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Scientific Research

Short Term Prognostic Utility of Tc-99m DMSA Renal Imaging in Sepsis Induced Acute Renal Failure; Provisional Data

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ABSTRACT

Background: Sound prognostic data in sepsis induced acute renal failure (SARF) are lacking especially on the short term outcome [STO] in the intensive care unit [ICU]. We addressed the use of Tc-99m DMSA [2,3-dimercaptosuccinicacid] renal cortical imaging as a prognostic tool in SARF. **Methods:** Forty patients with acute renal failure due to sepsis [age range 15 - 74 years; median 44.5] were subjected for full history taking complete physical examination, routine ICU monitoring, routine laboratory investigations, APACHE II [Acute Physiology and Chronic Health Evaluation] and SOFA [Sequential Organ Failure Assessment] together with Tc-99m DMSA cortical renal scintigraphy. Patients' death in the ICU or discharge was considered as the end point of the study representing the so-called short term outcome [STO]. **Results:** 25% mortality rate [10/40] was found along the admission period in the ICU. All non-survivors were abnormal with DMSA imaging [NPV & PPV 100% & 66.7% respectively]. Abnormal DMSA cases showed significant positive associations with serum creatinine at admission [r = 0.5; P 0.02]; admission duration [r = 0.4; P 0.002]; APACHE II score [r = 0.5; P 0.004] and STO [r = 0.4; P 0.03]. Statistically significant difference was elicited between subjects with normal and abnormal DMSA regarding the same parameters. **Conclusion:** This preliminary data could raise Tc-99m DMSA renal imaging as a prognostic tool in SARF that could allow influential interference to prohibit dramatic outcomes as mortality.

Keywords: Acute Renal Failure; Tc-99m DMSA; Sepsis Induced Acute Renal Failure

1. Introduction

Acute renal failure [ARF] is a sudden sustained decline in glomerular filtration rate [GFR] usually associated with uremia and a fall in urine output with a high mortality rate [1]. Factors affecting its incidence and outcomes are unclear therefore making optimal decision for patients' care is hindered [2]. Tc-99m labeled DMSA (2,3-dimercaptosuccinicacid) is avidly taken up by cells of the proximal tubule, with about 35% of the injected activity being localized in the renal cortex by one hour [3]. The renal uptake of Tc-99m DMSA parallels the renal function as determined by GFR and accordingly its uptake is significantly decreased in nephropathy [4,5] which is accepted as a poor prognostic sign [6]. Bernheim *et al.* in 1976 proposed renal scintigraphic scanning as a tool to assess the prognosis of ARF using hippuran and concluded that its uptake was a parameter which authorized the prognosis of a favorable course whereas its absence permitted one to envisage an unfavorable course [7]. However, in a case report published in 1986; a 35-year-old patient developed ARF on top of acute tubular necrosis requiring hemodialysis and they stated that failure to visualize acutely injured kidneys with Tc-99m DMSA did not preclude recoverable function [4], while the reverse was elicited in another two studies using hippuran [8,9]. Besides, much research is still needed because our understanding of what happens to the kidney in ARF is still poor [10]. Hence, we aimed to evaluate the predictive role of Tc-99m DMSA cortical scanning in predicting the short term outcome [STO] of the admission period in the intensive care in sepsis-induced ARF patients [SARF].

