Effects of Alcohol Reduction on Blood Pressure A Meta-Analysis of Randomized Controlled Trials

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Abstract—Alcohol drinking has been associated with increased blood pressure in epidemiological studies. We conducted a meta-analysis of randomized controlled trials to assess the effects of alcohol reduction on blood pressure. We included 15 randomized control trials (total of 2234 participants) published before June 1999 in which alcohol reduction was the only intervention difference between active and control treatment groups. Using a standard protocol, information on sample size, participant characteristics, study design, intervention methods, duration, and treatment results was abstracted independently by 3 investigators. By means of a fixed-effects model, findings from individual trials were pooled after results for each trial were weighted by the inverse of its variance. Overall, alcohol reduction was associated with a significant reduction in mean (95% confidence interval) systolic and diastolic blood pressures of −3.31 mm Hg (−2.52 to −4.10 mm Hg) and −2.04 mm Hg (−1.49 to −2.58 mm Hg), respectively. A dose-response relationship was observed between mean percentage of alcohol reduction and mean blood pressure reduction. Effects of intervention were enhanced in those with higher baseline blood pressure. Our study suggests that alcohol reduction should be recommended as an important component of lifestyle modification for the prevention and treatment of hypertension among heavy drinkers. (*Hypertension*. 2001;38:1112-1117.)

Key Words: alcohol ■ blood pressure ■ meta-analysis ■ clinical trials

A large number of cross-sectional and prospective epidemiological studies have repeatedly demonstrated that alcohol consumption is 1 of the most important modifiable risk factors for hypertension among populations from a variety of geographic regions, including North America, Europe, and Asia.¹⁻³ The positive association between alcohol intake and blood pressure (BP) generally persists after adjustment for important confounders such as age, body mass, smoking, exercise, and sodium and potassium intake. A number of clinical trials have been conducted to examine the effects of a reduction in alcohol consumption on BP.⁴⁻¹⁸ In general, these studies have had a small sample size and have reported inconsistent findings.⁴⁻¹⁸ A recently published large-scale, long-term clinical trial failed to show a significant reduction in BP associated with an alcohol treatment program.¹⁸

We conducted a meta-analysis of randomized controlled trials to examine the effects of alcohol reduction on BP. By pooling information from individual trials, we were able to obtain more stable statistical estimates of intervention effect and to explore the basis for heterogeneity in the study outcomes.

Methods

Selection of Studies

A comprehensive literature search was performed with the MED-LINE computerized database (for studies from 1966 through June 1999) with medical subject headings "alcohols," "alcohol drinking," and "blood pressure," as well as text words "alcohol reduction" and "alcohol restriction." Only full-length original journal articles were considered; no attempt was made to include abstracts or unpublished studies. The search was restricted to studies conducted in humans and classified as clinical trials in the MEDLINE database. Medical librarians were consulted during the literature search. A manual search was also conducted by using reference lists from original and review articles. The contents of 24 articles identified during the literature search were reviewed to determine whether they met the prestated criteria for inclusion in our meta-analysis. The literature search and the article review were conducted independently by 3 of the authors (X.X., M.G.F., and O.I.M.).

To be included, a study had to meet the following criteria: (1) the study was conducted in humans; (2) there was random allocation of study participants to alcohol reduction and control groups; and (3) alcohol reduction was the only intervention difference between the comparison groups. In studies with a factorial design, other interventions such as exercise or reduced sodium intake had to apply equally to the active and control groups or periods. (4) The intervention duration was ≥1 week; and (5) a change in systolic and/or diastolic BP was an outcome of the trial. Fourteen studies met these criteria and were included in our meta-analysis. One study included 2 independent strata (daily and weekly drinkers) and was treated as 2 trials.⁵

Major reasons for the exclusion of studies were (1) nonrandomized treatment assignment,^{4,19,20} (2) comparison of alcohol intake rather than alcohol reduction on BP,^{20–23} (3) comparison of the effects of different dosages of alcohol on BP,²⁴ (4) comparison of the

