Renal dysfunction after major surgical operation : the impact of age, gender, and obesity

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الخلاصة

الهدف: دراسة التغيرات الحاصلة في وظيفة الكليتين نتيجة إجراء العمليات الجراحية الكبرى ومدى تأثير العمر،الجنس ووزن الجسم.

الطريقة: أجريت هذه الدراسة على ٧٠ مريضا (٣٩ذكرا و٣١ أنثى) ممن اجريت لهم عمليات جراحية كبرى في مستشفى الصدر التعليمي في النجف الاشرف/ العراق ، للفترة من تشرين الأول ٢٠٠٩ ولغاية أيلول ٢٠١٠.وبأعمار تتراوح بين ٢٠-٦٠ سنة .حيث تم قياس تركيز الصوديوم، الكرياتنين ،و جوهر البول في الدم وتركيز الصوديوم، والكرياتنين في البول و حساب معدل تصفية الكرياتنين والافراغ التجزيئي للصوديوم للمرضى المشاركين بالدراسة قبل وبعد اجراء العملية الجراحية.

النتائج: أظهرت الدراسة وجود زيادة ذات أهمية إحصائية في مستوى الكرياتنين ،و جوهر البول في الدم و الافراغ التجزيئي للصوديوم ووجود نقصان معنوي في معدل تصفية الكرياتنين لدى كبار السن (٤١-٦٠ سنة) بعد اجراء العملية الجراحية بالمقارنة مع نتائج ما قبل العملية الجراحية($P\leq 0.0001$ ، $P\leq 0.0001$ ، $P\leq 0.0001$ ، $P\leq 0.0001$) . في حين لم تبدي الدراسة اختلافا معنويا في القيم المذكورة اعلاه لدى المرضى الدين تراوحت اعمارهم بين ٢٠ الى ٤٠ سنة. كما أظهرت نتائج الدراسة وجود زيادة ذات أهمية إحصائية في مستوى الكرياتنين ،وجوهر البول في الدم والافراغ التجزيئي للصوديوم ووجود نقصان معنوي في معدل تصفية الكرياتنين لدى المرضى المصابين بالسمنة بعد اجراء العملية الجراحية بالمقارنة مع نتائج ما قبل العملية الجراحية ($P\leq 0.0001$ ، $P\leq 0.0001$ ، $P\leq 0.0001$ ، $P\leq 0.0001$). في حين لم يظهر نتائج الدراسة اختلافا معنويا في القيم المذكورة اعلاه بين الذكور والاناث .

ألاستنتاجات :أظهرت نتائج الدراسة حدوث اعتلال كبير في وظيفة الكليتن اثناء اجراء العمليات الجراحية الكبرى خاصة لدى كبار السن والمرضى المصابين بالسمنة .

ABSTRACT

Aim: To study the effect of major surgical operation on renal function and to evaluate the role of age, gender and body weight.

Methods: seventy patients (39 males, and 31females) aged (20-60 years), who admitted to Al-Sader Teaching hospital for major surgical operation in Al- Nagaf Al-Ashraf, from October 2009 to September 2010. For every patient participate in the study plasma concentration of sodium, creatinine, urea, urine sodium , urine creatinin, creatinine clearance and fractional excretion of sodium were determined.

Results: The were statistically significant increase in plasma level of creatinine, urea, and fractional excretion of sodium ($P\leq 0.001$, $P\leq 0.0001$ and $P\leq 0.0001$) and statistically significant decrease in creatinine clearance ($P\leq 0.0001$) after surgical operation in comparison with preoperative values in elderly patients(41 - 60 years).

A similar statistically significant changes observed in obese patients when preoperative values are compared with postoperative values. While there was no significant changes in the preoperative and postoperative values of these parameters in younger age groups(20-40 years) or when patients classified into males and females.

Conclusion: major surgical operation had significant effect on renal function, specially on elderly and obese patients.

