RESIDUAL RENAL FUNCTION IN UREMIC PATIENTS UNDERGOING REGULAR HAEMODIALYSIS ASSESSMENT AND CLINICAL SIGNIFICANCE

Thesis

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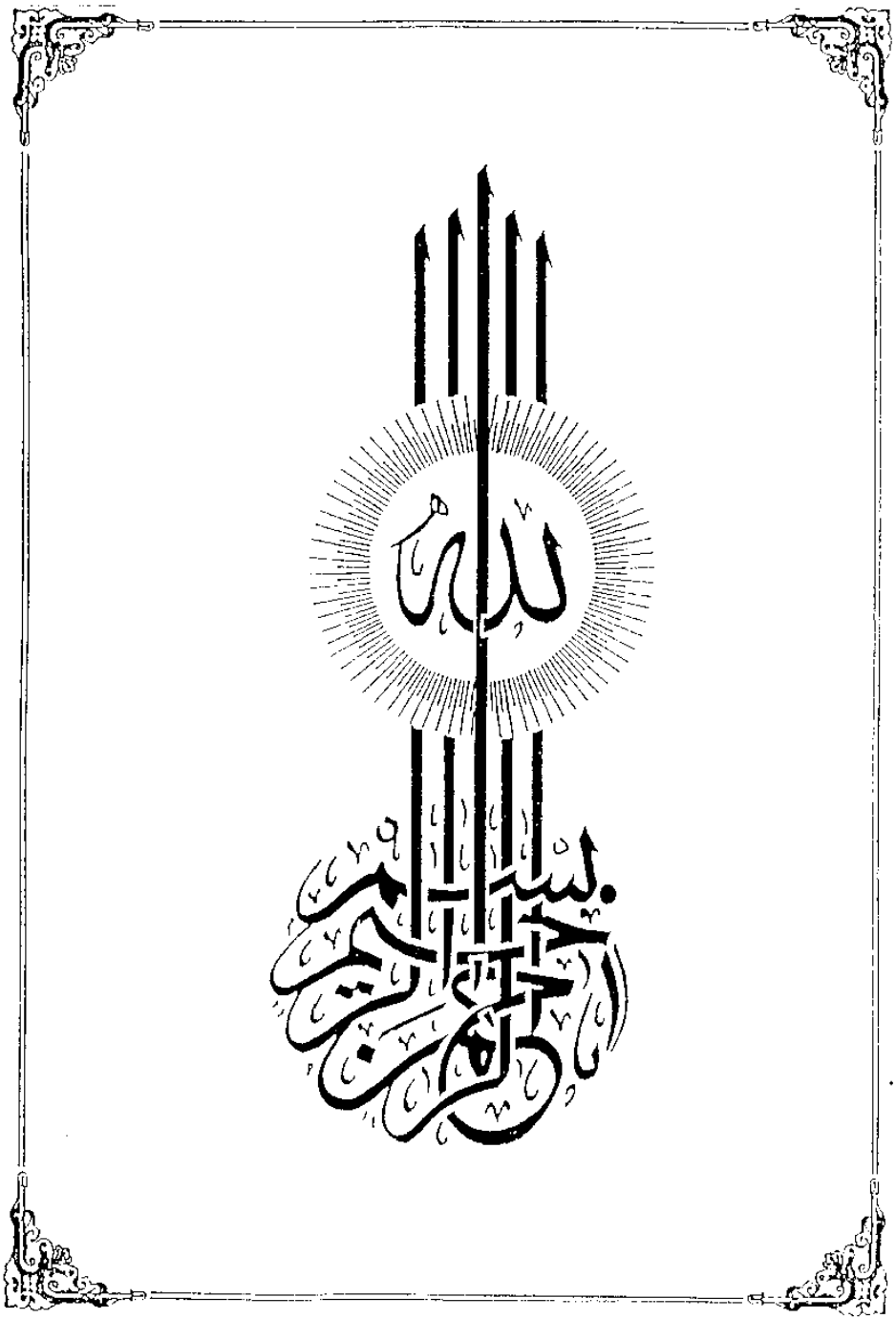

List of Abreviations

GFR = glomerular filtration rate.

