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Letter

Variability in Urate-lowering Therapy Prescribing: A Gout, Hyperuricemia and Crystal-Associated Disease Network (G-CAN) Physician Survey

To the Editor:

Gout is common in people with chronic kidney disease (CKD) and its treatment is frequently suboptimal in this special population due to concerns over adverse events and/or efficacy of medications. There is controversy about the use of urate-lowering therapy (ULT) in those with CKD and lack of agreement about the dosing of allopurinol, the recommended first-line ULT[1,2]. The aim of this study was to determine real-world ULT prescribing patterns among a group of medical practitioners with an interest in gout.

Members of the Gout, Hyperuricemia and Crystal-Associated Disease Network (G-CAN) were invited to participate in an online survey in May 2017. G-CAN is a multidisciplinary group (predominantly rheumatologists) with clinical/research interest in gout and crystalline arthritis. Ethical approval was not required for a professional online survey. Participants were asked for each stage of CKD and for various ULT whether they would never prescribe the drug, the maximum dose they would prescribe, or whether the drug was unavailable. CKD stages were defined as follows: stage 1–2 [glomerular filtration rate (GFR) > 60 mL/min/1.73m^2], stage 3 (30–59 mL/min/1.73m^2), stage 4 (15–29 mL/min/1.73m^2), and stage 5 (GFR < 15 mL/min/1.73m^2 or receiving dialysis). Participants were given the opportunity to provide a reason for not using the ULT based on the CKD stage.

Sixty-three individuals completed the survey: 55/63 (87%) rheumatologists, 5/63 (7.9%) nephrologists, and 1 each from cardiology and family practice. Fifty-two out of 61 (82.5%) had been practicing for > 10 years. The majority of respondents were from the USA (33.3%), with other participants from Europe (33.3%), Australasia (12.7%), and Asia (9.5%). Figure 1A shows the maximum dose of allopurinol used in each CKD stage. As expected, the willingness to use doses > 300 mg daily decreased as CKD stage increased. There were 4.8% who reported that they would not use allopurinol at all in CKD stage 4, and 11.1% would not use it in CKD stage 5. Safety and inefficacy were cited as reasons for not using higher doses of allopurinol in those with CKD. Five participants commented that ULT was not necessary in those receiving dialysis. The most frequent dose of febuxostat was > 80 to 120 mg daily in CKD stages 1–4, with the lower dose of > 0 to 40 mg in CKD stage 5 (Figure 1B). There were 7.9% who reported