INTRODUCTION

Adequate cardiac output is essential for proper perfusion and function of different organs and tissues of the body. Surgical procedure is associated with significant hemodynamic changes, and the maintenance of cardiovascular stability during surgical operation requires interplay between many compensatory and homeostatic factors such as systemic vascular resistance, venous compliance, and autoregulatory capacity of various vascular beds. The ultimate goal is to maintain regional perfusion at a level that supports optimal cellular and organ function[1]. The kidneys plays an important role in the regulation of body fluid volume and electrolytes concentration, normally the kidneys receive as much as 1/4th of the cardiac output. Impairment of kidneys perfusion may lead to impairment of renal function with subsequent body fluid and electrolyte imbalance[2]. Previous studies shows that a variable degree of impaired renal function, occurs in up to 30% of all patients who undergo cardiac surgery[3,4,5], approximately 1% of them requires dialysis[6,7]. The development of kidney injury is associated with a high mortality, a more complicated hospital course, and a higher risk for infectious complications[8]. Even minimal changes in serum creatinine that occur in the postoperative period are associated with a substantial decrease in survival[9]. These data highlight the importance of understanding the pathophysiology of kidney injury associated with surgery and implementing specific therapies that are based on this knowledge in well-designed clinical trials. The aim of this study was to investigate the incidence and pattern renal function impairment following major non-cardiac surgery among patients with previously normal renal function.

MATERIALS and METHODS

The present study was conducted on 70 (39males and 31 females) patients with various major surgical operation who were admitted to the surgical wards, at Al-Sader Teaching hospital/ Al- Nagaf Al-Ashraf, from October 2009 to September 2010. After recording the routine information, concerning name, age, gender, body weight and height for every patient included in the study, a careful history and physical examination was performed to exclude any history of renal diseases. The patients were divided into two groups according to their ages, group I included 34 patients aged 20 - 40 years, Their body weights were 45- 89 kilograms and heights 157-185 cm. and group II included 36 patients aged (41- 60) years, their body weights were 50-91 kilograms and heights were 132-183 cms. Depending on body mass index(BMI) the patients included in this study was divided into two groups, 41patients with normal body weights (BMI▪ 25 Kg/m^2) and 29 patients with overweight and obesity (BMI ▪ 25 Kg/m^2)[10].For every patients participated in this study 5 ml of blood was collected from anticubital vein one day before operation and one day after operation. The collected blood samples were placed in tubes containing lithium heparin. The plasma was separated within 30 minutes of blood collection and kept in capped plastic tubes in the deep freeze (-20 Ċ) until analysis. For each plasma sample we determined the concentration of sodium(P_{Na}), creatinine(P_{cr}) and urea(P_{Ur}). Five ml of random urine sample was collected from every subject participated in the study one day before and one day after operation for determination of urinary sodium (U_{Na}) and urinary creatinine(U_{cr}) concentration. Plasma and urine sodium concentration was measured using an emission flame photometer[11], creatinine are manually measured by Jaffe end point method using kit from Biosyr[12], and plasma urea concentration was determined enzymatically, using kit

Purchased from Bicon ,Germany [13]. Utilizing the plasma creatinine together with age, body weight and height the creatinine clearance (C_{Cr} ml/min/ 1.73 m^2) was calculated by the following formula [14]:

$$C_{Cr}\ (\text{mL/min}) = \frac{(140 - \text{age in years}) \times \text{lean body weight (kg)}}{P_{Cr}\ (\text{mg/dL}) \times 72}$$

The fractional excretion of the filtered sodium (FE_{Na}%) was estimated from plasma and urine creatinine and sodium concentration by the following formula [15]

$$FE_{Na}\ (\%) = \frac{U_{Na} \times P_{Cr}}{P_{Na} \times U_{Cr}} \times 100$$

Data are expressed as mean ± standard deviation. Comparisons of the variable data were considered using paired Student's t-test. Statistical analysis was performed with SPSS 18 for Windows (SPSS Corporation, Chicago, Illinois).

RESULTS

The mean of P_{cr}, P_{Ur}, Ccr , and FE_{Na}% in group I (20-40 years), and group II (41-60 years) are shown in table (1). The mean of P_{cr}, P_{Ur} ,and FE_{Na}% in group II showed a statistically significant increase after surgical operation in comparison with the preoperative values ($P \leq 0.0001$, $P \leq 0.0001$, and $P \leq 0.0001$), while there was a significant decrease in the mean of postoperative Ccr ($P \leq 0.0001$). On the other hand no significant changes observed in the means of postoperative values of P_{cr}, P_{Ur}, Ccr, and FENa% in comparison with preoperative values in group I.

Table (1): Mean ± SD of plasma creatinine, plasma urea, creatinine clearance and fractional excretion of sodium in group I, and group II before and after surgical operation.

Parameter	**group I** (n=34) (20-40 years)		**group II** (n=36) (41-60 years)	
	Before operation	After operation	Before operation	After operation
P_{Cr} µmol/L	**72.4 ± 5.4**	**72. 6 ± 65**	**73.2 ± 6.7**	**83.1± 9. 8***
P_{Ur} mmol/L	**5.5 ± 0.53**	**5.6 ± 0.52**	**6.1 ± 0.53**	**6.8 ± 0.45***
C_{Cr} ml/min/1.73m^2	**102.31 ± 5.5**	**101.6 ± 5.6**	**93.1 ± 5.87**	**85.8 ± 8.3***
FE_{Na}%	**0.81 ± 0.04**	**0.82 ± 0.06**	**0.76 ± 0.08**	**0.81 ± 0.09***

* The preoperative values are significantly differ from respective postoperative value in group II.

