KI REPORTS
KIReports.org

Realtime Remote Detection of Evolving Peritonitis in Peritoneal Dialysis

Mark Lambie[1] and Martin Wilkie[2]

[1]School of Medicine, Faculty of Medicine and Health Sciences, Keele University, Staffordshire, UK; and [2]Sheffield Kidney Institute, Sheffield Teaching Hospitals NHS Trust, Sheffield, UK

Kidney Int Rep (2024) **9,** 749–751; https://doi.org/10.1016/j.ekir.2024.02.1430

See Clinical Research on Page 929

Despite impressive reductions in infection rates over the past 3 decades with the global average decreasing from 0.600 in 1992 to 0.303 episodes/patient-year in 2019, peritonitis remains the major complication of peritoneal dialysis (PD) and cause of transfer to hemodialysis.[1,2] The detection of peritonitis continues to rely predominantly on the patient or their carers being able to promptly recognize its features, including the appearance of a cloudy dialysis effluent.[3] For PD users, there "remains a permanent and consistent awareness of the risk of infection, which provides a background hum of vigilance and anxiety."[4] Individuals who are potentially suitable to use PD as a treatment may have cognitive and physical barriers that increase the difficulty there is in confidently recognizing that they may be developing an episode of peritonitis. Added to this are logistical difficulties patients may have in presenting to their health care teams particularly in remote geographic locations. Furthermore, delays in presentation and initiation of antibiotics are associated with an increased risk of death or technique failure.[5] It is therefore not surprising that the International Society for Peritoneal Dialysis (ISPD) peritoneal infection guideline recommends prompt commencement of antibiotics once infection has been diagnosed.[3] Investigations that delay antibiotics, such as waiting for the results of radiological investigations, can be deleterious to patient care.[6]

There is, therefore, a need for near patient testing systems that promptly identify a possible peritonitis episode, enabling rapid confirmation, thereby shortening the time-to-treatment for peritonitis. These could include devices that routinely screen drained dialysate, most obviously as part of an automated PD machine, or point-of-care diagnostic devices used by either patients or health care professionals. Of these, the screening option has the greatest potential to reduce time between the development of infection and its treatment, which will depend upon whether there is a meaningful period of time during which infection is present before clinical signs developing. The value of any such screening tool will rest on this currently unknown natural history of peritonitis as well as the proportion of false positives and false negative results that such a screening system may generate and their consequences.

Due to these challenges, there will be considerable interest in the CATCH study published by Rajnish Mehrotra and colleagues from the University of Washington School of Medicine in this issue of Kidney International Reports.[7] The authors present results from the CloudCath system that monitors turbidity in dialysis effluent to detect possible episodes of peritonitis as they develop. This is done using an optical sensor in the drain line of the automated PD machine that sends data directly to a cloud-based portal. The primary end point of the 12 month, 19 site, multicenter U.S. study was based on ISPD white blood cell count criteria alone: effluent with WBC >100/μl and polymorphonuclear leukocytes >50%. The secondary outcome measure was the standard ISPD diagnostic criteria for PD peritonitis, that is, 2 out of 3 of abdominal pain, cloudy effluent, and raised effluent cell count as above or positive effluent culture.

Among 243 patients followed-up with for 179 patient-months of therapy, 51 events met the ISPD white cell count diagnostic criteria for peritonitis. Importantly the CloudCath system triggered notifications in 80% of these with a median lead time of 2.6 days. The study design did not permit intervention because the notification system was deactivated on the basis that the study was purely observational. Overall there were 140 total notifications in the study, with 96 that were not caused by peritonitis, which is perhaps not surprising given that there are other causes of

Correspondence: Martin Wilkie, Sheffield Kidney Institute, Sheffield Teaching Hospitals NHS, Herries Road, Sheffield S5 7AU, UK. E-mail: martin.wilkie@nhs.net

effluent turbidity with a wide differential as documented in the ISPD infection guideline.[3] Of these 96 notifications, 41 were associated with other events thought to have caused turbidity; however, for 55 of these, there was no apparent event, and these have different implications. Nonperitonitis events generating an alert included nonperitonitis infections, catheter dysfunction, bleeding, vaccination and a dry peritoneal cavity. For some of these events, contacting the team would have been desirable and in some that patient was likely to consult the health care team anyway. The 55 events with no other explanation are more concerning, because the implication is that the patients will have extra worry and inconvenience, and the health care team will have extra work.

The 96 nonperitonitis notifications were clustered by patient, with 22 patients responsible for 66, suggesting scope for identifying patients where misleading notifications are more likely to occur. It is possible that these notifications could be identifying hitherto unrecognized problems; therefore, there is a clear need to examine outcomes and possible pathophysiological explanations in this group in future studies. Having said that, as more data becomes available, any prediction model, including those based on machine learning, would be expected to improve, and the study team demonstrated this, with a modified algorithm only generating 33 false positives with no apparent event.