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TABLE 1. Study and Participant Characteristics in 15 Alcohol Reduction Trials

	Cubicata	Moon	Male, %	Hypertensive, %	Antihypertensive Medication,	Chudu	Study Duration, wk	Pretreatment BP, mm Hg			Ougliby
Source, y	Subjects, n	Mean Age, y			wedication, %	Study Design		SBP	DBP	Intervention	Quality Score
Puddey et al, ⁵ 1985	46	35.0	100	0	0	X0	12	133.1	75.6	Substitute	68
Howes and Reid, ⁶ 1986	10	26.5	100	0	0	X0	1	115.5	62.0	Substitute	51
Puddey et al,7 1986	44		100	100	100	X0	12	142.3	84.4	Substitute	75
Ueshima et al,8 1987	50	44.5	100	100	22.0	X0	4	149.0	97.0	Counseling	75
Wallace et al,9 1988	909	42.7	58.2	•••	0	P0	52	133.5	79.9	Counseling	91
Parker et al,10 1990	63	52.0	100	100	100	P0	4	138.3	84.6	Substitute	77
Mahaswaran et al,11 1992	41	44.6	100	100	51.2	P0	8	148.1	90.0	Counseling	74
Puddey et al,12 1992	86	44.3	100	0	0	P0	18	137.4	85.0	Substitute	87
Cox et al,13 1993	72	36.6	100	0	0	P0	4	132.4	72.7	Substitute	71
Ueshima et al,14 1993	54	44.5	100	100	0	X0	6	143.9	96.4	Counseling	75
Lang et al,15 1995	129	42.5	95.0	100	19.5	P0	104	162.5	98.0	Counseling	70
Kawano et al,16 1998	34		100	100	82.5	Х0	8	142.0	95.0	Counseling	70
Rakic et al (Study 1),17 1998	41	45.5	100	0	0	X0	8	123.5	75.7	Substitute	93
Rakic et al (Study 2),17 1998	14	45.5	100	0	0	X0	8	123.5	75.7	Substitute	93
Cushman et al,18 1998	641	57.3	98.8	42	0	P0	104	139.3	86.0	Counseling	91

X0 indicates crossover open design; P0, parallel open design; SBP, systolic BP; DBP, diastolic BP; substitute, low-alcohol beer substitute intervention; counseling, cognitive-behavioral interventions aimed at reducing alcohol intake.

effects of multiple interventions (including alcohol reduction) on BP, 25 and (5) intervention duration of <1 week. 21

Data Extraction

Using a standard protocol, 3 of the authors (X.X., M.G.F., and O.I.M.) extracted information on sample size, participant characteristics, study design, intervention methods, duration, and treatment results. Disagreements were resolved by discussion among the 3 abstractors and in some instances with input from 1 of the other authors (J.H.). The quality of the trials was independently assessed by 3 investigators according to the quality scoring system described by Chalmers et al.²⁶ Quality scores were not used to weight the effect size but rather as an exclusion criterion for sensitivity analysis.

Statistical Analysis

To calculate the overall effect size, each study was weighted by the reciprocal of the variance for BP change. Because variances for BP net changes were not reported directly for most studies, they were calculated from confidence intervals (CIs), t statistics, probability value, or individual variances for the intervention and control groups (periods). For parallel trials in which variance for paired differences was reported separately for each group, we calculated a pooled variance for net change using standard methods. Then the variance for paired differences was not reported, it was calculated using the variances at baseline and at the end of follow-up based on the methodology of Follmann et al. In this method, we assumed a correlation coefficient of 0.5 between the initial and final BPs²⁸ and equal variances during the trial and between intervention and control groups.

Fixed- and random-effects models were used to estimate the overall effects of alcohol reduction on BP.^{29,30} Homogeneity of effect size across studies was tested by means of Q statistics.³¹ Because no statistically significant heterogeneity was found among studies, the results from the fixed-effects model are reported.³¹ However, the 2 models yielded similar results.

