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Original Paper

Heavy Alcohol Consumption Effects on Blood Pressure and on Kidney Structure Persist After Long-Term Withdrawal

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Key Words
Ethanol consumption • Ethanol withdrawal • Blood pressure • Glomerular morphology • Stereology • AT1 receptor

Abstract
Background/Aims: Heavy ethanol consumption is a risk factor for hypertension and prompts organ damage. There is no information regarding the impact of long-term heavy ethanol consumption on kidney structure and function linking to their hypertensive effects nor the repercussions after withdrawal. ***Methods:*** Rats were exposed to ethanol for 24 weeks and, afterwards, a group was assigned to withdrawal for 8 weeks. Blood pressure (BP) was measured and serum biochemical parameters were quantified. Glomerular volume density, areal density of glomerular tuft and renal corpuscles were determined. Angiotensin II type 1 receptor (AT1R) protein expression was evaluated. ***Results:*** Twenty-four weeks of ethanol consumption causes atrophy of renal corpuscles and glomeruli and reduces the volume of glomeruli. Glomerular changes induced by ethanol consumption were still evident after withdrawal. Renal AT1R levels were increased in ethanol-treated rats and returned to control levels during withdrawal. Ethanol consumption also induced an increase in BP, uric acid and albumin levels. Upon withdrawal, systolic and mean arterial pressures decreased, but were still higher than in controls rats. ***Conclusion:*** Ethanol consumption induces changes in glomerular morphology associated with increased BP and AT1R expression. Long-term withdrawal was inefficient to restore the structural integrity of renal corpuscles and in lowering systolic pressure.

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Introduction

Kidneys play an integral role in blood pressure (BP) regulation and even the slightest impairment of renal function can contribute to the development of hypertension [1, 2], which remains the leading cause of morbidity and mortality worldwide [3]. Among the modifiable risk factors for the development of hypertension, heavy ethanol consumption is considered as one of the most relevant unhealthy lifestyle pattern [3, 4], and data from epidemiologic, clinical and experimental studies have provided a compelling link between these two conditions [4-10]. Although it is widely known that heavy ethanol consumption has hypertensive effects [4-13] and can induce impairment of several organs [6, 10-16], its effects on kidney structure and function remain to be elucidated [16-18]. Moreover, very few clinical and experimental studies evaluated BP alterations underlying alcohol withdrawal and particularly after acute withdrawal [19, 20], but there are no follow up studies in the absence of alcohol consumption, specifically its consequences on BP and kidney structure.

Chronic ethanol consumption elevates BP through different mechanisms [5, 8, 11, 12], including the activation of the renin-angiotensin system (RAS) [11, 21, 22], oxidative stress [11, 12, 18, 21-23] and enhancement of the sympathetic nerve activity [5]. Most of the angiotensin II (Ang II) evoked effects are mediated by Ang II type 1 receptor (AT1R) [21, 22, 24, 25], such as elevation of systemic BP, vasoconstriction, inhibition of renal sympathetic nerve activity, baroreceptor control, glomerular hypertension, and retention of sodium and body fluids [22, 24-26]. Moreover, there is evidence that the pathological activation of the intrarenal RAS enhances oxidative stress [2, 27, 28] and promotes kidney injury, namely of glomeruli, tubules and vasculature [22, 24, 28]. Data regarding the effects of ethanol consumption on kidney structure and function is divergent, probably due to differences in the amount of ethanol consumed in the several studies [6, 15-17, 29]. It is possible that, alongside the systemic hypertensive effects, heavy ethanol consumption may also impair kidney structure and function, therefore contributing to the maintenance of hypertension.

This work studied the impact of long-term heavy ethanol consumption on BP, kidney morphology and on AT1R expression. Additionally, we evaluated if withdrawal was able to revert these effects. To our knowledge this is the first prospective study in animals that examined whether kidney physiological and structural changes due to chronic alcohol consumption persists after 2 months of withdrawal. This follow-up assessment can offer a significant opportunity for improving our understanding of the prospective of cardiovascular comorbidity related with long-term heavy ethanol consumption.

