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HCV Can and Should Be Eliminated From Dialysis Units

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Upon the identification of Hepatitis C Virus (HCV) over 3 decades ago, HCV infection was recognized as a frequent complication of maintenance hemodialysis (HD), in part due to high rates of blood transfusion (1). Progressive improvements in testing blood donors by serological tests (and more recently by nucleic acid testing (NAT)), the increasing use of erythropoiesis-stimulating agents, and the improvement of hygienic precautions all contributed over the subsequent two decades to a reduction in the incidence and prevalence of HCV in HD patients. Yet, HCV prevalence still averaged 9.9% in the Dialysis Outcomes and Practices Patterns Study (DOPPS) in 2012-15, whereas incidence averaged 1.2 new cases per 100 patient-years (2). Worldwide, this incidence translates to a minimum of 20,000 new cases yearly among patients on maintenance HD. The vast majority of cases are nosocomial (3), resulting from substandard hygienic precautions, with a minority acquired outside the HD unit, mostly from intravenous drug use. These dire figures of incident HCV infection while on HD collide with the World Health Organization (WHO) vision to eliminate viral hepatitis as a public health problem by 2030 (4). The WHO commitment hinges upon the recent availability of extremely effective and safe direct-acting antiviral agents (DAAs). Indeed, cure of HCV infection is currently possible in almost every patient whose HCV infection is diagnosed. However, because HCV infection is frequently underdiagnosed in the general population, the concept of micro-elimination was developed (5): this strategy targets individuals with diagnosed HCV infection who are under regular medical care, such as HD patients. Yet, despite the availability of effective and well-tolerated DAA regimens for HD patients (6,7), there has been hitherto little evidence that HCV elimination from HD units is underway.

In this issue of AJKD, Hu et al. report a quality improvement initiative that describes the almost complete elimination of HCV from all 31 HD units of Changhua County in Taiwan (8). Importantly, Taiwan has a high HCV prevalence, largely as a result of transmission decades ago by health care delivered with sub-optimal hygienic precautions (9). Thus, Taiwanese authorities have prioritized meeting the WHO target as part of their public health policy and a collaborative care model was implemented. The dialysis population was the first target of a broader program aiming at covering other high-risk populations (people who inject drugs, prisoners, HIV-positive persons, etc). The major components of the first step of the collaborative care model included an emphasis on collaboration between gastroenterologists and nephrologists, access to DAAs (restricted to severe cases of HCV prior to 2019), nurse-

led case management, easy access to medical transportation for patients to attend the HCV clinic, use of mobile clinics to reach remote areas, integration of county- and national-level data, and collaboration between central and local governments.

A total of 3657 dialysis patients (92.7% receiving HD), either prevalent at the time of study start or incident over the study period (January 1 to September 30, 2019) were included. A positive anti-HCV antibody test was recorded in 403 of 3657 patients (11%). NAT was performed in 396 of 403 (98.3% diagnosis rate). Surprisingly, 176 of the antibody-positive patients were NAT negative, a higher proportion (44%) than in most dialysis studies, in which the proportion is only 10%-15%. This was explained by prior antiviral treatment in 65 patients and may represent false-positive antibody testing or spontaneous viral clearance from prior infection in the remaining 111 patients. Among the 216 viremic patients, 184 received a DAA regimen (mainly glecaprevir-pibrentasvir, or grazoprevir-elbasvir) (6,7), whereas the remaining 32 patients were not treated for various reasons (refusal (n=14), too unstable (n=8), death before DAA (n=9)). The SVR12 rate (equivalent to a cure) was 166 of 173 (96%) among patients completing the DAA regimen. These results demonstrate that the battle against HCV within HD units can be successful with multidisciplinary collaboration and adequate funding. Admittedly, some patients may have a too-short life expectancy to justify a DAA course (9,10), as illustrated by the 10% death rate over the relatively short study period.

Thus, similar initiatives are urgently needed in other countries, including lower income countries. Needless to say that the prerequisite is that actual HCV infection is diagnosed in HD patients by regular enzymatic immunoassay followed if positive by NAT (10,11). The next step in the cascade of care is starting a DAA regimen. Fortunately, the recent decision by the US Food and Drug Administration to extend the label of sofosbuvir-based therapies for use in patients with chronic kidney disease glomerular filtration rate categories 4-5 (12), including dialysis patients, is good news as it broadens the spectrum of DAA regimens available in dialysis patients. In some countries either the original sofosbuvir or generic sofosbuvir may be available at a very affordable cost. Admittedly, the collaborative care model used in Taiwan will need to be tailored to the way dialysis care is provided in each context, depending on the breakdown of satellite vs hospital-based units and the presence of large dialysis organizations, among other factors.

As in previous large-sized studies of HCV in HD (such as DOPPS), the study by Hu et al. relied on the widely used serologic tests, rather than the gold standard NAT. Thus, the actual prevalence of HCV infection probably has been slightly underestimated, as anti-HCV

antibody testing remains negative for a median of 5 months after infection in HD patients (13). Still, the results convincingly demonstrate that the prevalence of HCV infection can be reduced to a level close to zero, much lower than in the general population of the corresponding country. The benefits of this dramatic reduction of the prevalence of HCV infection are multiple. First, the hepatic complications of chronic HCV infection will largely be prevented. Second, the prognosis of patients cured from HCV infection likely is improved independently of hepatic benefits. There is indeed a large body of evidence demonstrating that chronic HCV infection is associated with micro-inflammation and insulin resistance and contributes to an increased cardiovascular risk, and that curing HCV is associated with a reduction of this risk (14). Lastly, the incidence of HCV infection in HD will drop sharply because of the reduction of number of source (infective) patients, thus creating a virtuous cycle. Ultimately, regular testing for HCV, as performed in Taiwan and recommended by both the CDC(11) and KDIGO (10), may no longer be needed in units from which HCV has been eradicated, except in patients starting HD. Testing every patient at dialysis initiation then would be particularly important; the prevalence of HCV at HD start is around 5% in countries with relevant DOPPS data (USA, UK, Germany, Italy, Spain, and Japan), substantially higher than in the general population of these nations, with this prevalence not changing much over 2000-2015 (2). Patients found to be anti-HCV antibody and NAT positive at dialysis initiation could be treated immediately and this would obviate the need for the isolation policy for HCV-positive patients used in Taiwan (8) and several other countries (2) that is burdensome, has been shown to be neither necessary nor effective, and is not currently recommended by either the CDC or the KDIGO guideline (10,11). Importantly, this policy of testing at HD initiation should not preclude testing patients returning from vacations during which they received treatment in another unit, especially in a high prevalence country,(15) as well as in those with risk factors for acquiring HCV outside of the dialysis setting.

In summary, Hu and colleagues should be congratulated for showing us the way: this is the right time to eradicate HCV from HD units. Their success sounds as a call for urgent action by all HD units and providers.

Article Information

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