SNGFR = single nephron glomerular filtration rate.

CRF = chronic renal failure.

RRF = residual renal function.

Chr. gl. N. = chronic glomerulo nephritis.

Chr. P. N. = chronic pyelonephritis.

obst. urop. = obstructive uropathy.

chest urop. = chest uropathy.

PTH = Parathyroid hormone.

Shist. Neph. = shistosomal nephropathy.

D.I. = dialysis index.

Diab. Neph. = diabetic nephropathy.

Content

INTRODUCTION
AND
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Measurement of Residual Glomerular filtration rate has several important applications in management of patients with chronic renal failure.

Residual Renal function is an important parameter in planning conservative and dietary management (Mackenzie W. et al., 1978), in deciding the time of onset of dialysis treatment (Bonomini V., 1975), in quantitation of dialysis therapy and short dialysis schedule (Milutinovic J., et al., 1974), in drug and middle molecule elimination, and finally in assessing the adequacy of dialysis therapy and its long term complications e.g. neuropathy and oesteodystrophy (Man N.K., et al., 1978; Saido A., et al., 1980; Oules R., et al., 1980).

Several methods are used in measurement of residual renal function. These methods include:

Urea and creatinine clearance, Inulin clearance, Manitol and other Hexitols clearance, Allantoin, Thiosulfate Ferrocyanide, Cyanocobalamine (Vit B_{12}), I^{125} iothalamate and finaly Ytterbium diethylemetriaminpentaacetic acid (YB-DTPA) clearance. (Herbert L. et al., 1967; Milutinovic J. et al., 1975).

In this work, measurement of RRF was done using the extended creatinine clearance (Milutinovic J. et al., 1975) in a group of dialysis patients.

The aim is to evaluate the RRF and certain laboratory and clinical findings to see how the presence or abscence of RRF would affect the findings and to plan the future management of those patients accordingly.

In addition, this study includes a review of literature emphasizing the importance of RRF, its progression, the factors that affect this progression and the methods used in its measurement.

REVIEW OF LITERATURE

CHAPTER I

STRUCTURAL AND FUNCTIONAL CHANGES IN THE KIDNEY IN DIFFUSE RENAL DISEASE

Chronic renal failure is the end result of several pathological mechanisms affecting the kidneys and leading to gradual loss of its nephron population. The aim of this chapter is to discuss the effect of progressive renal disease on glomerular filtration rate and factors affecting that progression.

Progressive Nature of Renal Disease:

Clinically, chronic renal insufficiency regularly progresses to end stage renal failure and several studies indicate that the rate of progress is predictable for any given patient (Mitch et al., 1976; Rutherford et al., 1977).

There are several postulated mechanisms which explain this progressive loss of renal functions:

1- The Underlying Cause of Renal Disease:

In some instances, the factor which initiates the process of renal destruction may persist throughout the entire course progressing to renal failure and hence be responsible, at least by inference, for the progressive

destruction (Brenner and Hostetter, 1981). Often however, such an initiating factor is not identifiable at the time this disease is detected clinically.

Moreover, on occasion, an identifiable initiating factor has clearly disappeared due either to its having been a single, evarescent insult or to effective specific therapy. Nevertheless, the patient progresses to renal failure (Brener and Hostetter, 1981). For example, the direct injury of bilateral cortical necrosis may often demonstrate a temporary period of recovery, only to be followed by eventual uremia (Kleinknecht et al., 1973). Also a recent report of nephropathy associated with vesico ureteral reflux has documented the appearance of a progressive glomerulopathic process in the abscence of indentifiable injurous factors such as hypertension or active urinary infection and even despite surgical correction of the reflux (Torres et al., 1980).

2- Hyperfiltration of Residual Nephrons:

Experimental uremia produced by surgical ablation or infarction of renal mass generally leads to increased filtration by remenant glomeruli, and has been considered an adaptive response (Brenner and Hostetter, 1980). The full increase in remenant kidney GFR probabally occurs within 2 to

4 weeks after nephrectomy in rats, dogs and human (Katz and Epstein, 1967; Deen et al., 1974; Kaufaman, Siegel and Hayslett, 1975; Rous and Wakim 1967).