Materials and Methods

Experimental animals

Male Wistar rats obtained from the Institute for Molecular and Cell Biology (Porto, Portugal) were housed in a temperature-controlled (22ºC) room with 12 h light/12 h dark cycle (lights on at 07:00 h). At 8 weeks of age, rats were randomly assigned to an ethanol-treated group (ET, n = 20) or to a water drinking control group (n = 10) as previously described [30]. ET rats received a 20% (v/v) ethanol (Merck KgaA) solution for 24 weeks. During the first 2 weeks, the ethanol concentration was progressively increased, starting with a 5% (v/v) solution and rising by 1% per day until the final 20% (v/v). At the end of the ethanol treatment period, half of Control and ET rats were euthanized. The remaining Control and ET rats were studied for a further 8 weeks. During this period, ET rats were submitted to withdrawal (W) (Fig. 1). Because in a preliminary study we did not find any difference between 24- and 32-weeks-old rats in all the parameters herein analysed, we did not include in the study an age-matched control group for withdrawn rats. The shift from ethanol treatment to water was performed gradually for the initial 2 weeks, by reducing the ethanol concentration in the drinking solution by 1% per day [30]. Rats received standard solid diet and water or ethanol solution *ad libitum*. Animals were weighed weekly and the amount of food and liquid intake was calculated daily.

All procedures were conducted according to the European Communities Council guidelines in animal research (2010/63/EU) and Portuguese Act 113/13 and approved by the animal welfare ethics review board (ORBEA) of the Faculty of Medicine, University of Porto.

Blood pressure measurements and blood biochemistry

Diastolic, systolic and mean arterial blood pressures were measured using the CODA tail-cuff blood pressure system (Kent Scientific Corporation, Connecticut, USA). The animals were submitted to an adaptation period during one week before measurements. BP measurements were recorded during the last two weeks of ethanol and withdrawal [14].

Blood samples (500 µl) were collected once per month after 2 h of light offset and of light onset, directly into Eppendorf tubes to measure blood ethanol concentrations. At the end of the experimental period, blood was collected directly from the left ventricle with heparinized needles, centrifuged twice at 2000 rpm for 10 min and the serum was collected and stored at −80°C. Blood alcohol concentrations were measured using a commercial kit (K620-100; BioVision, Mountain View, CA, USA). Blood ethanol concentration values are presented as mean of all monthly determinations. Serum creatinine, uric acid, urea and albumin levels were quantified using a PRESTIGE 24i® automated chemistry analyzer. Results of serum creatinine, uric acid and urea levels are expressed as mg/dl and serum albumin levels are expressed as g/dl.

Histomorphology and immunohistochemistry

At the end of the experimental period, rats (n = 6 per group) were anesthetized with sodium pentobarbital solution (80 mg/kg b.w.; i.p. injection, Abbott; North Chicago, IL) and perfused transcardially with 4% paraformaldehyde in phosphate buffer. The kidneys were removed, weighed and stored in the same fixative solution.

Tissue blocks of fixed right kidneys were embedded in paraffin, cut at 5 µm on a microtome and mounted on poly-L-lysine coated slides (Sigma-Aldrich, Madrid, Spain). Slides were deparaffinized in xylene and rehydrated through graded ethanol solutions (100%, 96% and 70%) to water. One set of slides was stained with Periodic acid-Schiff (PAS) and used for qualitative histological analyses and stereological estimations; the second set of slides was processed for immunohistochemistry, as described previously [31]. Sections were incubated with a rabbit polyclonal anti-AT1R antibody (1:1000 dilution, sc-1173, RRID: AB_2305402, Santa Cruz Biotechnology Inc.; Santa Cruz, CA) and processed for immunohistochemistry using avidin-biotin-peroxidase complex with diaminobenzidine tetrahydrochloride, and counterstained with hematoxylin. Previous studies have shown the AT1R antibody specificity, by performing peptide competition studies using the specific blocking peptide (sc-1173P) [32-34]. A good correlation was also demonstrated between Western blot using this antibody and the quantification of AT1R in tissue by radio-ligand binding with I125-labeled ANGII [32]. In human renal clear-cell carcinoma, the AT1R antibody also showed specific staining in IHC, corroborated by Western blot and rtPCR [35]. Tests with positive controls using PC12- adrenal pheochromocytoma cells and HTR-8/SV neo cells were also done using Western blot and flow cytometry, respectively, with specific results [34, 36].

The histomorphology of the renal glomeruli was analyzed in PAS-stained sections. The fraction of renal cortex occupied by glomeruli (Vv) was determined using a point counting system [37], at 400× magnification at the monitor level. In each section, the fields of view were systematically sampled at regular intervals of 2000 µm along the x and the y axis; the area of the counting frame was 511 mm^2. The areal density (N_A) of renal glomeruli was estimated in the same fields of view used for Vv estimations. The area of the glomerular profile tuft and of the renal corpuscle was measured by point counting [37], at 800× magnification at the monitor level. Fifty glomeruli were measured per kidney.

