ORIGINAL ARTICLE

Intravenous drug users who require dialysis: causes of renal failure and outcomes

Jemima K. Scott*, Dominic M. Taylor and Chris R. K. Dudley

Richard Bright Renal Service, North Bristol NHS Trust, UK

Correspondence and offprint requests to: Jemima K. Scott; E-mail: jemima.scott@nbt.nhs.uk
*Jemima Scott is an NIHR Academic Clinical Fellow.

Abstract

Background: Intravenous drug use is associated with progressive kidney disease of several aetiologies. It is associated with behavioural and lifestyle characteristics that make the provision of renal replacement therapies (RRTs) challenging. We observed that patients who use intravenous drugs [people who inject drugs (PWID)] present late to renal services and struggle to engage with treatment. We describe the experience of a UK centre providing renal services to a mixed city and rural population.

Methods: A review of electronic patient records (2003–16) was performed to identify patients actively using intravenous drugs at the time of dialysis initiation. Descriptive statistics were used to describe aetiology, treatment, complications and prognosis.

Results: Twenty-three patients were identified; 15 had a biopsy-proven diagnosis of AA amyloidosis. The median time from presentation to dialysis initiation was 47 days [interquartile range (IQR) 8–147.5]. Hepatitis C infection, venous thromboembolism and mental health disorders were common comorbidities. Eight patients attempted peritoneal dialysis; all failed after a median of 30 days (IQR 21.75–83). One-year survival was 65% (95% confidence interval 42–80), significantly lower than 2013 UK renal registry statistics for incident haemodialysis patients <65 years of age (94.2%).

Conclusions: PWID who develop end-stage kidney disease in our region predominantly have AA amyloidosis. Most present late to renal services and have poor outcomes on all forms of RRT. Rates of transplantation are low. Management challenges include coexisting alcohol and mental health problems, low socio-economic status, contamination of intravenous dialysis access and chaotic lifestyles. Multidisciplinary management with enhanced social support may be beneficial in improving outcomes for this patient group.

Key words: amyloidosis, dialysis, ESRD, hepatitis C, survival analysis, vascular access

Introduction

In a survey from 2000 by the Office of National Statistics, 1 person per 1000 in the UK reported injecting illicit drugs during the previous month [1]. People who inject drugs (PWID) are at higher risk of death from any cause: the standardized mortality ratio for PWID in the UK is reported to be between 10 and 20 [2]. Rates of intravenous drug use are higher in cities [3].

Intravenous drug use has been associated with kidney disease of several aetiologies, including focal segmental glomerulosclerosis ('heroin nephropathy'), membranoproliferative glomerulonephritis (including that associated with hepatitis virus

infection), AA amyloidosis, rhabdomyolysis and interstitial nephritis [4].

Haemodialysis patients with drug dependence have been shown to have 1.3-fold higher any-cause mortality [5]. This association varies with age, with the highest hazard ratio seen in individuals in the youngest age group. A review of PWID with end-stage renal disease (ESRD) secondary to AA amyloidosis demonstrated a median survival of only 19 months in the UK [6].

We have observed a number of patients developing dialysis-dependent kidney disease related to intravenous drug use. The management of ESRD for these individuals was challenging from a clinical point of view and because of concurrent psychosocial problems. We sought to describe formally the demographic, clinical details and prognosis of this patient group.

Materials and methods

A retrospective review of electronic patient records from January 2003 to December 2016 was carried out at the nephrology department of North Bristol NHS Trust, a regional centre providing nephrology services to a population of 1.5 million. A text search was performed using the terms 'amyloid' or 'amyloidosis' (diagnosis) and 'IVDU', 'IVD', 'IVDA', 'intravenous drug', 'heroin' (within summary records). Electronic case notes of patients identified by these searches were reviewed by two researchers (J.S. and D.T.). Figure 1 is a flow diagram of exclusions. Patients >18 years of age at the time of reaching ESRD

Fig. 1. Flow diagram of exclusions.

were included if they had reported active use of intravenous drugs at the time of dialysis initiation. Patients were excluded if there was recovery of renal function in >30 days.

Data were recorded on patient demographics, primary renal diagnosis, comorbidities, biochemistry at dialysis initiation, initial and subsequent dialysis modalities, number of access procedures and complications, admissions to intensive care facilities and survival. Positive hepatitis C viral antibody and polymerase chain reaction (PCR) tests were assumed to indicate previous and current infection, respectively. The postcode of residence at the time of data collection was linked to census data via the GeoConvert online portal [7] to obtain the English Index of Multiple Deprivation (IMD) 2015 decile, used to indicate socio-economic status. Patients were classified as suffering from a mental health disorder if a relevant diagnosis was documented in electronic case notes or they were prescribed antidepressant or antipsychotic medication with no explanation of alternative indication (excluding benzodiazepines).

