Clinical Considerations in Renal Failure, Depression, and Delirium

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By Norman B. Levy, MD [1]

Renal failure is not an uncommon disorder either in the general public or in patients with psychiatric disorders, but accompanying depression, anxiety, and loss must be attended to during such an illness.

CLINICAL

Renal failure is not an uncommon disorder either in the general public or in patients with psychiatric disorders. It is estimated that 27 million people in the US have chronic kidney disease; renal failure can occur in patients with an extreme form of the disease and is diagnosed in 117,000 people in the US yearly. There are 86,000 people in the US waiting for a kidney transplant and 355,000 on dialysis. The major causes of renal failure are diabetes mellitus—now nearly pandemic in our obese population—and hypertension. Other causes include autoimmune disorders, such as lupus, and congenital disorders, such as polycystic kidney disease.

Comorbidities
Both depression and anxiety are common in medical as well as surgical disorders. So-called exogenous depression may be viewed as a response to loss, whether actual, impending, or fantasized. There is usually a loss of freedom in the physical restraints of illness. These include general weakness and loss of body functions. Often there is financial loss (eg, reduced income, medical costs). Physical illnesses are commonly associated with a relative loss of some self-esteem and not uncommonly a loss of sexuality, since pain and disability do little in favor of a woman’s sense of femininity or a man’s masculinity. We know that persons with kidney failure have a marked loss in their interest and ability to perform sexually.

Belding Scribner, one of the originators of dialysis, estimated that one-third of men have total sexual dysfunction, one-third have partial dysfunction, and one-third have no sexual dysfunction at the start of dialysis for kidney failure. Surveys have shown that 70% of men on dialysis have partial or total impotence. Women are similarly but less affected. Interestingly, those who receive a kidney transplant have much less sexual dysfunction.

Delirium is usually characterized by an acute disturbance in attention and cognition. It is particularly common in older persons, especially as a comorbidity in hospitalized patients, and in those with a chronic medical condition, such as chronic kidney failure. It is notoriously underdiagnosed because clinicians tend to be focused on the patients’ primary illness and do not think about or test for it. Since testing for cognitive functioning can readily make the diagnosis, it should be a routine part of
an examination. Patients with renal failure are particularly vulnerable to delirium. Healthy kidneys filter out waste products every second of every hour, 24/7. Patients on dialysis have this process done for them 2 to 4 hours usually 3 times a week, rendering them relatively uremic at other times. The many causes of delirium in those with renal failure include the adverse effects of medications and/or a complicating medical condition, such as anemia, secondary hyperparathyroidism, or uremia. Before receiving and during a dialysis treatment, patients are uremic. The actual cause of a uremic state is not fully known. Uremia does not develop in animals that are experimentally injected with urea. Other waste products not filtered out by the kidney must be responsible for this condition.

**CASE VIGNETTE**

Morris Kramer is a 74-year-old retired rabbi who has been treated for hypertension for the past 25 years. About 2 years ago, he fractured his arm and was taken to an emergency department. Routine urinalysis showed red blood cell casts that were strongly positive for albumin. His blood tests revealed a BUN of 150 mg/dL and creatinine level of 4.5 mg/dL, with an elevated potassium level and mild anemia. Further workup by his internist resulted in a diagnosis of renal failure associated with hypertension or due to chronic glomerulonephritis.

Rabbi Kramer chose to be treated by home peritoneal dialysis and did well; nevertheless, he decided to retire because of frequent extreme fatigue. Several months later while taking a walk, he fell and was found unconscious. He was taken to the hospital, where a diagnosis of a subarachnoid hemorrhage was made. He underwent surgery, and dialysis was planned on his second postoperative day. During his first postoperative day, his wife noticed that he was not as sharp as usual. When asked what she meant by that, she said that his memory seemed foggy. This was attributed to the general anesthesia.

During that night, the nurse on duty reported the patient missing; he was found by the police wandering in his hospital bedclothes on a street adjacent to the hospital. An emergency psychiatric consultant recognized signs of impaired cognitive functions; delirium was diagnosed and low-dose haloperidol was prescribed.

The hospital staff attributed his delirium to the delay in dialysis, dehydration, and some hangover from the anesthesia. Both wife and patient were reassured of the nature of his problem and told that he would be his previous self after receiving dialysis. He slowly improved and was his usual self 2 days later. He continued on dialysis until his death from heart failure, 4 years later.

**Treatment considerations**

What about treatment of psychological problems in the physically ill and, in particular, in patients with kidney failure? In my experience, persons who are physically ill tend to be rather resistive toward talking therapies. As a group, with notable exceptions, they tend to use denial as a defense against a more insightful view of their problems. These patients often rationalize that their physical illness is the reason for their depression. Dialysis recipients often feel over-doctored and less inclined to engage with another medical specialist. Careful screening is required for the occasional patient who will accede to time-limited psychotherapy.

Group therapies have been used with success in large hemodialysis centers. Taking advantage of a “trapped audience,” some centers use an “educational” approach in addressing large groups of patients. For example, a social worker or psychologist may talk about complications seen in patients or a transplant surgeon may be invited to address the group about recent advances in his or her field.

Newer psychotropic medications offer relief of many psychiatric disorders, such as depression, anxiety, insomnia, and psychosis. For patients with kidney failure, it is obviously important to select an agent that is not metabolized by the kidneys. Also, for those on dialysis, the medication should not be a small molecule that can be dialyzed out. Fortunately, almost all medications used for psychiatric illnesses are detoxified by the liver, pass the blood-brain barrier, and are not dialyzable. An interesting exception is lithium, a small dialyzable molecule. It may be given as a single dose following a dialysis run, after which it stays in the patient’s body until it is completely removed during the next dialysis run.

