JIACM 2005; 6(3): 198-200

Protein Tolerance Test

Suresh C Tiwari, Sandeep Mahajan**, Umesh Gupta****

Glomerular Filtration Rate (GFR) is the most widely used indicator of kidney function in patients with renal disease. The severity and prognosis of the renal disease is often predicted on basis of this parameter alone[1]. The recent K-DOQI guidelines also recommend the stratification of renal disease according to the GFR and other risk factors[2]. Generally, it is a well accepted notion, that GFR is remarkably stable from day-to-day over a period of years. However, in their pioneering report, Bosch *et al*[3] described their findings in a group of studies performed to examine the influence of protein intake on GFR. They studied GFR in normal persons on a vegetarian diet and the effect of long term and short term protein intake on creatinine clearance. They demonstrated that a wide variation in creatinine clearance existed in these subjects. The subjects ingesting an *ad libitum* vegetarian diet had a significantly lower creatinine clearance as compared to those on high protein diets. A direct relationship was also found between the protein intake and GFR, i.e., with an increase in protein intake there was an increase in GFR in both short term and long term studies.

The possibility of a variation in GFR and the capacity of kidney to augment its level of function suggest a renal functional reserve. The renal functional reserve represents the capacity of the kidney to increase its level of operation under certain demands. This reserve may be considered analogous to the cardiac functional reserve. When increased physiological demands are placed on the heart, it responds with an increase in cardiac output. Similarly, when the kidneys are subjected to greater physiological demands, they also respond with an increase in GFR. Conceptionally, the renal capacity to increase GFR from the baseline to a maximal one can alter the results of GFR studies. Thus, in renal diseases, this functional reserve increases GFR of the residual nephrons, replacing the lost function and maintaining the whole organ GFR. Only after the residual nephrons can no longer compensate for the functional loss, will the changes in resting GFR and serum creatinine occur[2]. On the other hand, the patient with a renal disease on a low protein diet may have a reduction in GFR unrelated to the progression of renal disease. Resting GFR therefore is not only an insensitive index for early detection of renal disease but is also inappropriate for renal disease follow up.

Glucose tolerance test (GTT) has been used to assess the patient at risk of diabetes mellitus. The stress of glucose load in GTT unravels the patient with marginal pancreatic function. It has been suggested that analogous to GTT, a protein tolerance test (PTT) may help in identifying individuals with subnormal renal function before they manifest clinically. The stress of PTT will enable us to determine individuals with impaired functional reserve. Thus PTT is a better test than resting GFR or serum creatinine.

Mechanisms of renal haemodynamic response to protein feeding

Numerous mechanisms have been hypothesised for this increase in GFR subsequent to protein feeding. In an exhaustive review done by Woods[4], the author has proposed the following theoretical model (Figure 1).

A protein meal, on digestion, which acutely raises the plasma amino acid concentration; this increase can also be mimicked by an intravenous amino acid infusion. These amino acids are filtered at the glomerulus and act directly on the kidney to stimulate proximal tubular absorption in a healthy metabolic state. Amino acid may also change sensitivity of the macula densa sensing mechanisms by altering cell permeability. Sensing a reduced tubular sodium chloride concentration, the macula densa cells release EDRF and prostaglandins locally, which cause afferent arteriolar vasodilatation. This afferent vasodilatation results in increased blood flow and GFR.

** Professor, ** Assistant Professor, *** Senior Resident, Department of Nephrology,*
All India Institute of Medical Sciences, Ansari Nagar, New Delhi - 110 029.

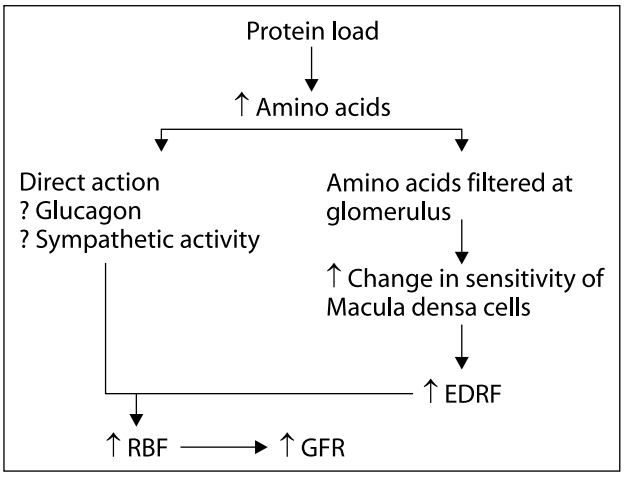

Fig. 1: *Mechanism of renal response to protein diet (Woods 1993)[4].*

Procedure for conducting PTT

The protein tolerance test has two components:

1. Stress GFR
2. Tubular stress test

Stress GFR

As described by Bosch *et al*[5], patients should be fasting and should receive oral hydration with 20 ml/kg of water. Once hydration is complete, urine volume is replaced by equal quantity of water. Endogenous creatinine clearance is used for assessing the test and baseline GFR.

Baseline GFR – Two blood samples are collected for serum creatinine measurement at the start and 30 minutes apart for calculation of creatinine clearance by Cockroft and Gault equation (CG formula) and the mean is taken as baseline creatinine clearance.

Test GFR – 100 gm of protein as cooked red meat or cottage cheese is given over 30 min. Blood samples are drawn at 60 and 120 minutes and mean value is used to calculate test creatinine clearance by CG formula.

We, at our institute, have conducted the PTT by using basal and post-protein loading DTPA GFR estimation to remove the fallacies which can occur due to estimation of GFR by CG formula. Spot urinary protein estimation is also done at baseline and 120 minutes after the test meal.

Interpretation

Any individual with normal protein tolerance test will show an increase in GFR from baseline in absence of urinary protein. In contrast, those with abnormal test will have proteinuria and no increase in GFR. The maximal filtration capacity attained after the protein load in various western studies is reported to be around 140 - 160 ml/min/1.73 m^2 with a percentage increase in GFR of 20 - 40% from basal state[2, 3, 5]. We, at our centre, have found similar results in Indian population. Increase in GFR without any proteinuria suggests normal response. While increase in GFR with proteinuria would suggest renal injury and no increase in GFR would suggest incipient renal failure.

Tubular stress test

Herrena *et al*[6] assessed the functional reserve of the kidney by performing tubular function. They examined increase in tubular secretion of creatinine (TScr) after a test meat meal. They demonstrated in normal individual TScr was three times the baseline, while patients with moderate renal failure were unable to raise their TScr. However, it requires standardisation and further studies to prove its utility.

Hence, protein tolerance test can be used to ascertain an individual's renal reserve, with incipient renal failure and normal GFR and serum creatinine. Thus, appropriate measures can be initiated at the earliest in such cases.

Utility of the protein tolerance test in clinical nephrology

The protein tolerance test can be utilised in:

a. Assessing the baseline and progression of renal disease in certain high risk groups – especially in disorders known to have a subsequent decline in renal function – like diabetics, hypertensives, polycystic kidney disease patients, and patients with a solitary kidney. These patients can be accurately prognosticated and planned for more aggressive intervention if required, by testing with stress GFR as compared to resting GFR.

b. Assessment of borderline donors. Due to shortage of live related donors, elderly and hypertensive individuals are now being taken up as potential renal donors. Stress GFR in atleast these high risk donors

will be desirable to reject those who are likely to have renal compromise subsequently, though they might be having a normal resting GFR.

Conclusion

Protein tolerance test can be very useful to detect incipient renal failure in a person with normal GFR and serum creatinine value, thus identifying the patients who are most likely to be benefited by an aggressive intervention. This is especially important in evaluating high risk persons like diabetics, post-renal transplants, and polycystic kidney disease patients. PTT can also be used to check the borderline renal donor, and to give accurate prognostication in a progressive renal disease. Tubular stress test still requires standardisation and further studies to prove its utility.