Data were summarized using descriptive statistics and summary statistics expressed as median [interquartile range (IQR)]. Kaplan–Meier survival analysis was performed and median survival was compared to incident dialysis patients from the UK renal registry report (2015 [8]). A P-value < 0.05 was selected *a priori* to indicate statistical significance. Statistical analyses were performed using Stata 12 (StataCorp, College Station, TX, USA).

Results

Figure 1 shows the process of patient selection. There was full agreement between the two reviewers as to which patients should be included. Twenty-three patients met the eligibility criteria. Sixteen were male and seven were female. The median age at the time of dialysis initiation was 40 years (IQR 33–46). Nineteen were white; ethnicity data were unavailable for the remainder. The median IMD tertile was 3 (IQR 1–5).

Clinical details are summarized in Table 1 (Causes of ESRD and co-morbidities). Hepatitis C infection (35%), mental health disorders (43%), venous thromboembolism and soft tissue abscesses were the most common comorbidities. Eight patients had active hepatitis C infection at the time of audit, two of whom were under the care of a gastroenterologist. One patient was receiving treatment with antiviral therapy. Twelve patients had evidence of previous infection. No patients had active hepatitis B or human immunodeficiency (HIV) infection at the time of presentation.

Seventeen patients underwent a renal biopsy, 15 of whom were found to have AA amyloidosis. One patient had anti–neutrophil cytoplasmic antibody–related vasculitis and another had acute kidney injury associated with streptococcal endocarditis. Six patients whose clinical presentation was consistent with AA amyloidosis (two), hepatitis C–related glomerulonephritis (one), hepatorenal syndrome (one) and unknown (one) were not biopsied. One patient developed ESRD from sarcoid-related hypercalcaemia following unilateral nephrectomy for renal cell carcinoma. The median time from presentation to renal services to dialysis initiation was 47 days (IQR 8–147.5). Prior to dialysis initiation, the median haemoglobin was 84 g/L (IQR 70–95), serum albumin 22 g/L (IQR 17–30) and urine protein creatinine ratio (uPCR) 1013 mg/mmol (IQR 229–2288).

Eighteen patients were commenced on haemodialysis and five patients started on peritoneal dialysis (PD) as their initial dialysis modality. The first haemodialysis access was via tunnelled line (nine patients), temporary line (seven patients) or fistula (two patients). All of those who started PD subsequently
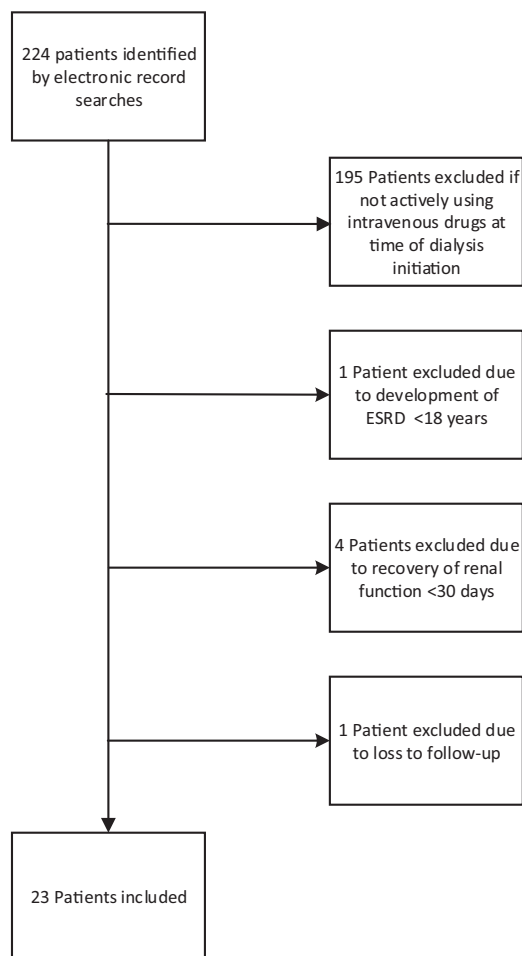
Table 1. Causes of end-stage renal disease and comorbidities