To explore the influence of covariates on the net change in BP, a series of prestated subgroup analyses were performed. Subgroups were selected on the basis of biological plausibility and our review of the literature. For each subgroup, pooled effects were calculated using the fixed-effects model, and statistical significance was tested

by ANOVA. Meta-regression analysis was used to estimate the effect of various study characteristics on the net change of BP weighted by the inverse of its variance. Covariates for meta-regression analysis were selected based on the results of the subgroup analysis and prior biologic knowledge. For each trial, the covariates were calculated as average values of the active treatment and control groups at baseline or average change from baseline. Where information on mean age was not reported in 2 trials, we used imputed values (the average age in the remaining 13 trials) in our meta-regression analysis. For crossover trials, we used the mean BP during the control period as the baseline value.

To examine potential publication bias, a funnel plot that related sample size to effect size and a correlation analysis between sample size and standardized BP were performed. Kendall's τ correlation coefficients between sample size and standardized systolic and diastolic BP reduction were calculated and tested for statistical significance.³²

Results

Participant Characteristics and Study Design

Participants and selected study design characteristics of the 15 clinical trials included in our meta-analysis are presented in Table 1. The trials, which were conducted between 1984 to 1996, varied in sample size from 10 to 909 participants. All of the trials were conducted in adults, with an age range of 27 to 57 years. Men were the majority or sole participants in most trials. Seven trials included only hypertensive persons, 6 included only normotensive persons, and 2 included both hypertensive and normotensive persons. Antihypertensive medications were used in 6 trials. Eight trials had a crossover design, whereas 7 had a parallel or 2-way factorial design. The study duration varied from 1 to 104 weeks, with a median length of 8 weeks. In 8 trials, a low-alcohol beer substitute was used in the intervention group or period, whereas in the remaining 7 trials, behavioral interventions were used as a means to encourage a reduction in alcohol consumption

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	Alcohol		Moon Weight				
Source, y	Reduction, %	Systolic	95% CI	Diastolic	95% CI	Mean Weight Change, kg	
Puddey et al, ⁵ 1985	80	-3.83	(-6.09 to -1.50)	-1.43	(-3.07 to 0.21)	-0.70	
Howes and Reid, ⁶ 1986	100	-3.04	(-5.99 to -0.00)	-3.12	(-5.45 to -0.74)		
Puddey et al,7 1986	86	-5.02	(-7.74 to -2.25)	-3.01	(-4.76 to -1.23)	-0.90	
Ueshima et al,8 1987	51	-1.35	(-5.12 to 2.52)	-0.63	(-3.26 to 2.06)	-0.62	
Wallace et al,9 1988	46	-2.12	(-4.19 to -0.00)				
Parker et al,10 1990	85	-5.40	(-9.20 to -1.59)	-3.20	(-5.35 to -1.04)	-1.00	
Maheswaran et al,11 1992	50	-2.22	(-9.84 to 5.44)	-6.00	(-10.8 to -1.15)	-0.50	
Puddey et al,12 1992	85	-4.82	(-7.30 to -2.29)	-3.37	(-5.24 to -1.35)		
Cox et al,13 1993	85	-4.71	(-7.99 to -1.40)	-1.92	(-3.50 to -0.29)	-0.43	
Ueshima et al,14 1993	54	-3.67	(-6.34 to -0.85)	-1.91	(-3.76 to -0.03)		
Lang et al,15 1995	16	-6.32	(-12.7 to 0.13)	-1.73	(-6.01 to 2.61)	•••	
Kawano et al,16 1998	84	-3.00	(-6.88 to 0.88)	-2.00	(-4.35 to 0.35)	-1.00	
Rakic et al (Study 1),17 1981	76	-2.00	(-5.25 to 1.25)	-2.00	(-4.11 to 0.11)	-0.42	

(-5.23 to 3.23)

(-4.54 to 0.54)

0

-1.91

Mean Net Change in Alcohol Consumption, BP, and Body Weight

76

29

-1.00

-2.00

among those assigned to the active treatment group. Average pretreatment BP ranged from 116 to 163 mm Hg for systolic BP and 62 to 98 mm Hg for diastolic BP. The quality score ranged from 51 to 93, with a median of 75.