Western blot method

For biochemical analyses, rats (n = 4 per group) were euthanized with pentobarbital administration at the end of the experimental protocol. Kidneys were collected and stored at −80°C for later processing.

Protein extraction and protein concentration determination were performed as previously described [14] using whole kidney homogenates. Immunoblotting was performed with the same rabbit anti-AT1R antibody at 1:500 dilution and mouse anti-α-tubulin (T6199, RRID: AB_477583; Sigma-Aldrich, Madrid, Spain) at 1:1000 dilution, followed by incubation with anti-rabbit (Sigma-Aldrich, Madrid, Spain) and anti-

mouse (Vector Laboratories, Burlingame, CA) secondary antibodies conjugated to horseradish peroxidase at 1:1000 dilution. Signals were visualized with the substrate Chemi-lumi (Chemidoc MP, Bio-Rad Laboratories). Optical density of the bands was measured using Image Lab software (Bio-Rad Laboratories) and quantified by densitometry using α-tubulin expression as endogenous control for normalization.

Statistical analysis

Comparisons between groups were performed by one-way ANOVA with treatment as the independent variable. Whenever significant results were found, pair-wise comparisons were made with post hoc Tukey's test using GraphPad PRISM version 6.0 (San Diego, CA, USA). Serum levels and blood pressure measurements are presented as means ± SEM. The remaining results are presented as means ± SD. Differences were considered to be statistically significant if $p < 0.05$.

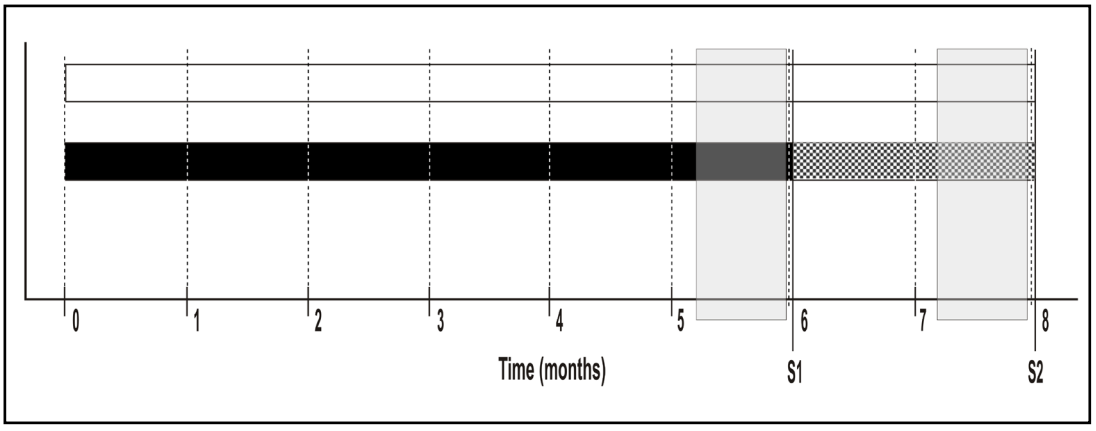

Fig. 1. Schematic drawing of the timeline of the experimental design. The study initiated with two groups of rats: control-8m, white column and ethanol, black column, and lasted 6 months. At that moment (S1) half of the animals of each group were sacrifice. The remaining animals continued the study, all drinking water (control-10m group, white column and withdrawal group, squared column), and were sacrificed two months later (S2). Because data from control-8m and control-10m did not differ, both control groups were plotted together. Dashed lines represent the moments for determination of blood ethanol concentrations. Shaded columns represent the three weeks of BP determination (1 week for preparation and two weeks for recording).

Results

General characteristics of animals

At the end of the experiment, results show that differences in body weight were dependent on the effect of treatment ($p < 0.0001$). ET rats were lighter than control and W rats (Table 1; Fig. 2A). The amount of food and fluid intake were dependent on treatment ($p < 0.0001$). ET rats consumed less food and liquid than Control and W rats (Table 1).