Micropuncture measurements of superficial single nephron glomerular filtration rate (SNGFR) in rats indicated that superficial SNGFR may be noticeably increased at an early stage after reduction in renal mass before whole kidney GFR is measurably increased (Diezi et al., 1976).

Together with increase in remenant kidney GFR, other changes take place. Hypertrophy of the remaining kidney tissue occurs, renal RNA content begins to increase 12 hours following uninephrectomy (Malt, 1969) and the incorporation of radiolabeled choline into renal membrane was demonstrated only 5 minutes after contralateral nephrectomy in mice (Toback, Smith and Lowenstein, 1974). The stimulus for this rapid alterations is uncertain.. Bonvalet and Coworkers (1972) reported that unilateral nephrectomy in the young rat led to increase in the number of glomeruli in the remaining kidney.

This was confirmed by Canter and Goss (1975); Imbert et al., (1974). Total renal blood flow is increased following surgical loss of renal mass (Krohn et al., 1970; Szocs et al., 1978).

3- Glomerular Enlargement:

Olivetti and coworkers, using light microscopy and morphometric techniques, studied rats 35 days after unilateral nephrectomy. Hypertrophy of the remenant renal mass was due to an increase of aproximately 70 per cent in mean glomerular volume with proportional increase in capillary length and surface area. Also, estimates of total mesangial, endothelial and epithelial cell volume indicated a tendency for all three cell types to increase after contralateral nephrectomy.
The growth of their volume was due primarily to an increase in cell number.

However, superficial glomeruli show slightly greater degrees of growth (Olivetti et al., 1977: Diezi et al., 1976; Pennell and Bourgoignie, 1978). Shea and Coworkers (1978) employing electron microscopy arrived at similar conclusions.

4- Factors Influencing Changes in GFR:

a. The amount of renal tissue which has been lost or, perhaps more importantly, the amount left intact. Unilateral nephrectomy alone led to 60 per cent augmentation of mean SNGFR values at 4 weeks, while

nephrectomy plus removal of approximately one half of the remaining kidney yield to an increase of approximately 150 per cent after the same time interval (Kaufman et al., 1974).

b. The age at which a reduction in renal mass is effected may determine whether an increase in glomerular number contributes to the functional hypertrophy. Studies of the augmentation in ispsilateral whole kidney GFR after donation of a contralateral kidney for transplantation in adult human indicates that the ultimate degree of functional hypertrophy is inversely related to age (Ogden, 1967; Boner et al., 1973).

Also, measurements of kidney weight and nucleic acid synthesis have generally demonstrated a greater potential for increase following unilateral nephrectomy in young animals (Barrows, Roeder and Olewine, 1962; Karp, Brasl and Wininck, 1971; Dicker and Shirley, 1973).

Nevertheless, the available evidence, particulary that in adult human kidney donors, suggests that the degree of compensatory elevation of SNGFR is age dependent (Brener and Hostetter, 1981).

c. Diet:

Diets high in protein lead to increase in weight of the remenant kidney as well as cellular evidence of renal growth (Moise and Smith, 1927; Mackay and Mackay, 1931). Furthermore, reduction in dietary protein below normal levels produce a reduction in kidney size in rats with both kidneys intact (Ichikawa et al., 1980). In both rats and dogs GFR and renal blood flow are directly related to protein intake (Ichikawa et al., 1980).

d. Hormones:

Variety of hormones influence renal growth and glomerular filtration rates. Growth hormone, Androgen and ACTH all have positive influences on renal growth but at what degree, this is uncertain (Ross J. et al., 1970; Schlondorf D. et al., 1977).

e. Internal shifts of filtrations and perfusion:

It has been apparent that distinct morphologic differences exist between superficial and juxtamedullary nephrons (Lameire, Lifschitz and Stein, 1977). Recently, these two nephron populations have been shown to exhibit important differences in a number of functional characteristics. In particular SNGFR is consistantly lower in superficial than in juxtamedullary glomeruli (Lameire, Lifschitz and stein, 1977).