References

1. Cameron JS, Greger R. Renal function and testing of function. In: Davison AM, Cameron JS, Grunfeld JP *et al*, ed. Oxford Textbook of Clinical Nephrology. Oxford University Press, New York, USA: 1998; 39-69.
2. K/DOQI clinical practice guidelines for chronic kidney disease: evaluation, classification, and stratification. Kidney Disease Outcome Quality Initiative. *Am J Kidney Dis* 2002; 39 (Suppl 2): S1-S246.
3. Bosch JP, Saccaggi A, Laner A *et al*. Renal functional reserve in humans. *Am J Med* 1983; 75: 943-50.
4. Woods LL. Mechanisms of renal haemodynamic regulation in response to protein feeding. *Kidney Int* 1993; 44: 659-75.
5. Bosch JP, Lauer A, Glabman S. Short term protein loading in assessment of patients with renal disease. *Am J Med* 1984; 77: 873-9.
6. Herrena J, Rodriguez Iturbe B. Stimulation of tubular secretion of creatinine in health and in conditions associated with reduced nephron mass. Evidence for a tubular functional reserve. *Nephrol Dial Transplant* 1998; 13: 623-9.

BOOK REVIEW

PRINCIPLES AND PRACTICE OF EMERGENCY MEDICINE

Published by B. I. Publications Pvt. Ltd., New Delhi 2005, 640 pp, Rs. 475/-

Dr. P Aggarwal, Dr. LR Murmu, Dr. CS Yadav

Recent years have witnessed an increasing interest in the speciality of Emergency Medicine in India. Furthermore, every clinician has to manage some form of an emergency or the other in their practice. However, very few comprehensive books on Emergency Medicine are available from India. The authors, who are senior faculty members at the All India Institute of Medical Sciences (AIIMS), New Delhi, have brought out the essence of their vast experience in the form of the book **"Principles and Practice of Emergency Medicine"**.

The authors have attempted to provide an account regarding the diagnosis and management of various kinds of emergencies encountered in the Indian scenario ranging from trauma, medical emergencies including poisioning and overdosage, and surgical emergencies. The book is divided into four parts. Part A covers the fundamentals of cardio-pulmonary resuscitation. Non-traumatic emergencies are covered in Part B. In Part C, traumatic emergencies are covered. Appendices containing information on drug use in pregnancy and prophylaxis for infective endocarditis are provided in Part D. The approach is logical and systematic and useful information regarding the important clinical, laboratory, imaging, and management aspects related to various emergencies are provided in this book. Keeping up-to-date with changing times, the book also covers acquired immunodeficiency syndrome (AIDS) in the emergency room and legal aspects in emergency care. Line diagrams, flow charts, and algorithms are judiciously used to effectively convey diagnostic and therapeutic principles. At the end of each chapter useful practical tips are provided in a box summarising the major concepts covered in the chapter. The layout is good and typeset is clear, rendering the book easy to read.

References were not provided in any of the chapters in the book. In the present era of 'evidence-based medicine', the authors should have provided at least a list of key references relevant to each chapter. With internet access being widely available even in small towns of India, a list of useful websites where futher detailed information on the key aspects covered in the book could be accessed would have been a welcome addition. Inclusion of representative radiological images in the future editions would considerably enhance the value of this book.

The book would be useful to undergraduate and postgraduate students and practitioners as a guide to rational management of various emergencies and is a good buy for any library.

Dr. Alladi Mohan
Asociate Professor
Department of Emergency Medicine,
Sri Venkateswara Institute of Medical Sciences, Tirupati - 517 507

oral protein tolerance test. Whether or not your blood glucose levels rise or decrease in response to a high protein meal with no carbohydrate is also a useful way to understand if you are insulin resistant. Someone who is metabolically healthy will release glucagon and insulin in response to protein as it is metabolised to maintain a stable glucose level.[28] Someone who is insulin resistant may not produce adequate insulin to counteract the glucagon released by the liver and hence they may see their blood glucose levels rise. Share. Tweet. Share. Share. Email. The Glucose Tolerance Test (GTT), also referred to as the Oral Glucose Tolerance Test (OGTT), is a method which can help to diagnose instances of diabetes mellitus or insulin resistance. The test is a more substantial indicator of diabetes than finger prick testing. What is an OGT test? The test is used to determine whether the body has difficulty metabolising intake of sugar/carbohydrate. Ornithine carbamoyltransferase deficiency: Improved sensitivity of testing for protein tolerance in the diagnosis of heterozygotes. M. Potter1 , J. W. Hammond1 , K.-G. Sim1 , A. K. Green1 &. B. Wilcken1. Journal of Inherited Metabolic Disease volume 24, pages5â€“14(2001)Cite this article.