2. Patients and Methods

Forty patients with SARF were enrolled in the study and monitored for their ICU prognosis and outcome. ARF patients with previous renal transplantation, known urinary tract abnormalities or surgery or those with pre-existing CKD requiring regular haemodialysis and advanced congestive heart failure were excluded. Patients were subjected for routine ICU monitoring, routine labs, Electrocardiography, APACHE II [Acute Physiology and Chronic Health Evaluation] and SOFA scores [Sequential Organ Failure Assessment]. APACHE II is used as an indicator of severity of illness and likelihood of survival [10]. The patients were allocated to Tc-99m DMSA cortical renal scintigraphy as performed in accordance with a standard protocol. Imaging was done 3 hours after injection of the trace 111 MBq [3 mCi] with obtained anterior and posterior views suing "PHILIPS AXIS-2 VT; the Netherlands" gamma camera. The scintigraphic study findings were blindly interpreted and defined as normal or abnormal. We classified abnormal DMSA scans as based on visual assessment of images into GRADE 1 [Gr1; mild to moderate reduction in overall uptake with mild to moderate elevation of background] and GRADE 2 [Gr2; severe reduction in overall uptake with severe elevation of background]. Patients' death in the ICU or discharge was considered as STO that was used in calculating positive and negative predictive values [PPV and NPV].

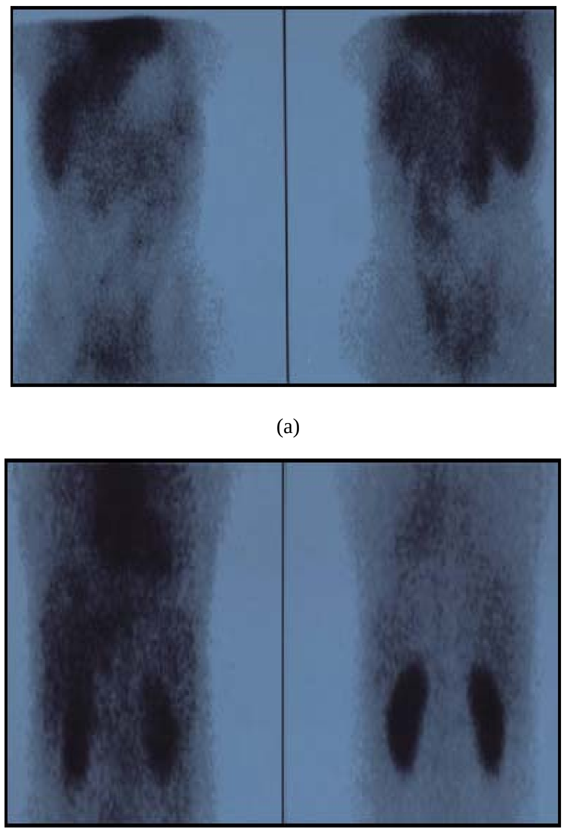
3. Statistical Analysis

Descriptive statistics included frequencies and percentages for each variable while numerical measures were represented as mean ± SD. Cross tabulation was utilized to describe the relations between variables using the contingency coefficient. T-test for testing the differences between samples was used. Correlations were done using Pearsons and Spearman correlation coefficients. Also; NPV and PPV were calculated and P value <0.05 was considered significant.

4. Results

40 patients [22 female & 18 males; mean age 47.2 ± 17 years] with ARF due to sepsis were enrolled in this study. Regarding their medical history; 32.5% were smokers and hypertensive (using B-blockers and Angiotensin converting enzyme inhibitors [ACE-I]), while diabetes was found in 17.5% [using oral hypoglycemic drugs]. Sepsis was the inducing factor for ARF with bronchopneumonia and pyelonephritis as the dominating clinical sources [27.5% and 22.5% respectively]. Other less sources included peritonitis and post-surgical sepsis [7 for each; 17.5%] and finally infected pace-maker [3 patients; 7.5%]. According to the STO in the ICU; patients were classified into survivors and non-survivors [**Figures 1(a)** and **(b)**] representing 30/40 [75%] and 10 [25%] respectively. Their characteristics are detailed in **Table 1**.