Table 1. Body and kidney weights and food and fluid intake. Results are expressed as mean ± SD. Significant difference compared to the Control group ($^{*}p < 0.05$, $^{**}p < 0.0005$) and to the ET group ($^{\#}p < 0.05$, $^{\#\#}p < 0.0005$). C, control; ET, ethanol-treated; W, withdrawal

	C	ET	W
Bodyweight mean (g)	521 ± 98	417 ± 17*	548 ± 22##
Fresh kidney weight, mg	1.50 ± 0.14	1.24 ± 0.08**	1.43 ± 0.04##
Relative fresh kidney weight (mg/g)	2.9 ± 0.3	3.0 ± 0.1	2.6 ± 0.1*,#
Food (g/d)	26.1 ± 1.6	14.3 ± 1.1**	24.5 ± 2.2##
Fluid (ml/d)	45.3 ± 4.6	30.4 ± 6.2**	39.2 ± 6.7#

The amount of food and liquid ingested by ethanol-treated rats decreased about 45% and 35%, respectively, of the food and water intake by controls during the first month of ethanol treatment and, then, remained relatively stable (Fig. 2B and C). After withdrawal, the amount of food and liquid consumed returned, approximately, to that consumed by Control rats.

The treatment had a significant effect on the absolute and relative kidney weights ($p < 0.0001$ and $p < 0.005$, respectively). The mean fresh kidney weight was smaller in ET rats than in Control and W rats (Table 1). There were no differences on the absolute kidney weights between control and W rats. When the kidney to body weight ratio was compared, this parameter was smaller in W than in Control and ET rats.

Effects of ethanol and withdrawal on BP

The exposure to ethanol had a significant effect on BP measurements, namely the systolic, diastolic and mean arterial pressures (Fig. 3). Systolic, diastolic and mean arterial pressures were higher in ET than in Control rats. Withdrawal induced a significant decrease in the systolic, diastolic and mean arterial pressures when compared to values of the ET group. However, in W rats the systolic and mean arterial pressures were still higher than in Controls.

Effects of ethanol and withdrawal on serum biochemistry

The mean daily ethanol consumption (g/day/kg b.w. ± SD) over the entire experimental period was 8.31 ± 0.04. Mean blood alcohol concentrations of all monthly determinations (mg/dl ± SD) in ET rats were 24 ± 0.33 after 2 h of light offset and 77 ± 0.45 after 2 h of light onset. In Control and W rats, mean blood alcohol concentrations were 0.0 mg/dl at both moments of the day. Ethanol treatment was associated with variations in serum uric acid and albumin levels (Table 2). Uric acid and albumin levels were higher in ET than in Control and W rats. Moreover, albumin levels were higher in W rats than in controls. No effects of treatment on serum urea and creatinine levels were found.