Patient	Age at RRT start (years)	Renal diagnosis	Comorbidities		
			Hep C	Mental health disorder	Other
1	41	AA amyloidosis	+	No	DVT, staphylococcal septicaemia
2	48	AA amyloidosis	+	Yes	DVT
3	33	AA amyloidosis	+	Yes	Epilepsy, previous osteosarcoma and limb amputation
4	37	AA amyloidosis	+	No	Multiple abscesses, DVTs, PE
5	28	AA amyloidosis	+	Yes	Groin abscess, aortic regurgitation
6	32	AA amyloidosis	+	Yes	DVT
7	42	AA amyloidosis	−	Yes	Multiple abscesses, aortic regurgitation and valve replacement, upper GI bleed, hypertension.
8	40	AA amyloidosis	+	No	Epilepsy, hypertension
9	36	AA amyloidosis	+	No	PE
10	35	AA amyloidosis	+	No	DVT, multiple abscesses
11	39	AA amyloidosis	+	Yes	Groin abscess, staphylococcal septicaemia, infective endocarditis
12	25	Presumed AA amyloidosis (biopsy not performed)	+	No	DVT, multiple abscesses, fungal infective endocarditis
13	28	Acute kidney injury associated with streptococcal endocarditis	+	No	Infective endocarditis requiring valve replacement
14	56	Presumed AA amyloidosis (biopsy not performed)	+	No	DVT, groin abscess
15	40	Hepatitis C related nephropathy (biopsy not performed)	+	No	Alcohol dependence, chronic liver disease
16	31	Nephrectomy for renal cell carcinoma, hypercalcaemia	−	No	Sarcoidosis, hypertension, renal cell carcinoma
17	60	Unknown (declined biopsy)	+	No	Alcohol dependence, soft tissue abscess, epilepsy
18	42	ANCA-associated vasculitis	+	Yes	Small bowel obstruction, alcohol dependence, chronic leg ulceration
19	36	AA amyloidosis	+	Yes	Tricuspid regurgitation secondary to infective endocarditis, treated hepatitis B
20	50	Hepatorenal syndrome (not biopsied)	+	Yes	Alcohol excess, chronic liver disease, treated hepatitis B
21	40	AA amyloidosis	+	Yes	Recurrent DVTs
22	46	AA amyloidosis	−	No	DVT
23	50	AA amyloidosis	+	No	Severe mitral regurgitation, soft tissue abscess

DVT: Deep Vein Thrombosis; PR: Pulmonary Embolism; RRT: Renal Replacement Therapy

transferred to haemodialysis after a median time of 52 days (IQR 24.5–88). During the dialysis lifespan, the median number of intravenous catheters required was 2 (IQR 1–4). Indications for line change/removal were the creation of permanent access (31%), infection (26%), blocked access (23%), poor flow (10%) and unknown (10%). Nineteen patients underwent a permanent access scan; suggested initial access was a graft in 58% and fistula in 37%. One scan report made no recommendation. Arteriovenous fistula or graft formation was performed on one or more occasion for 13 patients; 1 patient underwent four such procedures. The total number of access procedures was 23, 12 of which were grafts. The median survival for grafts and fistulae was similar [5 versus 6 months (IQR 3–6 and 4–24, respectively)].

Eight patients underwent peritoneal dialysis. One patient had two separate attempts. The median time to peritoneal dialysis failure was 78 days (IQR 30–156). Peritoneal dialysis failed due to infection (56%), failure to attend for dialysis education (22%), technique failure (11%) or surgical wound dehiscence (11%). One patient with ESRD secondary to nephrectomy (for malignancy) and sarcoidosis-related hypercalcaemia received a renal transplant. Renal transplantation was considered to be contraindicated in the other patients because of their chaotic lifestyle and lack of adherence to treatment.

Critical care admissions occurred at a frequency of 0.42 admissions per patient-year. One patient was admitted to a critical care unit seven times. At the time of data collection, 15 patients had died. The median survival from the start of dialysis was 20.4 months (IQR 7.4–63.1) and the age at death was 40 years (IQR 33–49). The cause of death was unknown in eight cases (53%) and in the remaining seven patients was line-related infection (two), withdrawal from dialysis (two), fungal infective endocarditis of the tricuspid valve (one), heroin overdose (one)

and cardiac arrest secondary to hyperkalaemia (one). Nine patients were alive at the end of the follow-up period; all but one continued to receive dialysis.

Discussion

This is the first UK-based review of the use of haemodialysis in PWID. In this 13-year retrospective case series we highlight some of the most challenging areas in the management of this group of patients, including late presentation, range of comorbidities, difficulties in haemodialysis access formation and low rates of transplantation. The poor outcomes seen in this UK population are similar to those seen in data from the USA [5], despite differences in patterns of drug use.