Lorazepam is an interesting and usable medication for anxiety in patients with kidney failure. In patients with functioning kidneys, it is removed by the kidneys. In those with renal failure, it is removed by the liver.

**Pharmacokinetics**

Drug absorption is not affected in kidney failure unless the patient has significant diarrhea or vomiting. However, changes in fluid balance and the effects of uremia can affect drug distribution. The amount of fluid required to contain the administered dose of a drug evenly throughout the body...
is termed the “volume of distribution.” Edema, not uncommonly seen in patients with renal failure, affects the volume of distribution. In such cases, water-soluble drugs, such as lithium, are most affected. Most psychiatric drugs are fat-soluble, making this a less significant factor in patients with renal failure. But these drugs tend to be protein-bound, making protein binding an important concept for the treating psychiatrist.

It is the unbound form of a drug that provides effectiveness or the potential for overdose; the bound form is essentially inert. Because patients with kidney failure have decreased albumin, the amount of a given drug binding to protein is less than in a person with normal kidney function. Thus, patients with kidney failure should be given a lower dose of drug than persons with normal renal function. Fortunately, the liver metabolizes almost all psychiatric medications. As previously discussed, the notable exception is lithium.

**Transplant**

An alternative to dialysis is renal transplant. This has advantages over other vital organ transplant (eg, heart, lungs) because if the kidney transplant is rejected, the patient can be treated by dialysis—the only artificial vital organ substitution now available. The most obvious advantage of renal transplant is freedom from dialysis, which in the case of hemodialysis is usually 3 times weekly. Furthermore, patients on dialysis have strict dietary limitations. They are placed on a low-protein, low-salt, low-phosphate (limited dairy products) diet. The worst is the restriction on fluid intake. This requirement is less of an issue with peritoneal dialysis than with hemodialysis—patients on the latter are told not to drink water, but rather substitute ice to quench thirst. Studies show that patients who receive a transplant have less sexual dysfunction, less depression, and fewer psychological problems altogether. In general, they assume a much more normal life than their counterparts who are on dialysis. However, transplant is not free of problems. The medications used to inhibit rejection have many adverse effects. For example, in the early postoperative period, patients receive large doses of prednisone, which can have myriad adverse effects, including moon facies, buffalo hump, acne, and worsening of diabetes. Recipients of immunosuppressants are prone to infections and neoplasms, the most common of which are skin cancers.

And finally, although most patients use denial successfully, the distinct possibility or inevitable probability of organ rejection is ever present. As one patient put it, “the sword of Damocles hangs over me.”

**CASE VIGNETTE**

Several years ago, a 35-year-old African American woman was called to my attention because she was depressed. Although raised by poor southern parents, because of her initiative and intelligence she made her way north, completed a master’s degree, and had recently been appointed an assistant principal in the New York City school system.

She saw her physician because of progressive lethargy, hiccupping, and nausea. Findings from her physical examination were normal, but blood studies showed a creatinine level of 3.5 mg/dL (normal, 0.67 to 1.17) and elevated BUN and potassium levels. The physician diagnosed a kidney disorder, and further workup revealed that she had polycystic kidney disease. The illness progressed to chronic kidney failure, and dialysis was needed. She chose in-center hemodialysis that required that she spend 3 hours 3 times a week at a neighboring dialysis center. Because of the illness and its treatment, she was not able to carry through the responsibilities of an assistant principal and decided to accept a half-time position as an adult education teacher. When I saw her, she was clinically depressed, had a sleep disorder, complained of poor self-esteem, said that she was less social than she had previously been, and told me in an almost confessional manner that she had suicidal thoughts but would not act on them.

Because of the significant reduction in salary, she was no longer able to support her aging parents. She complained that her appearance had changed: her skin was somewhat darker and she had snake-like bulging of the veins in her forearm. (To gain repeated access, surgeons had joined her left radial vein and radial artery subcutaneously, and the increased pressure caused an “arteralization” of her radial vein.) After some prodding, she mentioned that she felt “down” because the nephrologist had said that women on dialysis have a marked decrease in their ability to become pregnant.

Kidney transplant offers a close resemblance to normal life. Unlike the dialysis patient, those who receive a kidney transplant are no longer tied to a machine, a procedure, or a group of dialysis professionals. They can go and come as they like; can drink fluids in a relatively unrestricted way; and do not have to be on a low-sodium, low-protein diet. It is the rare patient who does not highly
prefer this type of intervention. Psychologically, these patients tend to use denial as a defense against the possibility of organ rejection. However, if the transplanted organ is rejected, patients can return to dialysis.

On the negative side, the anti-rejection medications that patients need to take for the rest of their lives have some serious adverse effects, including, as noted, an increased risk of cancers, especially skin cancers, and an increased vulnerability for infections. However, health outcomes are generally good.

**Conclusion**

Citing all the possible problems of patients with kidney failure tends to remove one from appreciating how far we have come and how fortunate these patients are. Although some dwell on their misfortune, the reality is that patients are fortunate to have been born at a time when kidney failure is no longer a death sentence. Many patients on dialysis and recipients of kidney transplants go on to lead productive and enjoyable lives.

**Disclosures:**

Dr Levy is Director of Psychiatry at the Southern California Mental Health Associates in Los Angeles and Professor Emeritus in Psychiatry at SUNY Downstate Medical Center in Brooklyn, NY. He reports no conflicts of interest concerning the subject matter of this article.

**References:**


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