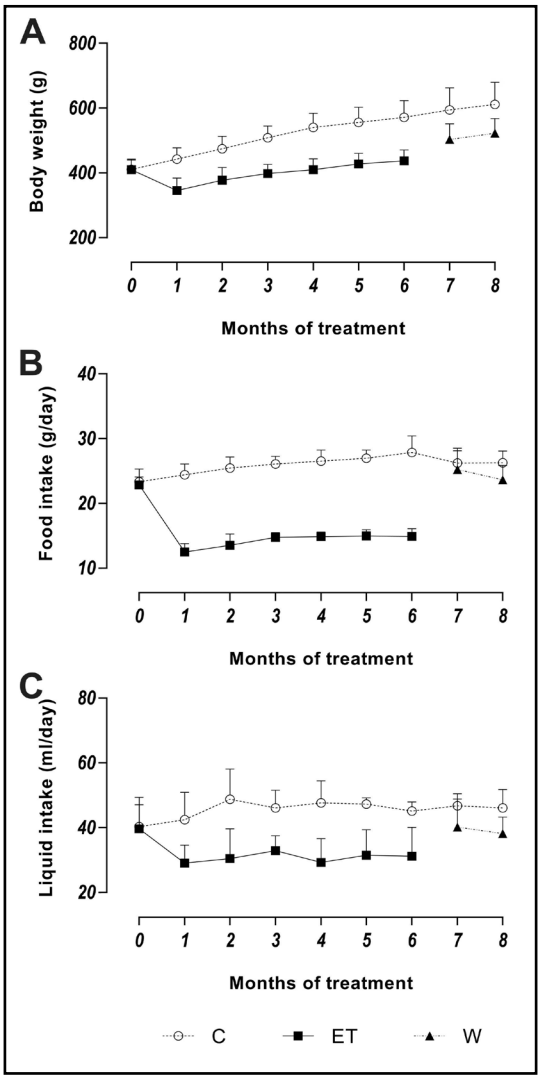

Fig. 2. Graphic representation of the effects of alcohol consumption on body weight (A) and food (B) and liquid (C) intake variations along the experimental period. Data correspond to monthly average of weekly determinations and are expressed as mean ± SD. C, control; ET, alcohol-treated; W, withdrawal. Determinations at point month = 0 correspond to water intake and were made in the 1st day of ethanol administration (at 5% in water). Measurements at month = 1 include the ethanol adaptation period. Measurements at month = 7 include the gradual ethanol withdrawal period. Determinations of liquid intake in ET group from 2nd to 6th month correspond to ethanol (20%) intake. At month = 6, half of the C and ET rats were sacrificed (n = 10 in ET group and n = 5 in C group). At the end of the study, remaining rats were sacrificed (n = 10 in W group and n = 5 in C group).

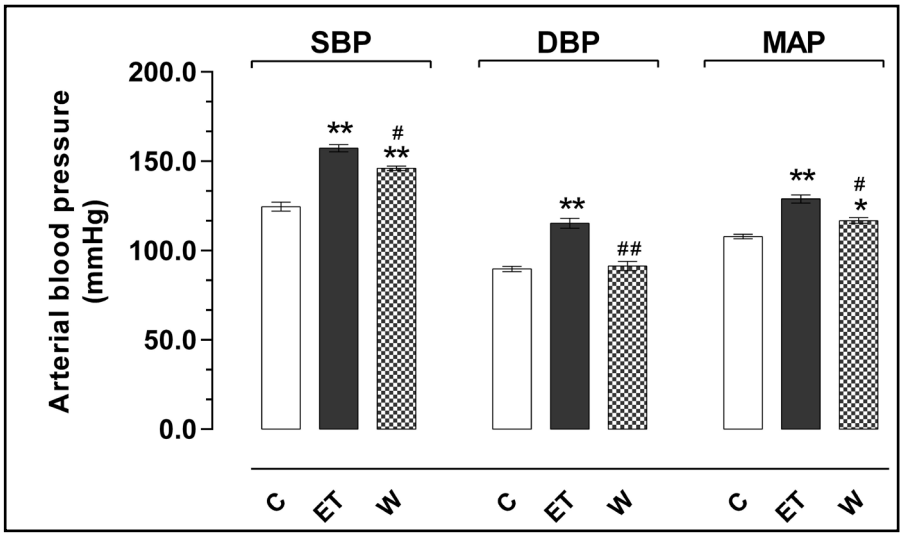

Fig. 3. Graphic representation of the effects of alcohol consumption on systolic (SBP), diastolic (DBP) and mean arterial pressures (MAP) from Control, ET and W groups (n = 10 per group). Data are expressed as mean ± SEM. *p<0.005, **p < 0.0005 versus C group. #p<0.005, ##p<0.0005 versus ET group. C, control; ET, alcohol-treated; W, withdrawal.

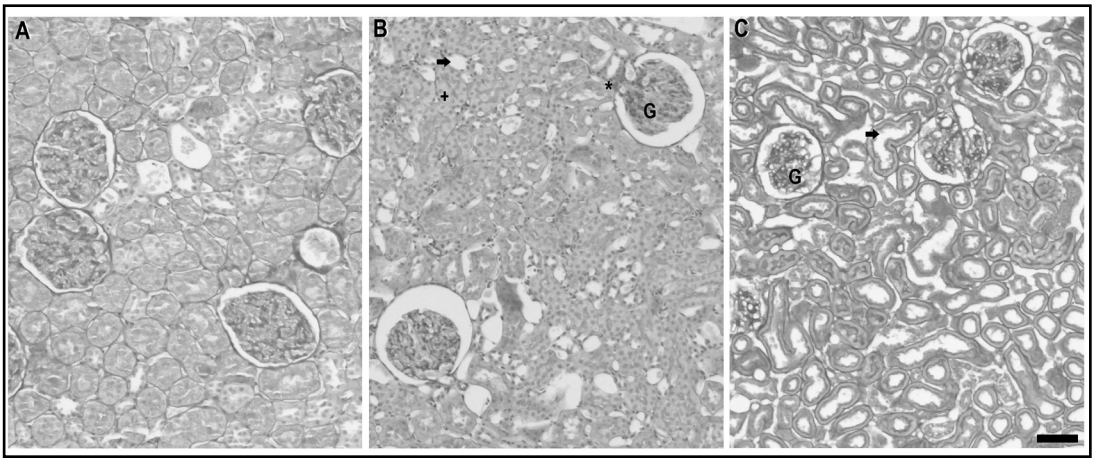

Fig. 4. Representative photomicrographs of kidney tissue stained with PAS. Normal histology of Control rats (A). Atrophy of glomeruli in ethanol-treated rats (B) and withdrawal (C). Dilatation of renal tubules (arrow), extraglomerular mesangial cells (asterisk) and hypertrophy of the epithelium (cross) was observed. G, glomeruli. Scale bar = 10 μm.

