

History of Medicine: The Emergence of Intestinal Dialysis

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1. Abstract

In 1923, Georg Ganter at the University of Würzburg performed the first peritoneal dialysis for patients with chronic kidney disease. During the period from 1924 to 1938, intermittent peritoneal dialysis was used in the USA and Germany as a short-term replacement for the renal functions. In 1946, Fine and colleagues described the use of peritoneal irrigation in a patient with severe anuria, who survived after four days of continuous peritoneal lavage. In 1943, a Dutch physician named Willem Kolff developed the first dialyzer which was called “Artificial kidney” with aim of cleaning the blood of patients with acute renal failure. Kolff moved to the USA and improved the early design of the dialyzer and was manufactured in the early 1950s.

During the 1980s and 1990s, experimental studies on animals suggested that dietary fibers including acacia gum have a urea lowering effect (Yatzidis et al., 1980; Rampton et al., 1984; Tetens et al., 1996). In 1996, Bliss et al. reported that the use of acacia gum supplementation in adult patients with asymptomatic early chronic renal failure on low protein diet was associated with urea lowering effect. The use of Intestinal dialysis in symptomatic chronic renal failure patients was first described by Aamir Jalal Al-Mosawi in 2002. The achievement of six-year dialysis freedom with the use of intestinal dialysis in patients

with end-stage renal failure was described by Aamir Jalal Al-Mosawi in 2009. Late during the 2000s, “Only medical talks” web site included Aamir Jalal Al-Mosawi in the list of famous physicians of all time for describing intestinal dialysis [9]. During the previous two decades there have been a plethora of publications describing the concepts, principles and use of intestinal dialysis including journal articles, conference papers and books. Some of these publications have been translated to eight languages confirming that intestinal dialysis has become an established medical therapeutic technology.

The aim of this paper is to review the milestones associated with intestinal dialysis which was considered by many experts as a Nobel Prize winning technology.

2. Keywords: History of Medicine; Intestinal Dialysis; Pioneers of medicine

3. Introduction

In 1923, Georg Ganter at the University of Würzburg performed the first peritoneal dialysis for patients with chronic kidney disease. He introduced 1.5 liters of a physiological saline solution, one with the same salt concentration as the human blood into the abdomen of a woman who had a blocked ureter.

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Treatment improved symptoms for short time and the patient died. During the period from 1924 to 1938, intermittent peritoneal dialysis was used in the USA and Germany as a short-term replacement for the renal functions. In 1946, Fine and colleagues described the use of peritoneal irrigation in a patient with severe anuria, who survived after four days of continuous peritoneal lavage.

In 1943, a Dutch physician named Willem Kolff developed the first dialyzer which was called “Artificial kidney” with aim of cleaning the blood of patients with acute renal failure. Kolff moved to the USA and improved the early design of the dialyzer and was manufactured in the early 1950s. Belding Scribner, a professor of medicine at the University of Washington used an access point in their arm for the use of dialysis in chronic renal failure and established the first hemodialysis clinic 1962.

During the 1980s and 1990s, experimental studies on animals suggested that dietary fibers including acacia gum have a urea lowering effect (Yatzidis et al., 1980; Rampton et al., 1984; Tetens et al., 1996). In 1996, In 1996, Bliss et al. reported a study included 16 adult patients with asymptomatic early chronic renal failure on low protein diet, they were randomly assigned to receive a supplement of acacia gum (50 g daily) or oral placebo (1 g daily). Acacia gum supplementation was associated with lower serum urea and the patients had greater fecal masses and greater fecal nitrogen excretion in comparison with period there were on low protein diet alone and in comparison, with a control patients on pectin supplementation instead of acacia. Emphasis was made that in contrast to locust bean gum and ispaghula, patients considered acacia gum to be palatable and the clinical use of acacia gum was considered applicable [1-5].

Intestinal dialysis involves the use of the conservative (dietary and pharmacologic) interventions of chronic renal failure plus the supplementation of a relatively large amount of soluble fiber “acacia gum” which is digested by colonic flora and cause a shift of urinary

excretion to intestinal excretion by modifying the entire hepatic urea cycle and increasing the amount of nitrogen eliminated as fecal waste. The use of Intestinal dialysis in symptomatic chronic renal failure patients was first described by Aamir Jalal Al-Mosawi in 2002 [6]. The achievement of six-year dialysis freedom with the use of intestinal dialysis in patients with end-stage renal failure was described by Aamir Jalal Al-Mosawi in 2009 [7].

