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Letter to the Editor

Klotho levels and ethanol consumption

Dear Editor

In the manuscript entitled "Alcohol consumption and S-Klotho plasma levels in sedentary healthy middle-aged adults", Jurado-Fasoli et al. (2018) analyze the relationship between soluble Klotho (s-Klotho) levels and the intensity of ethanol consumption in a cohort of healthy individuals, drinkers of "safe" amounts of ethanol (approximately 11 g/day, with an upper limit of the 95% confidence interval of about 48 g for men and 20 for women, roughly the mean +2sD of the values shown in Table 1 of the mentioned article, although one individual drank > 60 g (Fig. 1)). They found an *inverse* correlation between ethanol consumption and s-Klotho levels, in contrast with the results derived from our series composed of 124 heavy alcoholic men, aged 59.31 ± 11.23 years, drinkers of 158 g ethanol daily (interquartile(IQ) range = 100–248 g) during 32.5 years (IQ = 25–40 years). In this cohort s-Klotho was increased in alcoholic cirrhotics (but not in non-cirrhotics) compared with controls (González-Reimers et al., 2018). The patients drank only wine (n = 59), wine and spirits (n = 42), only spirits (n = 10), or only beer (n = 4). We observed a *direct* correlation between the daily ethanol consumption and s-Klothos ($\rho = 0.18$; $p = 0.044$), especially among the 73 non-cirrhotic patients included in the sample ($\rho = 0.29$; $p = 0.012$), but no relationship between s-Klotho and age ($\rho = 0.02$; $p = 0.80$). Among 88 patients who underwent total body composition analysis, s-Klotho was not related to total fat mass ($\rho = 0.13$; $p = 0.022$), but with total lean mass ($\rho = 0.23$; $p = 0.035$), a signification that disappeared when patients with ascitis were excluded ($\rho = 0.18$; $p = 0.13$). Interestingly, a significant direct correlation was observed between TNF-α and s-Klotho ($\rho = 0.23$; $p = 0.023$). This relationship was even closer among only-wine drinkers ($\rho = 0.36$; $p = 0.013$).

Jurado-Fasoli et al. concluded that plasma levels of s-Klotho are negatively associated with ethanol consumption in middle-aged sedentary adults. While this assertion is fully sustained by the results presented by the authors, and may be valid in a normal healthy population, their results are in sharp contrast with what we here report. Ethanol consumption leads to a proinflammatory situation (main mechanisms: increased intestinal permeability, oxidative damage, cytokine secretion, among others), but it is not known if there is a cut-off point that marks that this inflammatory state is clinically relevant. Klotho exerts an antioxidant effect, enhancing the expression of superoxide dismutase (Yamamoto et al., 2005) so that mice overexpressing Klotho are protected against oxidative damage (Kim et al., 2017). Also Klotho overexpression reduces the production of proinflammatory cytokines (Zhou et al., 2017) and some clinical studies show increased levels of Klotho in inflammatory conditions (tumors or sepsis), even directly related to increased mortality (Abdelmalik et al., 2018). It is tempting to speculate that, at least in some instances, inflammation triggers overexpression of Klotho gene in an attempt to compensate the enhanced proinflammatory state. Therefore, possibly a dual effect may define the relationship of ethanol and Klotho: low doses of ethanol may lead to decreased Klotho levels, but high doses may increase Klotho secretion, perhaps as a homeostatic mechanism directed to regulate enhanced ethanol-mediated inflammation.

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Conflict of interest

The authors declare that there are no conflicts of interest.

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