Effects of ethanol and withdrawal on kidney morphology

Examination of kidney histology from ET and W rats (Fig. 4B and 4C, respectively) showed moderated atrophy of glomeruli and an increase of Bowman's space when compared with control rats (Fig. 4A). It was also observed hypertrophy of the epithelium of proximal convoluted tubules, dilatation of distal convoluted tubules and increased extraglomerular mesangial cells in the kidney of ethanol-treated rats. In W rats it was observed dilation of both renal tubules.

Since in a preliminary study there were no differences in the morphological parameters analysed between 32 weeks and 40 weeks of age in Control rats, all the results were pooled together. Ethanol treatment had a significant effect on the glomerular V_V but not on the glomerular density (Fig. 5A and B). Glomerular V_V was smaller in ET rats than in controls. There was no difference on the glomerular V_V between ET and W rats, however, after 8 weeks of withdrawal the glomerular V_V was still smaller than in Control rats. Treatment was also

associated with variations in the mean area of glomeruli and renal corpuscles (Fig. 5C). When compared to Control rats, the mean area of glomeruli and renal corpuscles was reduced in both ET and W rats. No significant differences were found in these parameters between ET and W rats.

Effects of ethanol and withdrawal on AT1R expression

Treatment significantly influenced the levels of AT1R protein (Fig. 6). Ethanol consumption induced an increase of about 18% in the levels of AT1R protein when compared to the Control group. AT1R protein expression decreased by about 28% in W rats compared to ET rats.

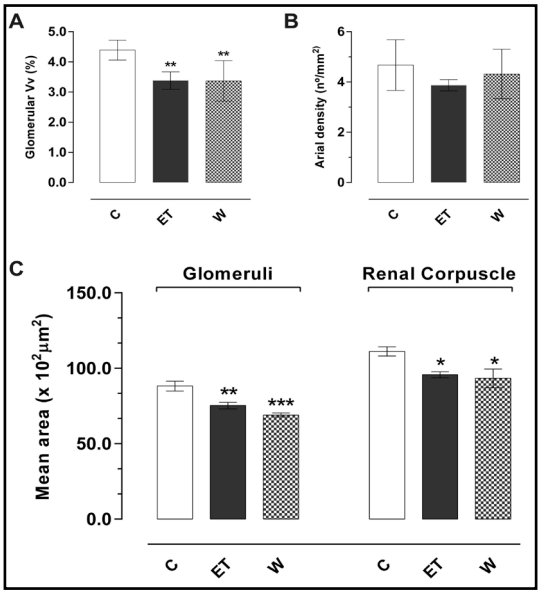

Fig. 5. Graphic representation of histomorphological data of renal glomeruli. (A) Glomerular volume density (V_V), (B) areal density (N_A), (C) mean area of glomerular tuft and renal corpuscles from Control, ET and W groups (n = 6 per group). Data are expressed as mean ± SD. * p<0.05, ** p<0.005, *** p<0.0005 versus C group. C, control; ET, alcohol-treated; W, withdrawal.

Discussion

Epidemiological and experimental studies have documented that heavy ethanol consumption causes more than 60 types of diseases and is, in a dose-dependent manner, a contributing cause to a large number of other medical conditions [3, 4, 7, 9, 17, 38, 39]. Several studies have provided a wealth of data linking heavy ethanol consumption to the development of hypertension [4-13]. Herein, we show that chronic ethanol consumption increases BP that is not completely reversed by withdrawal and that this effect is associated with changes in renal structure, namely atrophy of the glomeruli.