4. Review

The early research of Aamir Jalal Al-Mosawi was based on the fact that as peritoneal dialysis acts by shifting the urinary excretion of urea to the peritoneal excretion with use of intraperitoneal dialysis fluids, intestinal dialysis can be performed with the use of a dietary material (Acacia gum) to increase extra renal excretion and shift the urinary excretion of urea to the intestinal excretion [6-8].

Late during the 2000s, “Only medical talks” web site (Figure 1) included Aamir Jalal Al-Mosawi in the list of famous physicians of all time for describing intestinal dialysis [9]. During the previous two decades there have been a plethora of publications describing the concepts, principles and use of intestinal dialysis including journal articles, conference papers and books. Some of these publications have been translated to eight languages confirming that intestinal dialysis has become an established medical therapeutic technology [10-48].



Figure 1: Late during the 2000s, “Only medical talks” web site included Aamir Jalal Al-Mosawi in the list of famous physicians of all time for describing intestinal dialysis.

Early during the 2000s, children with chronic renal failure in Baghdad and Iraq were mostly treated with intermittent peritoneal dialysis using temporary peritoneal catheters and treatment was associated with a significant and an unacceptable risk of morbidity and mortality and many parents were taking their children to die at home without subjecting them to dialysis. During these years, Aamir Jalal Al-Mosawi was left with no choice other than trying something new to improve the management of childhood chronic renal failure [49-52].

Despite the significant lowering of urea levels associated with intestinal dialysis, the process of urea lowering is slow and its effectiveness remains less than the traditional dialysis especially in the more advanced stages of chronic renal failure. Therefore, the combined use of intestinal dialysis with intermittent peritoneal dialysis was the first reported use of intestinal dialysis in symptomatic urea [6].

Early during the 2000s, Al-Mosawi started adopting the practices of evidence-based medicine to deal with the therapeutic challenges and improve patients' care and he developed the strategy of intestinal dialysis accordingly. Al-Mosawi tried to share his early experiences in the practice of evidence-based medicine with world scientific leaders in the fields of pediatrics and nephrology. Therefore, Al-Mosawi wrote to Ira Greifer, a pioneer of pediatric nephrology (Figure 2) who was the secretary general of the International Association of Pediatric Nephrology during that time [49-53].

It was not long time when Al-Mosawi received a reply from Ira Greifer. He wrote "I was very pleased to receive your letter and know that you are working very hard to bring the benefit of modern knowledge, techniques and treatment to children in your country with Kidney and Urologic problems." Figures 3A and 3B show the 2-page letter of Ira Greifer.

Ira Greifer also wrote "I was most fascinated by your use of gum Arabic in children with chronic renal failure, in attempt to promote low protein diet. With

this experience and your general experience with acute glomerular nephritis in Iraqi children, should be considered for publication in our journal "Pediatric Nephrology", if it was presented for review to our editors" [49,50].



Figure 2: Ira Greifer, a pioneer of pediatric nephrology.



Figure 3A: The 2-page letter of Ira Greifer.

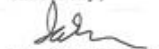
Dr. Jawad
Page 2

I would be most supportive of helping you become members, by subsidizing the membership of you and your colleagues for a short period of time.

Also, I am looking forward to the continuing development of the Pan Arab Pediatric Nephrology Association (PAPNA), whose next meeting will take place in Riyadh in the middle of November, 2000.

Looking forward to hearing from you.

Sincerely,



Ira Greifer M.D.
Professor of Pediatrics & Nephrology
Montefiore Medical Center/Albert
Einstein College of Medicine

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enclosure

Figure 3B: The 2-page letter of Ira Greifer.

Thereafter, the first clinical use of intestinal dialysis in symptomatic uremia was published during May, 2002, in *Pediatric Nephrology* [6].