Rakic et al (Study 2),17 1982

Cushman et al.18 1998

Net Change in BP

The intervention effect, as measured by reduction in selfreported daily consumption of alcohol, ranged from 16% to 100%, with a median of 76% (Table 2). Compared with the control subjects, the intervention group had an average net change in BP of -1.0 to -6.3 mm Hg for systolic BP and 0 to -6.0 mm Hg for diastolic BP (Table 2). Mean net change in body weight ranged from -0.42 to -1.0 kg, with a median of -0.56 kg. All 15 trials had an intervention-related trend toward a reduction in systolic BP, with 9 of the trials (60%) showing a statistically significant result (Figure 1). For diastolic BP, a trend toward intervention-related reduction in BP was also noted in all 14 trials, with a statistically significant reduction in 8 (57%) of the trials. One trial failed to report the net change in diastolic BP.13

(-1.78 to 1.78)

(-3.46 to -0.33)

-0.42

-0.50

Overall pooled estimates of the effect of alcohol reduction on systolic and diastolic BP were -3.31 (95% CI, -2.52 to -4.10) mm Hg and -2.04 (95% CI, -1.49 to -2.58) mm Hg, respectively (P < 0.0001 for both). After exclusion of a cluster-randomization trial. 15 the net reduction in systolic and diastolic BP was -3.26 (95% CI, -2.56 to -3.97) mm Hg and -2.04 (-1.45 to -2.63) mm Hg. After exclusion of studies with poor compliance in intervention (net self-reported reduction of alcohol consumption of <30%), 15,17 the net reduction in systolic and diastolic BP increased to -3.40(95% CI, -2.67 to -4.13) mm Hg and -2.06 (95% CI, -1.40 to -2.72) mm Hg, respectively. After exclusion of studies with a relatively short intervention duration (<4 weeks),6 the net reduction in systolic and diastolic BP was -3.33 (95% CI, -2.51 to -4.15) mm Hg and -1.98 (95% CI, -1.42 to -2.53) mm Hg, respectively. After exclusion of trials with poor

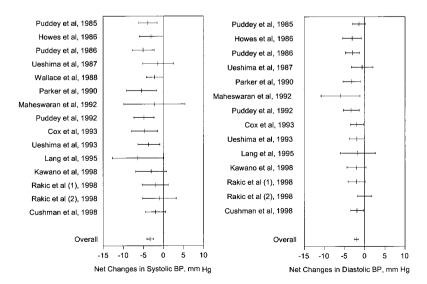


Figure 1. Average net change in systolic BP (left) and diastolic BP (right) and corresponding 95% Cls related to alcohol reduction intervention in 15 randomized controlled trials. Net change was calculated as the difference of the baseline minus follow-up levels of BP for the intervention and control groups (parallel trials) or the difference in BP levels at the end of the intervention and control treatment periods (crossover trials). The overall effect represents a pooled estimate obtained by summing the average net change for each trial, weighted by the inverse of its variance. Data on diastolic BP were not available in 1 trial.13

TABLE 3. Mean Net Changes in Systolic and Diastolic BP in Subgroups of Trials According to Participants and Study Design Characteristics