Intravenous drug use is associated with multiple comorbidities including venous thrombosis, soft tissue infection and endocarditis. The prevalence of active hepatitis C infection in this cohort was 35%, higher than the estimated 26% among PWID nationally [9]. Difficulties in treating hepatitis C in PWID include low levels of awareness of positive antibody status [9] and reduced rates of spontaneous clearance [10].

The cause of end-stage renal failure in this group was directly related to intravenous drug use in all but three patients, either as AA amyloidosis or infection. The high prevalence of AA amyloidosis is consistent with an observed change in the causes of kidney disease associated with intravenous drug use. Reported cases of 'heroin nephropathy' declined during the 1990s, while nephropathy related to blood-borne viruses (membranoproliferative glomerulonephritis associated with viral hepatitis infections, HIV-associated nephropathy) increased [4]. More recently, an increased prevalence of AA amyloidosis has been reported [6, 11]. Jung et al. [12] reported higher rates of AA amyloidosis among those infected with HIV and suggest that HIV-associated immunosuppression may promote the development of amyloidosis. The prevalence of HIV infection among PWID in the UK is believed to have been relatively stable since 2004 at between 1 and 1.6% [13]. None of the patients in this study were infected with HIV. In this cohort, AA amyloidosis was thought to be caused by chronic soft tissue sepsis associated with intravenous drug use and 'skin popping' (intradermal or subcutaneous injection of illicit drugs).

The rate of late presentation [<90 days from presentation to renal replacement therapy (RRT) start] was high (65% versus 17.8% nationally [14]), making timely formation of permanent vascular access difficult. Only two patients (9%) started dialysis on a fistula or graft, compared with 28.8% nationally [15]. The number of patients in this cohort on peritoneal dialysis as the initial RRT modality was similar to registry data (21% versus 20.1%) [15]. This may not be surprising in view of the median patient age and presumed clinician preference to avoid using intravenous catheters in those at risk of misuse of dialysis access. Despite the high peritoneal dialysis rate, technique success was very poor, with 63% transferred to haemodialysis before 90 days. Only one patient received a renal transplant. The primary renal disease in this case was unrelated to intravenous drug use and hepatitis C infection was absent, perhaps suggesting lower levels of intravenous drug use. No other patient was listed for renal transplantation.

Overall outcomes were very poor, with a median survival of 8.6 months. The median survival of patients starting RRT from a comparable age group from registry data (patients 35–44 years of age from the 2010–13 cohort) is >10 years [8]. For comparison, the crude mortality rate for all people who use intravenous drugs in western Europe is 2.31 per 100 person-years [2]. A case series from 2006 of patients with renal AA amyloidosis associated with intravenous drug use described similar mortality rates among those starting dialysis [6]. The mortality of those with AA amyloidosis not associated with intravenous drug use is unknown.

Managing patients requiring RRT who inject drugs is a challenge. Drug use is associated with unemployment, financial difficulty, lower educational level and lower levels of home ownership [1], all factors that associate with poorer health outcomes [16]. Dependence on drugs itself contributes to a chaotic lifestyle and is compounded by high levels of mental health disorders. These factors are likely to contribute to late presentation, making pre-emptive vascular access or transplant planning problematic. Fistula formation is technically challenging in those with venous damage from intravenous drug use. The use of dialysis catheters by patients as a portal for drug abuse risks infection and catheter occlusion. Peritoneal dialysis as a treatment modality had a dismal success rate due to a combination of poor housing, chaotic lifestyle and self-neglect. In our unit, no intravenous drug user has been started on peritoneal dialysis since 2010, suggesting a change in management over time with increasing clinician experience.

Patients who use intravenous drugs may struggle to comply with the demanding treatment regimens characteristic of RRT. Previous studies have documented a lack of stable housing and competing interests (the need to access drugs and money) as barriers to compliance [17]. Missing dialysis sessions carries significant risk wherein mismanagement of fluid or potassium can easily lead to death. Nutrition and adherence to low potassium or phosphate diets is usually poor. Access to transplantation depends on demonstration of compliance as well as attendance at preoperative assessments, and is likely to be difficult.

This study benefits from a clearly defined search strategy, a high level of clinical detail afforded by our electronic notes system and a long study period of 13 years. As a local study, relatively few patients were identified for inclusion compared with studies of registry data. In addition, the data were taken from electronic case notes that rely on the diligence of clinicians in entering relevant information. However, more detailed information on comorbidities and clinical course were available compared to registry data. Socio-economic status was assessed by area-level deprivation score only.