Heavy ethanol consumption effects on BP were predictable on the basis of data from our [14] and others studies [8, 12]. In the present study, we extend those observations by showing that the hypertensive effect of ethanol consumption was not completely reversed after long-term ethanol withdrawal. Indeed, the systolic and mean arterial pressures in W rats, although lower than in ET rats, were still significantly higher than in controls. Little is known about the effects of withdrawal on BP and the few existing studies have focused on the effects of acute withdrawal [19, 20]. It was previously shown that BP increases after acute ethanol abstinence both in humans [19] and in rats consuming low doses of ethanol for 20 days [20]. Despite the differences between our animal model of ethanol consumption and those from Gonzaga and collaborators [20], which was longer and with a higher amount of ethanol consumed (24 weeks of 20% v/v *versus* 21 days of 3-9% v/v), we extended their results by showing that the increase in BP persists even after long-

Table 2. Biochemical serum levels. Results are expressed as mean ± SEM. Significant difference compared to the Control group ($^{*}p < 0.05$, $^{**}p < 0.0005$) and to the ET group ($^{\#}p < 0.05$, $^{\#\#}p < 0.0005$). C, control; ET, ethanol-treated; W, withdrawal

	C	ET	W
Serum creatinine, mg/dl	0.41 ± 0.02	0.44 ± 0.03	0.41 ± 0.02
Serum urea, mg/dl	38.1 ± 3.1	43.7 ± 2.0	43.2 ± 2.7
Serum uric acid, mg/dl	1.28 ± 0.10	2.12 ± 0.13**	1.28 ± 0.12##
Serum albumin, g/dl	2.50 ± 0.15	3.91 ± 0.16**	3.27 ± 0.18*,#

term withdrawal. This is a relevant finding since it provides evidence for an increased risk for later onset of cardiovascular diseases [19].

The daily amount of food and liquid intake by Control, ET and W rats is in line with previous research [13, 14, 30, 38] in which the same experimental model of alcohol consumption and withdrawal was used. The blood alcohol concentrations presented herein are comparable to those previously observed in human [40] and in rats [13, 14, 30, 38, 40]. Our results also show that ET rats ingested less liquid and had lighter kidneys than Control rats, corroborating a previous study that showed that ethanol consumption induces a decrease of urine volume and liquid intake [6]. Similarly to other reports [18, 23], our results show that ethanol consumption induced no changes in the relative kidney weight. However, our results extend these observations by showing an increase of absolute kidney weight in the withdrawn animals, suggesting that this recovery may be related with an increase of liquid intake. Together, these findings indicate that the long-term ethanol consumption alters hydric balance [6], which could be partially reversed by withdrawal. It was shown that moderate ethanol consumption for 15 weeks does not change matrix protein production in glomerulofibrosis [29], but heavy ethanol consumption for 6 and 12 weeks induced tubular necrosis [16] and hypertrophy and degeneration of the epithelia of the renal tubules [15]. Our results further extend those previous studies by showing that 24 weeks of ethanol consumption causes atrophy of renal corpuscles and glomeruli and reduces the volume density of glomeruli without changing their areal density, which indicates that it does not lead to a marked loss of glomeruli. Since the values of glomerular size were averaged, a decrease in this parameter does not exclude the possibility that some glomeruli might undergo atrophy while others became hypertrophic. Changes in glomerular size could be related to the hypertensive effects of ethanol since there is evidence that hypertension initially induces an increase in their size, followed by glomerular atrophy with detrimental progression to glomerular sclerosis [41]. Studies using renal biopsy samples had reported a correlation between hypertension and glomerular size [42], however, these studies exhibit a selection bias since the renal biopsies were collected from patients with kidney disease and were not able to identify the risk factors underlying hypertension.