The mean of P_{cr}, P_{Ur}, Ccr, and FENa% in obese patients, and patients with normal body weight are shown in table (2). The mean of P_{cr}, P_{Ur} ,and FE_{Na}% in obese patients showed a statistically significant increase after surgical operation in comparison with the preoperative values ($P \leq 0.0001$, $P \leq 0.0001$, and $P \leq 0.0001$), also there was a significant decrease in the mean of postoperative Ccr ($P \leq 0.0001$). while there were no significant changes in the means of postoperative values of P_{cr}, P_{Ur}, Ccr, and FENa% in comparison with preoperative values in patients with normal body weights. The result of the study showed no significant changes in the means of postoperative values of P_{cr}, P_{Ur}, Ccr, and FENa% in comparison with preoperative values when patients are scored according to gender.

Table (2): Mean ± SD of plasma creatinine, plasma urea, creatinine clearance and fractional excretion of sodium in overweight and obese patients, and patients with normal body weight before and after surgical operation.

Parameter	**Obese patients** (n=29) **BMI** (31.2 ± 2.5)		**Normal body weight** (n=41) **BMI** (20.1 ± 4.5)	
	Before operation	After operation	Before operation	After operation
P_{Cr} µmol/L	**74.4 ± 5.4**	**82. 6 ± 65***	**71.2 ± 6.7**	**71.5± 9. 8**
P_{Ur} mmol/L	**6.1 ± 0.53**	**6.8 ± 0.45***	**5.1 ± 0.53**	**5.3 ± 0.52**
C_{Cr} ml/min/1.73m^2	**93.7 ± 6.5**	**86.6 ± 7.6***	**103.1 ± 9.87**	**102.8 ± 8.3**
FE_{Na}%	**0.71 ± 0.04**	**0.82 ± 0.06***	**0.76 ± 0.08**	**0.81 ± 0.09**

* The preoperative values are significantly differ from respective postoperative in The obese patients.

DISCUSSION

The result of the present study showed a significant reduction in the renal function after surgical operation among elderly patients , specially when it associated with obesity. Further more, renal dysfunction was more common among patients with major surgical operation and those who had normally high preoperative $P_{Cr.}$. Acute kidney injury usually defined as a rise in P_{Cr} > 1.4 mg/dL at any time during the stay with an increase of P_{Cr} of > 0.3 mg/dL from the baseline value during the first postoperative week[16]. one out of the 70 patients (1.4 %) developed postoperative acute kidney injury, he had BMI greater than 30Kg/m^2 and more than 55 years old. In general the impairment in renal function as manifested by increase P_{cr} and P_{ur} and decrease in C_{cr} was more common in elderly patients, this was expected, because the glomerular filtration rate is known to decline with increasing age[17,18]. Being obese with a BMI > 30 kg/m^2 was also identified as a significant risk factor[19,20]. In fact there are a large number of studies concerning the effect of cardiac surgery on renal function[21]. However, the number of studies dealing with renal function during general surgery is not too much, even those which done in this field was retrospective in nature and used

to utilize P_{cr} levels rather than an estimation of C_{cr} as an index for renal function[22]. Although a rise in P_{cr} usually represents a reduction in C_{cr}, with the exception of certain drugs that interfere with the creatinine assay or secretion or conditions such as rhabdomyolysis[23,24].However, the efficiency of P_{cr} as an accurate determinant of renal function had been challenged[25,26].

The physiological and clinical implications of the FE_{Na}% is of considerable importance, the test precisely defines the renal handling of sodium, thus it can differentiate between impaired renal function due to hypoperfusion of the kidneys and acute tubular damage[27]. Epsinal found that patients with acute tubular necrosis had FE_{Na}% values > 3, whereas patients with decreased renal blood flow had values < 1[28]. The value of FE_{Na}% in all patients who manifested renal dysfunction in this study was < 1, and according to Epsinal, this would suggest that the majority of patients who develop postoperative renal dysfunction had hypoperfusion of the kidneys rather than acute tubular damage. In conclusion the study demonstrated that elderly and obese patients undergoing major, non cardiac surgery liable to have a significant decrease in renal function.

