Outside Europe

Acute renal failure in tropical Africa

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Summary

Between 1972 and 1975, 55 adult patients with acute renal failure were admitted to the renal unit of Korle Bu Hospital. Fourteen patients died, giving an overall death rate of 25%. Massive intravascular haemolysis after a short febrile illness was the commonest cause of acute renal failure. Clinically these patients presented with blackwater fever but in only one could Plasmodium falciparum malaria be confidently diagnosed. In half the patients various bacterial and viral infections (especially typhoid) could be incriminated as causing this blackwater fever syndrome. The incidence of glucose-6-phosphate dehydrogenase deficiency was 22·5%, but we could not confirm the impression of a greater predisposition to acute renal failure in patients with this enzyme defect.

Introduction

Despite the introduction of dialysis, acute renal failure remains an important and potentially lethal complication of many serious medical, surgical, and obstetric conditions. There are many reports on the natural history of acute renal failure,[1 2] and clearly this largely depends on the prevailing spectrum of disease.[3-5]

We suggest that acute renal failure is more common in tropical Africa than is evident from reports. Acute renal failure in tropical areas is well recognised as a complication of blackwater fever induced by *Plasmodium falciparum*, a condition that was described mainly in non-indigenous inhabitants of holoendemic malarious areas.[6 7] Although blackwater fever has recently been reported in Africans,[8] there is now considerable evidence to suggest that this syndrome is more commonly a sequel to haemolysis due to drugs or bacterial infections particularly in people with glucose-6-phosphate dehydrogenase (G6PD) deficiency.[9 10] The association between G6PD deficiency, infection, and acute renal failure is now well established[11 12] and may be of great importance in areas such as Southern Ghana with an incidence of this enzyme deficiency of 24·3%.[13] The prominence of typhoid fever as a cause of haemolysis and acute renal failure in parts of Africa appears to be related to the high incidence of G6PD deficiency in these areas,[10 11] although typhoid is also reported as causing disseminated intravascular coagulation and a haemolytic uraemic syndrome in people with normal G6PD.[14]

In tropical areas, where medical attention is usually delayed and often inadequate, a high incidence of acute renal failure may be expected. The widespread use of traditional herbal remedies before seeking medical attention may be particularly hazardous in the light of reports of the nephrotoxicity of some herbal preparations.[5]

We present an analysis of the work carried out by the first haemodialysis unit established in Ghana, which was set up in 1972.

Patients and management

Between April 1972 and April 1975 55 patients with acute renal failure were admitted to the renal unit of Korle Bu Hospital. Adequate data are available for analysis in 50 patients. The many patients presenting with an acute uraemic emergency from chronic renal failure, obstructive uropathy, and primary renal disease have been excluded from this study and will be reported elsewhere. Acute renal failure was diagnosed from the history; the presence of progressive uraemia, usually but not always with oliguria; a failure to respond to rehydration plus mannitol when given; and a urine of specific gravity less than 1·014. The clinical course, pattern of functional recovery, and mean duration of oliguria of 11 days in our patients suggest that we were dealing with acute tubular necrosis as reported.[2]

Our major difficulty was in distinguishing between acute renal failure and acute on chronic renal failure. The lack of facilities for chronic dialysis made this distinction one of critical and agonising importance. The most useful pointer to chronic renal disease in our experience was hypertension, particularly when complicated by retinopathy or left ventricular hypertrophy. Uraemic pigmentation is undetectable on black skin, and anaemia has too many causes in the tropics to be useful. We rarely encountered radiological or biochemical evidence of renal osteodystrophy in our patients with chronic renal failure. We were unable to detect renal outline and size on plain abdominal radiography and are making increasing use of high-dose urography for this purpose.[15]

The choice of treatment was dictated by clinical and biochemical considerations.[3 16] All patients were put on a 30-g protein, high carbohydrate diet and fluids were restricted to 600 ml a day plus measured losses over the previous 24 hours. We managed 14 patients by these conservative measures alone. We treated 32 patients, most of whom fell into the hypercatabolic group of Parsons *et al*,[3] with haemodialysis. Four patients received peritoneal dialysis.

Haemodialysis was performed using an RSP (Travenol) machine and UF 100 coils. Vascular access was by means of a Teflon-Silastic arteriovenous shunt inserted into the arm or leg.[17] Low-dose heparinisation with 6000 units of heparin each six-hour dialysis was the preferred form of anticoagulation. Using a dialysate bath glucose concentration of 83 mmol/l (1500 mg/100 ml) for the first three dialyses we rarely encountered a disequilibrium syndrome.[18] The number of haemodialyses per patient ranged from one to 10 with an average of four. Peritoneal dialysis was performed along standard lines[19] using commercially prepared fluids.

