to drink three liters of water. Regardless of excluding the high-risk group, the consultant doctor performed a clinical judgment for the instruction of oral hydration. Hence, the volume of oral hydration was distributed within 12 hours to avoid hypervolemia. Furthermore, the commitment of patients for drinking oral hydration was followed and monitored by the patient's family. Serum creatinine and urea levels were obtained at 48-72-hours post-procedure from the same reference laboratory where pre-CT levels were determined.

Data analysis was done using SPSS version 25.0 software. The numerical variables are presented as mean and standard deviation. The categorical variables are shown as frequencies and percentages. A P-value of less than 0.05 was considered statistically significant.

Table 1. Medical history prior to the CT procedures

Patients' medical history	Categories	Frequency (%)
History of heart disease	Yes	10 (8.3%)
	No	110 (91.7%)
Diabetes Mellitus	Yes	21 (17.5%)
	No	99 (82.5%)

Table 2. Paired t-test differences in creatinine and urea pre- and post- contrast-enhanced CT

Test	Category	Mean ± SD	t	P-value
Creatinine	Pre-CT	0.96 ± 0.27	0.07	0.942
	Post-CT	0.95 ± 0.48		
Urea	Pre-CT	35.3 ± 15.2	0.52	0.608
	Post-CT	33.9 ± 25.4		

RESULTS

Gender distribution in the sample shows that there are 68 (56.7%) male and 52 (43.3%) female. Concerning age, the mean age of all patients in the sample is 52.3 years with a standard deviation of 7.2 years. Medical histories of the study subjects are illustrated in **Table 1**. Ten (8.3%) patients had a history of heart disease, and 21 (17.5%) had a history of diabetes.

All study subjects were administered Omnipaque (Iohexol) 350, a non-ionic, low osmolality, water-soluble radiographic contrast medium with a molecular weight of 821.14 and an iodine content 46.36%. The injection flow rate was 4-5 per second, and the administered volume ranged from 80 to 120 with an average of 96 ml.

A paired t-test was used to identify differences in urea and creatinine levels pre- and post- contrast-enhanced CT. Results are shown in **Table 2**. The test revealed no statistically significant differences in urea pre- (mean= 35.3, SD = 15.2) and post- (mean= 33.9, SD = 25.4) CT, with t = 0.52 and P-value = 0.608. Similarly, there were no statistically significant differences between pre- (mean = 0.96, SD = 0.27) and post- (mean = 0.95, SD = 0.48) CT creatinine, with t = 0.07 and P-value = 0.942.

DISCUSSION

A prevention strategy based on hydration and utility of low osmolality contrast media is effective, resulting in no significant changes in urea and creatinine. Consistent with

these results, a study conducted by Persson et al. [13] has recommended that hydration is the most effective treatment to prevent CIN through increased urine flow rates and dilution of the concentration of contrast media, which accelerates excretion.

Studies that showed that oral hydration before the contrast exposures are parallel in term of CIN prevention compared with intravenous hydration [12,14]. A more systemic review recommended that oral hydration may be as effective as intravenous fluid for CIN prevention [15]. In addition to the timing and route of hydration, the fluid composition may also contribute to prevention of CIN. Consistent long-term studies to regulate the optimal hydration strategy are needed. Several potential mechanisms can contribute to the beneficial effect of volume expansion [16].

With respect to the type of contrast media, studies comparing high versus low osmolality contrast media indicated that low osmolality reduced the incidence of CIN [17,18]. Guidelines on the use of intravascular iodinated contrast material administration recommend intravascular volume expansion with isotonic saline as standard prophylaxis for those considered at risk of CIN [19-24]. Consequently, the burden of huge budget's effects on patient and hospital because the pre and post CT procedural prophylactic treatment requires hospitalization for up to 24 h.

Regarding CIN risk stratification, Davenport et al. [25] used estimated glomerular filtration rate (eGFR), which indicated that intravenous low-osmolality iodinated contrast (IV LOCM) does not appear to be a nephrotoxic risk factor in patients with stable renal function. Furthermore, non-confounded post-CT CIN is rare in hospitalized adults with a stable renal function [26]. In parallel to the use of LOCM, careful consideration of procedural technique can reduce contrast load. Thus, the medical imaging specialist should be familiar with low contrast volume dose CT. The use of lower contrast media doses significantly reduces CIN [27].

The present study has several limitations. First, selection bias may be present because the study did not adequately recruit from a high-risk group. Second, due to the logistic barriers to follow-up, the study excluded outpatients. This is an area needing further study, as the strategy is readily adaptable to this group. The IV fluid can be administered before the CT procedure in the preparation room. The post-CT oral hydration can easily be done at home and monitored by the patient's family. Third, previous studies [28-30] investigated CIN by estimated glomerular filtration rate (eGFR), whereas the current study could not test the eGFR pre- and post-CT. Thus, further studies of outpatients and high-risk groups in Gaza Strip-Palestine are necessary.

CONCLUSION

The present investigation has attempted to investigate the preventive approach to control the incidence of CIN among patients undergoing CT procedures involving intravenous contrast in the Gaza Strip-Palestine hospitals. There is little evidence that IV iodinated contrast material is an independent risk factor for CIN when applying a preventive strategy involving good hydration pre- and post-CT together with the use of low osmolality contrast media.

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