	Systolic BP					Diastolic BP					
Characteristic	Studies, Subjects,		Effect Size 95% Cl		P*	Studies,	Subjects,	Effect Size	95% CI	P*	
Sample size											
≤41	5	140	-3.98	-5.29 to -2.67		5	140	-2.48	−3.37 to −1.58		
42 to 63	5	257	-2.62	−3.54 to −1.70	0.61	5	257	-1.54	-2.79 to -0.28	0.87	
>63	5	1837	-3.19	-4.46 to -1.92		4	928	-2.04	-2.76 to -1.32		
Design											
Parallel	7	1941	-3.43	-4.59 to -2.27	0.40	6	1032	-2.49	−3.35 to −1.64	0.11	
Crossover	8	293	-3.21	-4.29 to -2.12		8	293	-1.73	-2.43 to -1.02		
Duration, wk											
≤4	5	281	-2.37	−3.09 to −1.64		5	281	-1.72	-3.18 to -0.26		
6 to 8	5	184	-3.92	-5.05 to -2.79	0.81	5	184	-2.10	-2.96 to -1.24	0.85	
≥12	5	1769	-3.24	-4.64 to -1.84		4	860	-2.22	-2.91 to -1.54		
Intervention											
Substitution	8	376	-3.91	-4.96 to -2.86	0.15	8	376	-2.10	-2.77 to -1.44	0.89	
Counseling	7	1858	-2.52	−3.73 to −1.32		6	949	-1.90	-2.85 to -0.95		
BP measurement											
Automatic recorder	10	1319	-3.46	-4.43 to -2.60	0.30	9	410	-2.09	-2.73 to -1.46	0.80	
Random-zero sphygmomanometer	5	915	-2.69	-4.27 to -1.09		5	915	-1.88	-2.91 to -0.84		
Hypertensive											
Yes	7	415	-3.90	-5.04 to -2.76	0.54	7	415	-2.41	-3.25 to -1.57	0.35	
No	6	269	-3.56	-4.61 to -2.51		6	269	-1.80	-3.03 to -0.58		
Antihypertensive medication											
Yes	6	361	-4.01	−5.45 to −2.57	0.31	6	232	-2.56	-3.88 to -2.30	0.20	
No	9	1873	-3.09	−3.88 to −2.30		8	964	-1.83	-2.50 to -1.16		

*From ANOVA.

quality (average quality score of <60),^{5.6} net changes in systolic and diastolic BP increased to -3.41 (95% CI, -2.68 to -4.14) mm Hg and -2.05 (95% CI, -1.41 to -2.69) mm Hg.

There was no significant heterogeneity among trials in the effects of alcohol reduction on BP. The Q test for homogeneity was not significant (P>0.50 for systolic BP and P>0.25 for diastolic BP), even without taking into account the variation in study design, duration of intervention, percentage of alcohol reduction, mean age of the participants, and pretreatment BP. However, the statistical power for testing heterogeneity may not be sufficient because only 15 trials were included in this meta-analysis.

Subgroup and Meta-Regression Analysis

Table 3 summarizes the pooled estimates of the treatment effect among subgroups of trials defined according to participant and study design characteristics. The effects of alcohol reduction on both systolic and diastolic BP were consistent in each of the subgroups included in the analysis.

Meta-regression analysis identified a significant and positive relationship between mean percentage of reported alcohol reduction and corresponding net reduction in both systolic and diastolic BP (P=0.003 and P=0.03, respectively; Table 4). There also was a significant and positive relationship

between average pretreatment BP and mean reduction in systolic BP (P=0.008). Approximately 78.6% of the variation in systolic BP and 50.3% of the variation in diastolic BP net change was explained by 5 variables included in the multivariate model (Table 4). Percentage reduction of alcohol intake and average pretreatment BP accounted for the majority of the variance for systolic BP, whereas percent reduction in alcohol intake, sample size, and pretreatment BP accounted for almost half of the total variation for diastolic BP.

Testing for Publication Bias

The possibility of publication bias was explored by plotting the net change in BP against sample size for each trial (Figure 2). Net change in BP tended to be larger for studies with the smallest number of participants, and there was a trend for the variation of net change to diminish with increasing sample size. Kendall's τ correlation coefficients between sample size and standardized systolic and diastolic BP reduction were 0.096 (P=0.345) and -0.088 (P=0.337), respectively. Thus, the totality of the evidence failed to document the presence of publication bias.