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Analysis and comment

Age and sex—The age range was from 15 to 65 with a mean age of 29 years. There were 29 men and 21 women (table I).

Precipitating factors—Although acute renal failure has many causes we divided the suspected precipitating factors as in table II. The most striking feature was the high incidence of infection and haemolysis as causes of acute renal failure.

TABLE I—*Age distribution of 50 patients*

Age in years	<15	15–25	–35	–45	–55	–65
No of patients	0	18	17	9	5	1

TABLE II—*Precipitating factors of acute renal failure*

Causes	No of patients	Men	Women	Died
Haemolysis and infection	19	15	4	4
Typhoid fever	7	5	2	0
Obstetric	12	0	12	1
Surgical	2	2	0	1
Diabetes mellitus	2	1	1	2
Obscure	4	3	1	1
Pancreatitis	1	1	0	0
Acute intermittent porphyria	1	0	1	1
Nephrotoxic herbal remedy	1	1	0	0
Lysol ingestion	1	1	0	0
Total	50	29	21	10

Infection and haemolysis—In 26 (52%) of our patients acute renal failure occurred after infection and massive intravascular haemolysis (table III). Clinically these patients presented with blackwater fever but 13 had a variety of bacterial and viral infections which could be incriminated in causing this syndrome. Only one patient with G6PD deficiency had a proved infection with *P falciparum*. In 12 patients presenting with haemolysis after a febrile illness no pathogenic organism could be identified, probably as a result of antibacterial and antimalarial treatment on admission. Massive intravascular haemolysis was diagnosed from the presence of anaemia; reticulocytosis, or increased normoblasts on a blood film; a positive Schumm's test; and the presence of haemoglobinuria. Blood cultures were performed on admission in 42 patients and are now routine. Positive cultures were obtained in 10 patients, and in another two there was serological evidence of typhoid giving an incidence of proved septicaemia of 12 out of 50 (24%).

TABLE III—*Haemolysis and infection*

Causes	No of patients	No with G6PD deficiency	No with jaundice	No died
Typhoid	7	4	5	0
E coli septicaemia	3	0	1	1
Falciparum malaria	1	1	1	0
Viral infection	3	1	3	1
Obscure	12	1	9	2
All groups	26	7 (27%)	19 (73%)	4 (15%)

Typhoid fever—The most common infective cause of acute renal failure, typhoid in 7 (14%) of our cases, has been reported in detail.[10] G6PD deficiency was present in four of these patients, one of whom also had haemoglobin SC disease.

Urinary infections were found in 24 out of 40 patients usually in the early diuretic phase. All the pathogens were Gram-negative bacteria (in order of frequency), *Escherichia coli*, *Klebsiella*, *Proteus*, and *Pseudomonas*.

Shunt infections—Five out of 32 patients developed a shunt infection, the commonest pathogen being *Staphylococcus pyogenes* in three cases.

G6PD deficiency was found in nine out of 40 patients (22·5%) (table IV). This represents a minimum estimate of G6PD deficiency, as in the acute phase of haemolysis in Africans reticulocytes and young red blood cells often have sufficient enzyme activity and are present in sufficient numbers to give normal enzyme activity on assay.[20] Six men and three women showed this enzyme defect. The major mechanism of acute renal failure was intravascular haemolysis after infection.

TABLE IV—*G6PD deficiency and acute renal failure*

No	Age and sex	G6PD	Infection	Haemoglobin at uraemia (g/dl)	Total bilirubin (μmol/l)
1	31 M	Total defect	Typhoid	5·0	363
2	18 F	Total defect	Typhoid	2·8	137
3	18 M	Total defect	Typhoid	6·4	29·1
4	30 M	Total defect	Typhoid	2·8	581
5	29 M	Total defect	Chickenpox	4·6	68·4
6	25 M	Total defect	Obscure	2·7	
7	48 M	"Partial" defect	Obscure	10·3	
8	24 F	Partial defect	Septic abortion	3·2	154
9	30 F	Total defect	Falciparum malaria	5·9	640

Conversion: SI to traditional units—Bilirubin: 1 μmol/l ≈ 0·058 mg/100 ml.