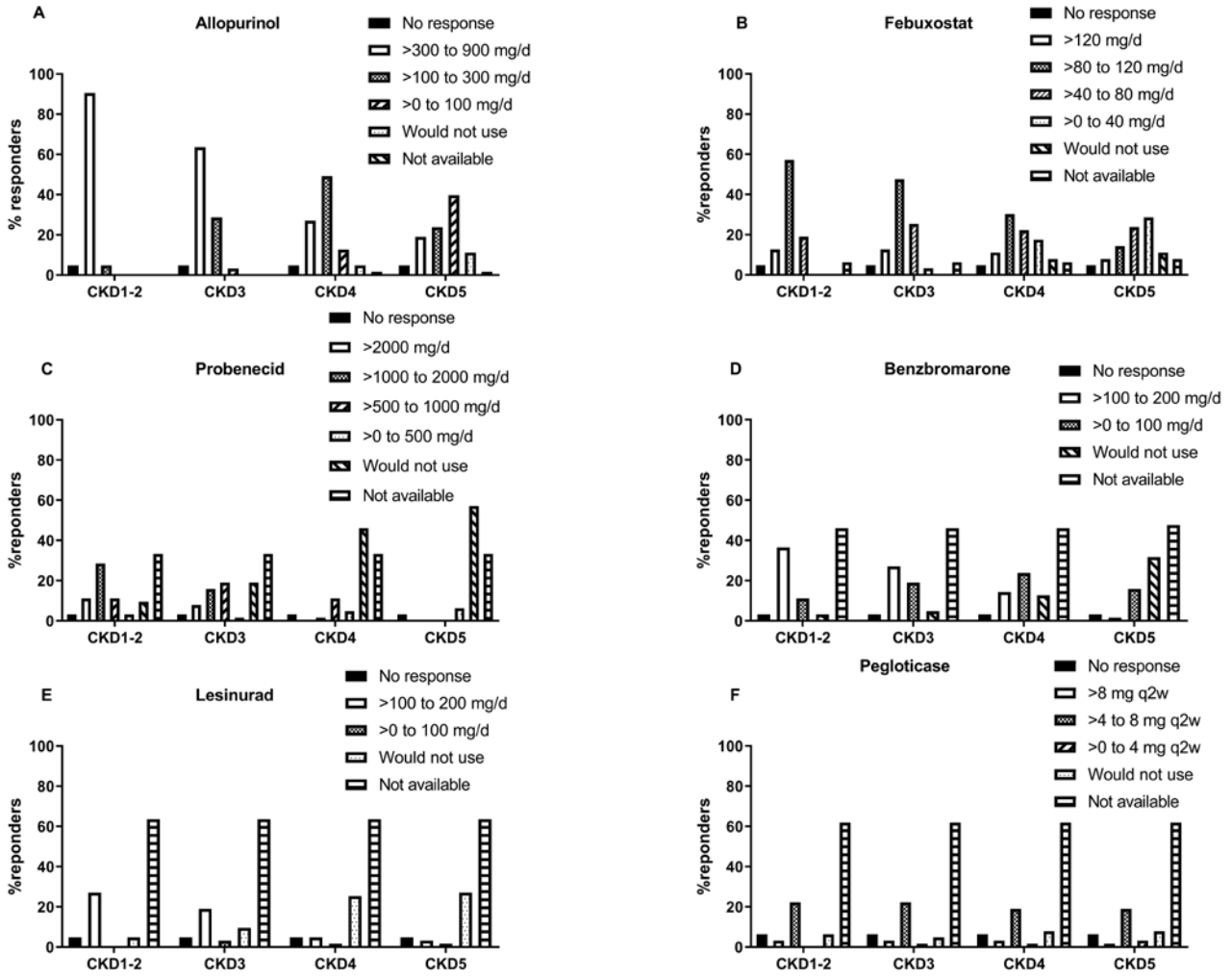

Figure 1. Use of individual urate-lowering therapies in CKD. CKD: chronic kidney disease.

that they would not use febuxostat at all in CKD stage 4, and 11.1% would not use it in CKD stage 5. Lack of data with regard to safety was the main reason for limiting the dose or not using febuxostat. There was no clearly agreed preferred maximal dose of allopurinol or febuxostat for CKD stages 4 or 5. As CKD stage increased, so did the proportion of respondents that would not use probenecid increased (Figure 1C). Most respondents felt probenecid was ineffective in CKD stages 4 or 5 and that there were better and safer options available. Availability of benzbromarone, lesinurad, and pegloitcase was limited for many, creating some bias in the reporting with these agents. There were a number of respondents that would use benzbromarone at > 100 mg/day. In comparison to lesinurad and probenecid, benzbromarone was used in CKD stages 4 and 5 (Figure 1D). Some felt this was a good ULT for those with more severe CKD, whereas others felt it was ineffective. For the majority, lesinurad was unavailable for use (Figure 1E). Concerns were raised about worsening renal function, lack of efficacy, and lack of safety data in severe CKD. There was little variation in the maximal pegloticase dose that would be used by CKD stage (Figure 1F).

Even among medical practitioners with an interest in gout, there is significant variability in ULT prescribing in people with CKD. The paucity of data on the safety and efficacy of ULT in people with CKD drives the variability. However, even with increasing evidence for safety of allopurinol in CKD, changing prescribing patterns is hard. Further research is needed to investigate the safest and most appropriate therapy for people with CKD and gout.

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