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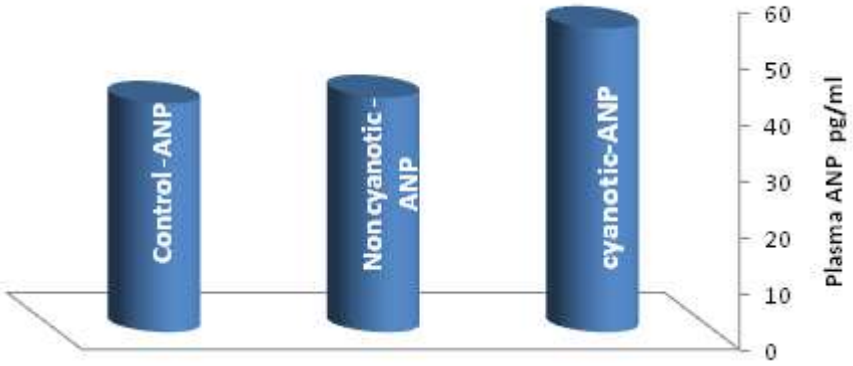

Figure (1) : Mean ± SD of Atrial natriuretic peptide, in cyanotic and non-cyanotic subjects with congenital heart disease and control group .

The mean of LVEF% was significantly lower in cyanotic subjects compared with non-cyanotic subjects (P≤ 0.0001) and control group(P≤ 0.0001), but there was no significant difference in the mean of LVEF% between non-cyanotic subjects and control group. The mean plasma BNP was significantly higher in non-cyanotic subjects with congenital heart disease compared with control group(P≤ 0.0001). However, there was no such differences in the mean of ANP between the non-cyanotic subjects and control group.

The averages mortality rate associated with the development of post operative kidney injury is about15 to 30%, (1–15). In patients who require dialysis, the mortality is uniformly high in all studies and averages 60 to 70% (1–15).. Lassnigg *et al.* (16) demonstrated that the 30-d mortality of patients who developed a 0- to 0.5-mg/dl and >0.5-mg/dl rise in serum creatinine was 2.77- and 18.64-fold higher, respectively, than patients without a change in serum creatinine. These results are qualitatively similar to studies by Thakar *et al.* (20) in which 31,677 patients who underwent cardiac surgery were analyzed. Mortality was 5.9% ($P < 0.0001$) when GFR declined 30% or more but did not require dialysis and 0.4% ($P < 0.001$) in patient with <30% decline in GFR. The development of post-CPB ARF also influences long-term mortality as identified by Loef *et al.* (21), who found that the hazard ratio for death at 100 mo after hospital discharge was 1.63 in patients who de

CPB provokes a systemic inflammatory response syndrome (SIRS; Figure 2) (84,85). Contact of blood components with the artificial surface of the bypass circuit, ischemia-reperfusion injury, endotoxemia, operative trauma, nonpulsatile blood flow, and pre-existing left ventricular dysfunction all are possible causes of SIRS in this setting (86–88). In its most severe form, a spectrum of injury that includes one or more of the following clinical manifestations may be observed: Pulmonary, renal, gastrointestinal, central nervous system, and myocardial dysfunction; coagulopathy; vasodilation and increased capillary permeability; hemolysis; pyrexia; and increased susceptibility to infection (89). During CPB, both neutrophils and vascular endothelium are activated with upregulation of adhesion molecules such as CD11b and CD41 (89–92). Platelets also undergo activation, degranulation, and adherence to vascular endothelium (91,93). These events led to elaboration of cytotoxic oxygen-derived free radicals (94), proteases (95), cytokines (96), and chemokines (96,97). These inflammatory mediators, such as IL-6, IL-8, and TNF-α, show a considerable rise in serum levels during CPB and generally reach peak levels 2 to 4 h after termination of CPB (84).

Furthermore, episodes of preoperative hypotension may lead to sublethal endothelial injury, which may impair the production of vasodilatory substances such as endothelial nitric oxide and promote vasoconstriction as a result of the release of endothelin, catecholamines, and angiotensin II, promoting further tubular ischemia and injury (64–66).

معلومة

In a recent study, recombinant human ANP (rhANP) was used to treat ARF after cardiac surgery in patients who required inotropic support for heart failure (138). In patients who received rhANP, there was a significant reduction in the incidence of dialysis at day 21 after the start of treatment. In this trial, ANP was infused at a lower rate (50 as opposed to 200 ng/kg per min; thus lowering the incidence of hypotension) and for a more prolonged period than previous studies. These changes may explain the benefit seen in this study as opposed to earlier ones.

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