According to the STO; patients were classified into survivors and non-survivors representing 30/40 [75%] and 10 [25%] respectively. DMSA cortical imaging showed 25 and 15 cases as normal and abnormal [5 Gr1 and 10 Gr2 cases] respectively and all the non-survivors were Gr2. Correlations between DMSA cortical imaging and patients' STO [survivors and non-survivors] with various patients' factors are shown in **Table 2**. There was statistically significant difference between subjects with normal and abnormal DMSA regarding need of mechanical ventilation, serum creatinine on admission, admission duration, APACHE II Score and STO [P 0.02, P 0.03, P 0.01, P 0.01 and P 0.03 respectively]. Abnormal DMSA showed significant positive associations only with serum creatinine at admission time [r = 0.5; P 0.02], admission duration [r = 0.4; P 0.002]; APACHE II score [r = 0.5; P 0.004] and STO [r = 0.4; P 0.03]. Calculated



(a)

(b)

Figure 1. Tc-99m DMSA cortical renal scan [Left: anterior and right: posterior]. (a) Non-survivor case where G2 was elicited and the patient died a week after admission to ICU and (b) Survivor images with normal cortical uptake.

Table 1. Clinical and investigatory characteristics of the studied patients.

	Survivors [*n*. 30]	Non-survivors [*n*. 10]
Age [Mean ± SD]	47.4 ± 16.0	46.6 ± 20.3
Gender [*n*. %]		
• **Male [n. 18]**	13 [72.2%]	5 [27.8%]
• **Female [n. 22]**	17 [77.3%]	5 [22.7%]
ICU admission duration [Days]	12.9 ± 7.7	19.1 ± 13.7
Creatinine [mg/dl]		
• **At admission**	4.4 ± 1.6	3.6 ± 0.9
• **At discharge**	2.2 ± 1.7	2.9 ± 1.4
APACHE II score	19.6 ± 4.2	23.9 ± 3.2
SOFA score	7.1 ± 1.6	8.3 ± 1.7
Abnormal renal sonography	8/30 [26.5%]	3/10 [30%]
Echocardiographic findings		
• **Normal [n. 40]**	30 [75%]	10 [25%]
• **Abnormal [n. 0]**	-	-
Need for mechanical ventilation	7/30 [23.3%]	9/10 [90%]
Need for dialysis	4/30 [13.3%]	1/10 [10%]
DMSA scan		
• **Normal [n. 15]**	15/15 [100%]	0/15 [0%]
• **Abnormal [n. 25]**	15/25 [60%]	10/25 [40%]

Table 2. Correlations between DMSA cortical imaging and patients' short term final outcome with various patients' factors.

Patients' parameters	**DMSA scan**			**Short term final outcome**		
	Normal [n. 15]	**Abnormal [n. 25]**	**r-value P value**	Survivors [n. 30]	Non-survivors [n. 10]	r value P value
Age	43.3 ± 21	40.5 ± 19	r = 0.1 P 0.7	47.4 ± 16	46.6 ± 20.3	r = 0.1 P 0.8
Sex						
Male	6 [40%]	12 [48%]	r = 0.2	13 [43.3%]	5 [50%]	r = 0.1
Females	9 [60%]	9 [52%]	P 0.5	17 [56.7%]	5 [50%]	P 0.7
Smoking	5 [33.3%]	8 [32%]	r = 0.1 P 0.9	9 [30%]	4 [40%]	r = 0.2 P 0.6
Source of sepsis	-	-	r = 0.2 P 0.3	-	-	r = 0.2 P 0.1
Need of hemodialysis	0	5 [20%]	r = 0.2 P 0.07	4 [13.3%]	1 [10%]	r = 0.2 P 0.7
Need of mechanical ventilation	5 [33.3%]	11 [44%]	r = 0.5 P 0.02	7/30 [23.3%]	9/10 [90%]	r = 0.5 P 0.0001*
Serum creatinine						
On admission	3.8 ± 1	5.5 ± 2	r = 0.5 P 0.02*	4.4 ± 1.6	3.6 ± 0.9	r = 0.2 P 0.1
On Discharge	2.2 ± 1.7	2.9 ± 1.5	r = 0.2 P 0.9	2.2 ± 1.7	2.9 ± 1.4	r = 0.1 P 0.2
Abnormal renal sonography [n. 11]	0	11 [44%]	r = 0.3 P 0.06	7/30 [23.3%]	2/10 [20%]	r = 0.1 P 0.8
Admission duration	10.65 ± 7.8	18.1 ± 14.2	r = 0.4 P 0.002	12.9 ± 7.7	19.1 ± 13.7	r = 0.3 P 0.08
APACHE II score	16.2 ± 6	22.4 ± 8.1	r = 0.5 P 0.004*	17.6 ± 4.2	23.9 ± 3.2	r = 0.5 P 0.001*
SOFA score	5.5 ± 2	8.5 ± 3	r = 0.3 P 0.051	7.1 ± 1.6	8.3 ± 1.7	r = 0.3 P 0.052
Short term final outcome survivors	15/15 [100%]	15/25 [60%]				
Non-survivors	0/15 [0%]	10/25 [40%]	r = 0.4 P 0.03*	-	-	-