More strikingly, the device identified peritonitis events at a median of 2.6 days before peritonitis was apparent clinically. This provides the first published evidence supporting the concept that infection is often present for a prolonged period before signs and symptoms of PD peritonitis develop, a key principle to establish when evaluating the promise of screening tests for peritonitis. Some patients had alerts more than 3 weeks before confirmed peritonitis, which does raise the question of how long after a notification teams need to be concerned about possible infection developing and whether every notification before peritonitis in this study was truly related to peritonitis. Further studies should help to clarify these issues, as well as the significance of notifications without any event to explain it.

Although the study demonstrates significant potential to improve peritonitis outcomes, there are limitations in the system described. Clearly, for the CloudCath system to work, it is necessary that the peritoneal catheter is draining well and in use during the clinically silent infection period, an issue that may need to be considered with incremental PD, or when flow problems or alarms prevent continuous usage. In the current form, the CloudCath system would not be available for people using manual continuous ambulatory PD, a major limitation to any country where this is the prevalent modality, especially given that this is likely to affect developing countries more. It is also crucial to recognize that the current study has not assessed improvements in patient outcomes to weigh up against the downsides of false positives. The team reports that future studies will address these issues, and we have to hope that commercial considerations do not prevent an appropriate randomized trial examining the impact on peritonitis outcomes from occurring.

The ISPD guideline reports a number of novel diagnostic techniques for PD peritonitis, including point-of-care devices and this is an evolving field. Hopefully in the near future, there will be a suite of systems that provide early alerts and diagnostic confirmation of peritoneal infection to improve patient outcomes. Already, there is evidence that remote monitoring can improve outcomes on PD; however, these systems currently report only catheter function and drain alarms as well as patient entered data, and to be able to include infection alerts would be an important development.[8] The CATCH study reported in this issue of Kidney International Reports describes a system that could be incorporated routinely into automated PD systems adding to the potential for remote monitoring to improve outcome on PD.

DISCLOSURE

ML has received speaker honoraria from Baxter Healthcare and Fresenius Medical Care; and a research grant from Baxter Healthcare in 2013. MW has received speaker honoraria from Fresenius Medical Care and Baxter Health Care and has conducted research funded by Baxter; he acts as a consultant to Triomed AB.

REFERENCES

1. Marshall MR. A systematic review of peritoneal dialysis-related peritonitis rates over time from national or regional population-based registries and databases. *Perit Dial Int*. 2022;42:39–47. https://doi.org/10.1177/08968608219960962. Lambie M, Zhao J, McCullough K, et al. Variation in peritoneal dialysis time on therapy by country: results from the peritoneal dialysis outcomes and practice patterns study. *Clin J Am Soc Nephrol*. 2022;17:861–871. https://doi.org/10.2215/CJN.163412213. Li PK, Chow KM, Cho Y, et al. ISPD peritonitis guideline recommendations: 2022 update on prevention and treatment. *Perit Dial Int*. 2022;42:110–153. https://doi.org/10.1177/08968608221080586
4. Ho H. Infection control: making it my own. *Perit Dial Int*. 2022;42:105–107. https://doi.org/10.1177/08968608221082850
5. Muthucumarana K, Howson P, Crawford D, Burrows S, Swaminathan R, Irish A. The relationship between presentation and the

time of initial administration of antibiotics with outcomes of peritonitis in peritoneal dialysis patients: the PROMPT study. *Kidney Int Rep*. 2016;1:65–72. https://doi.org/10.1016/j.ekir.2016.05.003

6. Muthucumarana K, Howson P, Burrows S, Swaminathan S, Irish A. The effect of radiological imaging on treatment delay and hospitalisation in patients with peritoneal dialysis-related peritonitis: A secondary analysis of the PROMPT study. *Perit Dial Int*. 2022;42:154–161. https://doi.org/10.1177/08968608211065871
7. Mehrotra R, Williamson DE, Ross Betts C, et al. A prospective clinical study to EvaluAte the AbiliTy of the CloudCath system to detect peritonitis during in-home peritoneal dialysis (CATCH). *Kidney Int Rep*. 2024;9:929–940. https://doi.org/10.1016/j.ekir.2024.01.033
8. Corzo L, Wilkie M, Vesga JI, et al. Technique failure in remote patient monitoring program in patients undergoing automated peritoneal dialysis: A retrospective cohort study. *Perit Dial Int*. 2020;42:288–296. https://doi.org/10.1177/0896860820982223