Oral K Binders: lessons from the COVID pandemic and clinical experience

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Successful and safe management of hyperkalemia gained particular importance in the extraordinarily demanding conditions that arose due to the coronavirus disease (COVID-19) pandemic when medical staff faced delayed transfer of patients into nephrology clinics, difficulties providing short-term hemofiltration in intensive care units (ICUs), and restructuring hemodialysis (HD) units to accommodate for isolated COVID-19 areas. Even more, adjustments were necessary to keep ICU beds available to critical patients and cope with limited staff. A panel of nephrologists shared their experiences in treating hyperkalemia in these exceptional circumstances.

Italy was the first country to encounter these challenges, with hospitals declaring a state of emergency in February 2020. Dr. Lucia del Vecchio and her dialysis unit in Lecco at that time experienced a growing number of COVID-positive dialysis patients and a surge of COVID-related acute kidney disease cases requiring renal treatment. Although the hospital was able to guarantee dialysis for chronic dialysis patients, dialysis in the acute setting was difficult to provide. In this regard, the possibility of using a potassium binder to delay treatment and relieve pressure on the healthcare system would have been extremely useful. Since the novel potassium binders were not available in Italy in 2020, the existing binders were employed in the acute setting to treat mild hyperkalemia. Unfortunately, these medications cannot be administered to acute patients for an extended period, and are not an alternative to dialysis treatment. In addition, many COVID 19 patients experienced diarrhea and nutritional problems, therefore therapy with sodium polystyrene sulfate was not a viable option.

At Dr. David Thomas's center in North West London, a tertiary dialysis facility, healthcare professionals had to use potassium binders extensively, since smaller satellite facilities did not perform dialysis, and patients were required to wait for the transfer. Since renal patients commonly have a high prevalence of COVID-19 risk factors, such as advanced age, hypertension, diabetes mellitus, cardiovascular disease, and residual immunosuppressive regimens due to glomerulonephritis or failed transplantation, the mortality was unsurprisingly high. The statistics from the first wave of the pandemic show that there were 4360 cases and 1403 deaths in adult renal patients across the UK and Northern Ireland as of 17 June 2020, and the North West London clinic was one of the earliest places that the pandemic hit, registering 300 cases and 94 deaths among 1530 HD patients. Renal services were overburdened due to a large number of admissions, and there was a need to modify outpatient pathways. Nephrologists provided remote help for serum potassium management to protect patients admitted to non-renal centers and reduce ICU admissions. Standard hyperkalemia treatment entails the administration of insulin/dextrose, salbutamol, and sodium bicarbonate. Nevertheless, their usage carries the risk of hypoglycemia, tachyarrhythmia, and fluid overload. New oral, non-absorbed potassium binders such as sodium zirconium cyclosilicate (SZC) - Lokelma, an inorganic crystalline compound, and Patiromer, a cation exchange polymer, have been registered in the United Kingdom for the management of acute hyperkalemia in adults who are not on renal replacement therapy (RRT). In addition, the Phase IIIb DIALIZE trial demonstrated the safety of SZC in HD patients, and tests are currently underway to establish the efficacy of Patiromer. Besides hemodialysis patients, potassium binders were also used in patients with acute kidney injury (AKI) who often required RRT, with hyperkalemia frequently being the predominant indication, and pre-dialysis patients, where some elective procedures, such as line lists and PD catheter insertions, needed to be canceled, postponing the initiation of dialysis. Four pre-dialysis patients were

administered SZC to treat asymptomatic hyperkalemia. At the time of SZC initiation, the mean potassium and urea concentrations were 6.1 mmol/L (range 5.9–6.4) and 74.49 mg/dL (range 61–92.97), respectively. Two patients initiated HD on an average of eight days after starting SZC. The remaining two patients stayed normokalemic on SZC and were monitored on an outpatient basis. SZC was administered to 19 COVID-19-positive HD patients (inpatients and outpatients), and the average time between dialysis treatments for patients was 3.4 days. Before receiving HD, peak serum potassium levels for the nine patients who remained on SZC were 6 mmol/L, and peak urea levels were acceptable at a median of 75.89 (interquartile range: 54.33–107.02) mg/dL. Therefore, after the initial fear that delayed dialysis and hypokalemia would cause further issues, the overall experience of using potassium binders was positive. In the 26 dialysis units in the UK that took part in the survey on the use of potassium binders in conditions of COVID-19,73 % of the units reported that they had used binders even before the pandemic and intensified at the onset of the pandemic, that the most frequently used binders were Lokelma and Patiromer, and the context of hyperkalemia treatment was a high incidence of managing AKI to prevent or delay the requirement for acute dialysis while awaiting renal recovery. Two of the twenty-three units reported that the twice-weekly dialysis regimen was implemented in approximately 20% of their patients with residual function. This regimen necessitates a complex clinical judgment based not only on potassium levels but also on the clinician's confidence in controlling hyperkalemia with a potassium binder in this setting.