Al-Mosawi described the use of intestinal dialysis (acacia gum supplementation and low protein diet) with intermittent peritoneal dialysis to treat a seven-year-old boy with the most extreme form of end-stage renal disease (anuric with no renal function). The patient was treated initially with intermittent peritoneal dialysis and conservative medical treatment (low protein diet and fluid restriction). He was treated with peritoneal dialysis sessions intermittently whenever became symptomatic with marked nausea, tachypnea (acidotic breathing) and generalized edema from fluid overload. When the patient described by Al-Mosawi was symptomatic, blood urea usually ranged from 37.4 to 53.9 mmol/l. After each 24 to 72 hours peritoneal dialysis session, blood urea usually fell to below 16.6 mmol/l. During 108 days of anuria, he was treated with 12 sessions of intermittent peritoneal dialysis (average frequency: one session of dialysis/9 days). Despite the earlier institution of low-protein diet and fluid restriction, the patient required 12 sessions of peritoneal dialysis and was receiving nifedipine 2 mg/kg daily to control hypertension. His diastolic blood pressure was reduced to 100 mmHg. He was also given frusemide for 3 days, but the effect was almost negligible. Propranolol was added at a dose of 2 mg/kg daily and lowered blood pressure to 120/80 mmHg.

Intestinal dialysis was initiated and continued for 48 days. Dietary protein was restricted to 0.5 g/kg per day given largely in the form of egg albumin. Fluid and salt were also restricted. A high-caloric diet was encouraged, together with supplements of water-soluble vitamins, calcium and iron. Acacia gum powder was given at a dose of 0.5 g/kg per day in 2 to 3 divided doses. Acacia gum was diluted with the minimal amount of water to make it acceptable.

The patient became symptomatic with anorexia, tachypnea (acidotic breathing) and edema 27 days after the initiation of intestinal dialysis. His blood urea was 49.8 mmol/l and he required a dialysis session. The child became symptomatic and needed the second session of intermittent peritoneal dialysis after another 21 days. The child found acacia gum acceptable (palatable), but taking it was associated with one or two voluminous stools per day that had an unusual smell (similar to the smell of urine). This effect of acacia on stool did not interfere with compliance. A suitable dose of acacia gum powder in this patient was 0.5 g/kg per day. A trial of a higher dose of 1 g/kg per day was performed in an attempt to increase the efficiency of intestinal dialysis. However, this increase resulted in abdominal distention and discomfort that interfered with sleep at night. The dose of acacia gum powder was reduced again to 0.5 g/kg per day.

In this child, intestinal dialysis was associated with a beneficial antihypertensive effect. Before the initiation of intestinal dialysis, diastolic blood pressure was maintained at 80 mmHg with nifedipine and propranolol. Diastolic blood pressure was maintained at 80 mmHg with intestinal dialysis alone for three weeks. During the first three weeks after the initiation of intestinal dialysis therapy, blood urea was maintained below 33.2 mmol/l.

The child remained relatively well without being significantly symptomatic. His appetite was good and he was not clinically acidotic. The child became symptomatic 27 days after the initiation of intestinal

dialysis and required a second intermittent peritoneal dialysis session after another 21 days. Compliance with all of the components of intestinal dialysis was better during the first 27 days of therapy. After two weeks of the initiation of intestinal dialysis, it was necessary to stop antihypertensive medications (nifedipine and propranolol) because the diastolic blood pressure dropped to 45 to 50 mmHg for no obvious reason such as gastrointestinal bleeding. Although the parents noticed the beneficial effect of intestinal dialysis, they couldn't ensure the child's compliance with treatment. The child and his parents were overwhelmed by the illness. Non adherence to intestinal dialysis therapeutic components led to severe hypertension (blood pressure 160/140 mmHg) and the uremic symptoms reappeared and the child died shortly after an intermittent peritoneal dialysis session [6].

In 2006, Al-Mosawi published a research paper describing the use of intestinal dialysis in 11 patients with symptomatic uremia. Their ages ranged from 14 to 65 years (Mean 41.45 year). Two of them were on hemodialysis. The remaining patients were on low protein diet combined with other medical treatments of chronic renal failure, including one patient has undergone one peritoneal dialysis session before referral. The intestinal dialysis therapeutic regimen included dietary proteins restriction to 0.5 g/kg with at least 50% of the total intake given as egg albumin. Protein and phosphorus restriction was primarily achieved by restriction of meat, poultry, fish, milk, cheese, yogurt and legumes. Additional restriction of potassium rich foods was made during elevation of serum potassium above 5 mmol /L. Powder acacia gum 1 g/kg/day (Maximum 75 g) in 2 to 3 divided doses diluted with desired amounts of water.