Improving outcomes in this patient group is likely to require a multidisciplinary approach with enhanced access to drug rehabilitation and social support as well as innovative approaches to providing dialysis. Further research into barriers faced by intravenous drug users in accessing secondary care and dialysis, as well as attitudes of clinicians towards this population, would assist in developing appropriate services. General practice has led the way in recognizing that medical services need to adapt to meet the needs of disadvantaged populations rather than asking the population itself to change. Numerous cities now have practices specifically for homeless, refugee and other vulnerable individuals, offering easy registration, drop-in clinics and a wide range of targeted services such as podiatry, social and mental health practitioners [18, 19]. However, it is hard to imagine how a dialysis regimen could be made similarly flexible. Screening of known intravenous drug users in hostels and day centres may offer an opportunity for earlier detection of renal disease, but changes to current services will have to be made before better engagement of this patient group is likely to be seen.

Conflicts of interest statement

None declared.

References

1. Coulthard MFM, Singleton N, Meltzer H. *Tobacco, Alcohol and Drug Use and Mental Health*. London: Office of National Statistics, 2002
2. Mathers BM, Degenhardt L, Bucello C *et al.* Mortality among people who inject drugs: a systematic review and meta-analysis. *Bull World Health Org* 2013; 91: 102–123
3. Health and Social Care Information Centre. *Statistics on Drug Misuse: England 2014*. http://content.digital.nhs.uk/catalogue/PUB15943/drug-misu-eng-2014-rep.pdf. 2014 [29 March 2017, date last accessed]
4. Jaffe JA, Kimmel PL. Chronic nephropathies of cocaine and heroin abuse: a critical review. *Clin J Am Soc Nephrol* 2006; 1: 655–667
5. Grubbs V, Vittighoff E, Grimes B *et al.* Mortality and illicit drug dependence among hemodialysis patients in the United States: a retrospective cohort analysis. *BMC Nephrol* 2016; 17: 56
6. Connolly JO, Gillmore JD, Lachmann HJ *et al.* Renal amyloidosis in intravenous drug users. *QJM* 2006; 99: 737–742
7. UK Data Service. GeoConvert. http://geoconvert.mimas.ac.uk/ [10 December 2016, date last accessed]
8. Steenkamp R, Rao A, Fraser S. UK Renal Registry 18th Annual Report: Chapter 5 Survival and causes of death in UK adult patients on renal replacement therapy in 2014: national and centre-specific analyses. *Nephron* 2016; 132: 111–144
9. Public Health England. Hepatitis C in the UK: 2016 report. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/565459/Hepatitis_C_in_the_UK_2016_report.pdf [9 February 2017, date last accessed]
10. Grebely J, Raffa JD, Lai C *et al.* Factors associated with spontaneous clearance of hepatitis C virus among illicit drug users. *Can J Gastroenterol* 2007; 21: 447–451
11. Manner I, Sagedal S, Røger M *et al.* Renal amyloidosis in intravenous heroin addicts with nephrotic syndrome and renal failure. *Clin Nephrol* 2009; 72: 224–228
12. Jung O, Haack HS, Buettner M *et al.* Renal AA-amyloidosis in intravenous drug users–a role for HIV-infection? *BMC Nephrol* 2012; 13: 151
13. Public Health England. HIV-STIs. Unlinked anonymous HIV and viral hepatitis monitoring among PWID: 2016 report. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/538321/hpr2316_uampwid.pdf [February 2017, date last accessed]
14. Gilg J, Caskey F, Fogarty D. UK Renal Registry 18th Annual Report. Chapter 1: UK renal replacement therapy incidence in 2014: national and centre-specific analyses. *Nephron* 2016; 132(Suppl 1): 9–40
15. Rao A, Evans R, Wilkie M *et al.* UK Renal Registry 18th Annual Report. Chapter 11 2014 multisite dialysis access audit in England, Northern Ireland and Wales and 2013 PD one year follow-up: national and centre-specific analyses. *Nephron* 2016; 132(Suppl 1): 253–278
16. Caskey FJ, Roderick P, Steenkamp R *et al.* Social deprivation and survival on renal replacement therapy in England and Wales. *Kidney Int* 2006; 70: 2134–2140
17. O'Donnell P, Tierney E, O'Carroll A *et al.* Exploring levers and barriers to accessing primary care for marginalised groups and identifying their priorities for primary care provision: a participatory learning and action research study. *Int J Equity Health* 2016; 15: 197
18. Inclusion Healthcare. Anchor Centre. http://inclusion-healthcare.co.uk/anchor-centre/ [23 January 2017, date last accessed]
19. Oxford Health NHS Foundation Trust. Luther Street Medical Centre. http://www.oxfordhealth.nhs.uk/service_description/luther-street-medical-centre [23 January 2017, date last accessed]