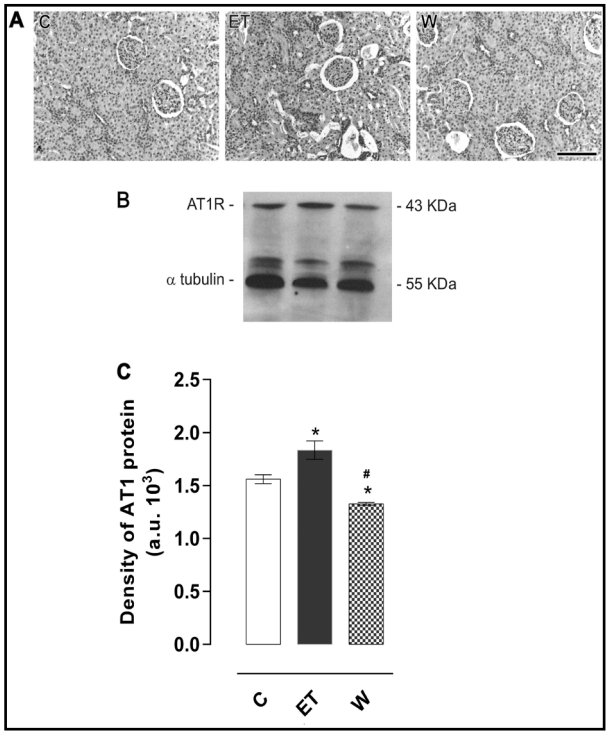

Fig. 6. (A) Representative photomicrographs of kidney tissue immunostained with anti-AT1R antibody and counterstained with hematoxylin. Scale Bar = 150 μm. (B) Representative Western blots of AT1R protein and (C) summary data for AT1R protein from Control, ET and W groups (n = 4 per group). Protein expression was normalized to α-tubulin. Data are expressed as mean ± SD. *p<0.05 versus C group; #p<0.0005 versus ET group. AT1R, angiotensin II type 1 receptor; C, control; ET, alcohol-treated; W, withdrawal.

After verifying the effects of ethanol consumption in kidney structure, we postulated that chronic ethanol withdrawal could reverse these changes. Yet, our data negate this hypothesis as they show that in W rats the glomerular volume and areal density do not differ

from those of ET rats, which are smaller than those of Control rats. It is known that ethanol induces endothelial dysfunction [11, 12, 43], namely due to oxidative stress and changes in the expression of vascular endothelial growth factor [16, 44]. Alterations in these angiogenic signals may contribute to aggravate glomerulosclerosis [44] and, consequently, hinder the possible benefits of withdrawal. Therefore, it is suggested that mechanisms of glomerular repair are impaired during ethanol withdrawal, warranting this issue further investigation.

Present data also shows that heavy ethanol consumption induced an increase in serum albumin and uric acid levels, without affecting creatinine and urea serum concentrations. The high serum albumin levels found can be ascribed to the effects of ethanol consumption on dehydration. These results are in line with earlier studies that have shown the effects of ethanol consumption on kidney dysfunction [6] and can be a risk factor for the development of albuminuria [17] and kidney injury [10, 15, 23]. Furthermore, high serum levels of uric acid have been associated with both hypertension and proteinuria, afferent arteriolopathy and glomerulosclerosis [10, 45], and can predict the development of chronic kidney disease [46]. Since urine creatinine levels were not measured in the present study, we cannot rule out the possibility that renal filtration rate might be altered by ethanol consumption as there is evidence that in these conditions the renal creatinine clearance is decreased [23]. Because the alterations we have detected in serum albumin and uric acid levels in the ET rats are improved after withdrawal, it might be argued that they could be the result from ancillary effects of alcohol consumption, such as dehydration. Yet, since we have not included in this study a water-deprived control group nor evaluated these biochemical parameters in urine, we cannot discard the possibility of kidney dysfunction after withdrawal.

There is accumulating evidence that Ang II plays a key role in the progression of kidney damage, contributing to renal fibrosis and glomerulosclerosis [2, 22, 24, 28]. Studies have shown that Ang II exerts a key role in the pathogenesis of both hypertension and renal injury [2, 3, 22-28]. In the present study, we show an increase in AT1R immunoreactivity in afferent and efferent arterioles, glomeruli and luminal surface of renal tubules in rats exposed to ethanol consumption. It is also shown an increase in kidney AT1R protein expression in ET rats, which points to the involvement of local RAS activation in renal impairment due to ethanol consumption. However, it deserves to be mentioned that the expression of AT1R protein was evaluated in whole kidney, which is a limitation of the present study. Despite the finding that after withdrawal the AT1R protein levels returned to control levels, we cannot safely discharge the hypothesis that the RAS may be involved in withdrawal-related effects. Another possible explanation for the glomerular changes and the rise of BP following withdrawal could be the involvement of other mechanisms, such as oxidative stress [18, 21, 23], impairment of renal autoregulation [41] and activation of renal sympathetic nerve [26]. Indeed, it was shown that acute withdrawal reduces nitric oxide bioavailability in blood vessels without affecting RAS activity [20], proposing that oxidative stress could be a more relevant mechanism underlying the effects of ethanol withdrawal on kidney structure and BP.

Conclusion

The present data provides new insights into the effects of long-term heavy ethanol consumption on kidney structure and function. Alongside with a rise of BP, ethanol consumption induced changes in glomerular morphology that are associated with an increase in renal AT1R protein levels. Withdrawal induced beneficial effects on kidney function and decreased renal AT1R levels, but it was not able to normalize BP nor to revert glomerular changes.

Disclosure Statement

All authors disclose that they have not any potential Disclosure Statement.

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