The use of intestinal dialysis in this study was associated with amelioration of the uremic symptoms and improved general wellbeing as long as the patients were compliant with the therapeutic protocol. The patients were followed for 2 to 16 weeks.

However, the most significant finding in this study was the achievement of hemodialysis freedom in two of these patients, both of them has a vascular access, but they considered hemodialysis to be associated with a significant amount of discomfort and suffering and they were not satisfied with the quality of life associated with hemodialysis. Two patients who didn't comply with the therapeutic protocol died, one during treatment with intermittent peritoneal dialysis and one within one month after renal transplantation [8].

Al-Mosawi (2004) described the management of six patients with end-stage renal disease and significant uremia that required at least one dialysis session to maintain life [54].

Intestinal dialysis was used in three of the six patients with the aim of improving wellbeing and reducing the need for dialysis. The other three patients were treated with intermittent peritoneal dialysis; all died with in less than six months. The three patients treated with intestinal dialysis aged between 11 to 13 years (each with, oxalosis, cystinosis and end-stage renal disease of undetermined etiology). They had symptomatic uremia that required at least one session of intermittent peritoneal dialysis despite low-protein diet and other conservative measures of chronic renal failure. They had no reductions in urine output or edema and were normotensive. Their pre-dialysis creatinine clearance was less than 5 ml/min when by a formula developed by Cock and Gault.

One of the patients complied with intestinal dialysis treatment for only ten days and died after six months despite treatment with intermittent peritoneal dialysis. Two of the three patients were treated for one year with intestinal dialysis. Both patients reported improved wellbeing. Neither became acidotic or uremic and neither required dialysis during the one year of the study period. Both patients-maintained serum creatinine and urea levels not previously achieved without dialysis. Of the two surviving patients treated with intestinal dialysis, one patient

couldn't comply with therapy and stopped most of the components of intestinal dialysis after one year and died within one month despite treatment with intermittent peritoneal dialysis [54]. The other patient continued to be treated with intestinal dialysis and continued to experience improved wellbeing and dialysis freedom during 6 completed years [7,55]. The patient who achieved six-year dialysis freedom was an 11-year-old girl with end-renal failure who initially required four sessions of intermittent peritoneal dialysis to control uremic symptoms despite conservative measures. The parents refused further treatment by dialysis. Thereafter, she was treated with intestinal dialysis [7].

During six years of therapy the girl continued in experiencing improved well-being and good participation in outdoor activities. Mild uremic symptoms occurred only during periods of noncompliance. Periods of decreased compliance with pharmacologic therapies were associated with anemia and renal osteodystrophy and some degree genua vulgum has resulted. The chronicity of her illness was confirmed by the presence of small contracted kidneys, a finding that has not changed during the subsequent follow-up [7].

Al-Mosawi (2019) reported the use of intestinal dialysis in eight patients and the achievement of eight years dialysis freedom [17].

During the period from December, 2005 to October, 2009, nine patients (5 males and 4 females) with various renal disorders associated with symptomatic uremia were referred for treatment due to their unwillingness to undergo dialysis. Ages ranged from 3.5 year to 72 years (mean 28.8). All patients considered dialysis in their circumstance to be associated with an unacceptable degree of discomfort and suffering. Five patients had severe uremic symptoms (fatigability, tachypnea and anorexia). All the patients were unable to walk independently. The patients were treated with the new technology of intestinal dialysis.

All the patients experienced amelioration of symptoms of uremia with improved general wellbeing in association with lowering of urea levels and creatinine during the period of therapy. The patients were followed for a period ranging from 8 weeks to 8 years. It was possible to follow three patients for more than 2 years on this therapy including one patient followed for 8 years. The three patients continued to experience low urea levels and didn't develop any symptoms of uremia. No important side effect was observed. However, most patients experienced some degree of abdominal distention associated with increased passage of gases (flatulence).

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