*P < 0.05 is considered significant.

PPV and NPV for DMSA imaging were 66.7% and 100% respectively.

5. Discussion

This study was carried out on 40 SARF patients and showed a mortality rate of 25% along the ICU admission period. Abnormal Tc-99m DMSA revealed a significant positive association with STO [r = 0.4; P 0.03]. Although different modalities for this clinically relevant task has been proposed, to our knowledge no previous studies have reported using Tc-99m DMSA cortical imaging as a prognostic tool; hence, this prospective study was addressed.

Our patients were recruited from ICU unit, as in Egypt ARF is usually treated in ICU and attributed mostly to sepsis. The latter was reported as the commonest causative factor of ARF (up to 50%) [2,10,11]. In fact, ARF is nowadays mostly observed as part of the multi-organ dysfunction syndrome in severe sepsis and septic shock [12]. 10/40 [25%] of our patients died in the ICU admission period and this agrees with Prescott *et al.* study as many of his deaths [20% - 30%] were very early where ARF was sepsis-induced. They concluded that the presence of sepsis increased the risk of death; both as an etiological factor and poor indicator of prognosis in a startling manner [2].

Also, we have chosen the German Prevalence Study [GPS] [13] for comparison with our elicited data as they studied a cohort of ARF patients with and without sepsis and compared both groups regarding patients' various factors and reported significant differences between serum creatinine at admission, APACHE II and SOFA scores. They reported a higher mortality rate [64.4% vs. 25%]. This disagreement could be explained by our small patients' number and the relatively younger age of our cases that carries in general an expected better outcome. Also, pulmonary infection was the most frequent source for sepsis as in our study [59% vs. 40%]. In our study significant statistical associations were found between DMSA and STO, serum creatinine at admission, APACHE II and need for mechanical ventilation in concordance with the same significant parameters of GPS.

We tried to find an explanation for our findings; as DMSA is avidly taken up by cells of the proximal tubule and with sepsis damage of the proximal tubules might occur and [3], so the higher the damage the lower is DMSA uptake and the worst is outcome. Hence in Gr2 pattern extensive damage of the proximal tubules was found in non-survivors.

Finally, since kidney injury in SARF plays an important role in prognosis; this preliminary data could raise Tc-99m DMSA cortical imaging as a tool to predict STO in such patients with 100% and 66.7% NPV and PPV respectively. As said by Niccolo Machiavelli [The Prince, 1513], "It ought to be remembered that there is nothing more difficult to take in hand, more perilous to conduct or more uncertain in its success than to take the lead in the introduction of a new order of things" hence, we tried to introduce DMSA renal imaging as a promising prognostic radiopharmaceutical with subsequent interference to ban serious sequences as mortality. However, we recommend further larger studies to support these provisional data.

6. Conclusion

Tc-99m DMSA cortical imaging could be raised as a diagnostic tool to predict short term outcome in such sepsis induced acute renal failure patients with 100% NPV and 66.7% PPV respectively that could allow influential interference to prohibit dramatic outcomes as mortality.

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