The twice-weekly dialysis program was also utilized by Dr. Dimitrios Poulikakos's team at the Salford Royal hospital of the Northern Care Alliance NHS Foundation Trust. During the pandemic, the center treated 432 in-center hemodialysis patients, with the main hospital and four satellite units providing care. Since London was the first city to be afflicted by the pandemic, the centers from the interior had a few weeks' head starts but faced various obstacles. The first was the anticipated rise in staffing requirements for dialysis patients precipitated by the necessity for isolation. It was necessary to rearrange the services to create a unit for suspected and proven cases and separate units for non-Covid patients. Thankfully, a very useful document created by the Renal Association during the 2009 influenza pandemic was available. It relied on a model that anticipated a peak staff absence of 30 to 55 percent for two to three weeks, should a similar pandemic occur. Experience from Italy and London at that time demonstrated a significant increase in AKI, resulting in a greater requirement for dialysis to support ICU units. To meet the local and regional demand for increased ICU care, the center used the influenza pandemic strategy to identify patients who may reduce their dialysis schedule if staff illness prevented the center from managing the population. Taking into account the circumstances in London, where the number of dialysis nurses was insufficient to cover the dialysis program, the center attempted to develop a contingency plan in case a similar situation occurred there since it was deemed unfeasible to implement an elective reduction of dialysis assessment at the height of the pandemic. The center also relied on modeling from Imperial College Healthcare NHS Trust, which suggested that 40 to 45 percent of patients could become infected, necessitating a difficult decision. A few weeks before the onset of the pandemic wave, the consultants were instructed to select patients who could transition to a twice-weekly hemodialysis regimen. Initially, the criteria were not stringent - patient compliance in the past, normal pre-dialysis potassium levels based on historical data, normal weight gain between dialysis sessions, and average metabolic demands. Approximately 160 of the 432 patients were deemed suitable for transition, representing 38% of the overall population. A program was established to undertake this regimen in a controlled fashion, and the clinic assigned five consultants, including the dietetic team and pharmaceutical staff to this program. The patients underwent weekly blood testing upon the first weekly session to assess potassium levels and interdialytic weight gain and were independently evaluated by two consultants. Potassium level above 6.5 mmol/L was an absolute indicator to revert to a three-times-a-week schedule. When the potassium level was between 5.7 and 6 mmol/L, the patients were provided dietary recommendations over the phone and re-evaluated the following week. If potassium levels were between 6.0 and 6.5 mmol/L, the potassium binder Lokelma was administered and the patients' diet and dialysis parameters were reviewed during the following week's dialysis session. Therefore, patients underwent intensive monitoring in the event of hyperkalemia and large interdialytic weight gain (ultrafiltration rate greater than 10 ml/kg or more than five percent of the target weight change). This practice was initially pursued for four weeks to publish the results, but monitoring continued until the patients were reverted to a three-times-weekly dialysis program following the initial pandemic wave. There were 12 deaths (5 owing to COVID-19) in the HD population, of which 6 were in the twice-weekly HD group. No deaths were conclusively linked to a change in a dialysis procedure. Nineteen patients were either hospitalized or developed COVID-19, prompting a protocol-mandated return to thrice-weekly dialysis. By the completion of the 4-week study, 113 (68.1%) individuals were still receiving twice-weekly HD. Transfer to thrice-weekly was driven by fluid overload, persistent hyperkalemia, patient request, and patient compliance. During the project, there were statistically significant increases in systolic blood pressure and pre-dialysis potassium. The program continued to support the ICU for the duration of the pandemic. Ten percent of COVID-related AKI in critical care was supported by dialysis nurses, and there was an overall mortality rate of 1.5 percent

after the first wave, along with an infection rate of 10 percent, which is comparable to national statistics. These shared experiences showed that in times of crisis it is possible for a significant portion of dialysis patients to be transferred to a twice-weekly dialysis regimen and subsequently return to a three-times-weekly dialysis regimen, assuming the transition is regulated and monitored.

Written by Jasna Trbojevic-Stankovic.
All the speakers reviewed and approved the content.

KEY POINTS

1. Many COVID-19 patients experienced diarrhea and dietary issues thus hindering therapy with old potassium binders, such as sodium polystyrene sulfonate therapy.

2. Besides hemodialysis patients, new oral, non-absorbed potassium binders were also used in patients with AKI who often require renal replacement therapy, with hyperkalemia as a frequent predominant indication.

3. By utilizing novel potassium binders, a significant portion of dialysis patients could be safely transferred to a twice-weekly dialysis regimen and subsequently return to a three-times-weekly dialysis regimen.

Further readings

1. Dattani R, Hill P, Medjeral-Thomas N, Griffith ME, Ashby D, McAdoo S, Corbett RW, Lucisano G, Beadle J, McCafferty K, Frankel A, Thomas D. Oral potassium binders: increasing flexibility in times of crisis. Nephrol Dial Transplant. 2020 Aug 1;35(8):1446-1448. doi: 10.1093/ndt/gfaa202. PMID: 32871590.
2. Lodge, M.D.S., Abeygunaratne, T., Alderson, H. et al. Safely reducing haemodialysis frequency during the COVID-19 pandemic. BMC Nephrol 21, 532 (2020). https://doi.org/10.1186/s12882-020-02172-2.