Haemoglobinopathy—Haemoglobin electrophoresis was performed in 28 patients (table V). The incidence of 36% of haemoglobin AS compared with 20% in the general population merits further study. The one patient with haemoglobin SC disease and G6PD deficiency developed acute renal failure as a consequence of typhoid and haemolysis. He recovered after peritoneal dialysis and chloramphenicol. Haemodialysis was not used in this patient because of the theoretical risks of thrombotic and haemolytic complications with an extracorporeal circulation. Recently, however, successful and complication-free haemodialysis in three patients with sickle cell anaemia and chronic renal failure has been reported.[21]

TABLE V—*Haemoglobin electrophoresis*

Haemoglobin electrophoresis	AA	AS	AC	SC
No of patients	15 (54%)	10 (36%)	2 (7%)	1 (3%)

Discussion

The most striking feature in our series compared with those from temperate areas is the high incidence of infection and haemolysis as causes of acute renal failure. In 26 (52%) of our patients, acute renal failure developed in the context of a blackwater fever syndrome but in only one patient with G6PD deficiency could *P falciparum* malaria be clearly implicated as a cause. In 13 patients G6PD deficiency and a variety of bacterial and viral infections provided an alternative and in the case of typhoid therapeutically important mechanism of haemolysis and acute renal failure. Clearly many cases of blackwater fever in Africans are due to haemolysis from G6PD deficiency and infections such as typhoid.[9 10]

The association between G6PD deficiency, infection, and acute renal failure is well established.[11 12] The incidence of G6PD deficiency of 22·5% in our series approximates to that of 24·3% in Southern Ghana.[13] This surprisingly low incidence may be explained by the difficulty of diagnosing this enzyme defect in the acute phase of haemolysis. Our findings highlight the importance of infection as a cause of as well as a complication of acute renal failure.[19] The importance of early bacteriological investigation, particularly blood cultures, in these patients is clear. Of the seven patients with typhoid four had G6PD deficiency. Probably not only are patients with this enzyme deficiency more susceptible to typhoid[22] but they also run a greater risk of developing massive intravascular haemolysis and acute renal failure with this infection.[10]

Choice of antibiotics during this period was severely restricted by availability. Although bacteriostatic, chloramphenicol proved extremely valuable in the initial management of Gram-negative septicaemia and is, of course, the drug of choice for typhoid. Recently we have increasingly used kanamycin, and with the

dose modification of Mawer *et al*[23] have not encountered ototoxicity.

In managing acute renal failure, we, like most renal units, believe that intensive care, early dialysis, and an aggressive approach to infection provide the basis on which improvements in survival might take place. The mortality of 25% in our series compares favourably with that found elsewhere[2 5 19] and partly reflects the good survival attainable in acute renal failure from haemolytic and obstetric causes present in 76% of our cases.

Our results justify the establishment of units for managing acute renal failure in tropical Africa. From our analysis of the causes it seems likely that acute renal failure is more common in our environment than is generally realised. The comment by Lee[24] that the most important factor in recognising acute renal failure is an awareness of the clinical conditions during which it may arise remains a valid one today.

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Letter from . . . South Australia

New thoughts on organising medical education

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The *Report of the Committee of Inquiry into Hospital and Health Services in Victoria*, with Sir Colin Syme and Professor Sir Lance Townsend as its only members, has just been published and contains some interesting ideas on medical education. They have some relevance for Britain.

Present medical education

At present the medical course in Melbourne consists of three preclinical years, three clinical ones, the award of the MB BS degree, an intern preregistration year, and then registration. Thereafter comes vocational training, varying with the specialty chosen. The universities have the major control over the years to registration, while doctors and the Royal Colleges have their special concern with vocational training. The difficulties are apparent, and a plea is made for better integration of the two parts. Moreover, account has to be taken of continuing education for those who have already specialised, and may have acquired a diploma of one of the Royal Colleges. There are also problems of the supply of doctors and their maldistribution among the specialties, which, of course, include general practice. The universities control the numbers of entrants to medicine, but there is no readily visible control over the numbers in each specialty. The uneven distribution of doctors between cities, towns, and country is probably more a matter for government than for education.

The medical course is a long one and it takes many years to produce a specialised doctor capable of independent practice. One reason is that entry to the profession, before vocational training can begin, is through the graduate degree, which is followed by at least one year's supervised practice. It is recognised that much of the undergraduate course contains material which is irrelevant to a particular doctor's subsequent career. The problem is that the choice of career for most only emerges; it is not fixed at the outset. Because of this fact the report resists schemes for streaming in the medical course. Streaming implies that if enough students know what they ultimately want to do, then a special shortened course can be devised for them. The fallacy here might well be that education is intended to modify behaviour. Without seeing the full range of medicine the future doctor makes choices on inadequate evidence. Moreover, there is emotional resistance in developed societies to having apparently substandard doctors, whatever they may be called.

Proposals

The report attempts an ingenious solution to these problems, though it emphasises that it is tentative and meant as a basis for discussion. It suggests four years with the university, consisting of three years' basic medical sciences and one year of clinical science. (I have altered the wording slightly, for the authors still refer to preclinical teaching on the university campus and a clinical year in the teaching hospital.) At the end of these four years the student should proceed to the MB, BS. This

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