



## Neglected facts in digoxin intoxication



### Letter to Editor:

We have read the article titled “Retrospective evaluation of patients with elevated digoxin levels at an emergency department” by Limon G et al.<sup>1</sup> with great interest; however, there are some key aspects to take into account for consistent practical implications.

Firstly, it seems interesting that chronic kidney disease (CKD) wasn't included to comorbid disease in the study population. CKD and chronic heart failure (CHF) are frequently encountered diseases in the population and they are often seen together. The incidence of CKD is high in patients with CHF since both diseases have common risk factors including hypertension (HT), diabetes mellitus (DM) and atherosclerosis. The frequency of CHF is increased by reduction in renal function, reaching up to 65–70% in patients with end-stage renal disease. In recent meta-analyses, it was shown that impaired renal functions may be considered as an independent risk factor for development of cardiovascular disorder.<sup>2</sup> In a study on CKD patients using digoxin, Maurizio Sessa et al. found that 36% of patients were on antihypertensive medication while 14% had DM and 37% had CHF.<sup>3</sup> In the design of the study, it would be more appropriate to include patients with known baseline creatinine levels by estimating glomerular filtration rate (GFR).

Secondly, K<sup>+</sup> levels were found to be markedly high in intoxication group. In the section “Discussion”, authors mentioned that hyperkalemia isn't anticipated in chronic digoxin intoxication unless there isn't comorbid renal failure. However, it was found that there was acute kidney injury (AKI) in 13.9% of the patients. In addition, it is unknown whether the patients had underlying CKD. The angiotensin converting enzyme inhibitors and angiotensin-renin blockers are choice of treatment in many of patients with comorbid diseases listed such as CHF, HT, DM and coronary artery disease (CAD). In addition, aldosterone antagonists are recommended at class I level in CHF due to their favorable effects on mortality. K<sup>+</sup> retention is well-known adverse effect of spironolactone which is most commonly used aldosterone antagonist.<sup>4</sup> In addition, it was shown that spironolactone prolongs half-life of digoxin, which may result in increased serum digoxin levels and consequent digital toxicity. As similar to spironolactone, diltiazem, verapamil, amiodarone and warfarin may also increase plasma digoxin levels.<sup>5</sup> Thus, lack of information about medication may be another reason

for inability to explain elevation in K<sup>+</sup> levels in the study patients.

### Conflict of interest

Authors declare have no conflict of interest.

### Abbreviations

CKD	Chronic Kidney Disease
CHF	Chronic Heart Failure
HT	Hypertension
DM	Diabetes Mellitus
GFR	glomerular filtration rate
AKI	Acute Kidney Injury
CAD	Coronary Artery Disease

### References

1. Limon G, Ersoy G, Oray NC, Bayram B, Limon O. Retrospective evaluation of patients with elevated digoxin levels at an emergency department. *Turkish J Emerg Med.* 2016;16(1):17–21.
2. Said S, Hernandez GT. The link between chronic kidney disease and cardiovascular disease. *J Nephropathol.* 2014 Jul;3(3):99–104.
3. Sessa M, Mascolo A, Andersen MP, et al. Effect of chronic kidney diseases on mortality among digoxin users treated for non-valvular atrial fibrillation: a nationwide register-based retrospective cohort study. *Berger T, ed. PLoS ONE.* 2016;11(7): e0160337.
4. Van Vark LC, Bertrand M, Akkerhuis KM, et al. Angiotensin-converting enzyme inhibitors reduce mortality in hypertension: a meta-analysis of randomized clinical trials of renin–angiotensin–aldosterone system inhibitors involving 158 998 patients. *Eur Heart J.* 2012;33(16):2088–2097.
5. Cascorbi I. Drug interactions—principles, examples and clinical consequences. *Dtsch Arztl Int.* 2012;109(33–34):546–556.

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