Discussion

To our knowledge, this is the first systematic overview of clinical trials that have investigated the effect of alcohol

	Sy	/stolic BP ($R^2 = 0.786$)	Diastolic BP (R ² =0.503)				
Characteristic	Regression Coefficient	SEM	Partial R ²	Р	Regression Coefficient	SEM	Partial R ²	Р
Alcohol reduction, %	0.097	0.024	0.383	0.003	0.076	0.030	0.1944	0.031
Pretreatment BP, mm Hg	0.128	0.037	0.285	800.0	0.081	0.044	0.0929	0.106
Duration, wk	0.019	0.017	0.085	0.280	0.019	0.026	0.038	0.484
Sample size	0.001	0.001	0.085	0.336	0.003	0.004	0.154	0.404
Age, y	-0.005	0.048	0.0003	0.912	-0.032	0.057	0.022	0.588

TABLE 4. Meta-Regression Analysis of Study Characteristics on Average Net Reduction in BP

Analysis weighted by inverse of variance of effect size.

reduction on BP. The overall effect size estimates in our meta-analysis were impressive: -3.31 mm Hg reduction in systolic BP and -2.04 mm Hg reduction in diastolic BP. The effect of alcohol reduction on BP was consistent across subgroups, including those defined by presence or absence of hypertension. Furthermore, a dose-response relationship was observed between mean reduction in reported consumption of alcohol and net change in both systolic and diastolic BP. These findings strongly support recommendations for moderation of alcohol consumption as a means to prevent and treat hypertension.^{33,34}

The effect size estimated from our meta-analysis is consistent with experience from observational epidemiologic studies. In the International Study of Salt and BP (INTERSALT) study, men who drank 300 to 499 mL alcohol/wk (≈2.8 to 4.8 drinks/d) had a 2.7-mm Hg higher level of systolic BP and 1.6-mm Hg higher level of diastolic BP than did nondrinkers after adjustment for age, body mass index, smoking, and urinary excretion of sodium and potassium.³5 The mean baseline alcohol consumption in our study population was 3 to 6 drinks/d. With an average 67% reduction in alcohol consumption, the net change in BP was −3.31 mm Hg for systolic and −2.04 mm Hg for diastolic, which were well within the range expected from observational epidemiological studies.

There are several limitations to our meta-analysis. First, only 1 of the trials⁹ that we could include had woman as study participants. Therefore, our study provides little direct evi-

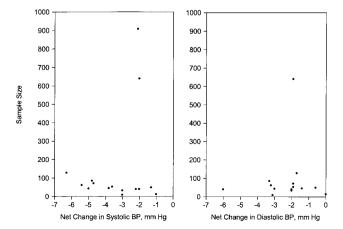


Figure 2. Funnel plots of net changes in systolic BP (left) and diastolic BP (right) vs sample size.

dence regarding the effect of alcohol reduction on BP in women. However, experience in observational epidemiological studies indicates that the association between alcohol consumption and BP is similar in men and women.1-3 Another limitation of our meta-analysis is that the participants in the 15 trials we studied tended to be fairly heavy alcohol drinkers (≥ 3 drinks/d). Therefore, we were not able to examine the effect of moderate alcohol consumption on BP. Prospective epidemiological studies have indicated that persons with a low to moderate alcohol consumption have a reduced risk for coronary heart disease, stroke, and all-cause mortality compared with nondrinkers.^{36–39} The effect of moderate alcohol consumption on BP is not fully understood. A linear, J-shaped, or threshold association between alcohol consumption and BP has been reported in observational epidemiological studies.1-3

The BP-lowering effects of alcohol reduction in the present study are similar to those noted with potassium supplementation or sodium reduction.^{40,41} It has been estimated that a small downward shift in the distribution of BP in the general population could substantially reduce the risk of hypertension and cardiovascular disease. Data from overviews of observational studies and randomized trials suggest that a 2-mm Hg reduction in diastolic BP would be expected to result in a 17% decrease in the prevalence of hypertension, a 6% reduction in the risk of coronary heart disease, and a 15% reduction in the risk of stroke and transient ischemic attacks.⁴²

It has been suggested that BP-reduction effect of a reduced intake of alcohol is smaller in long-term than in short-term intervention trials because study participants continually adapt to the depressor effects of alcohol withdrawal.4 However, in the current analysis, we did not recognize a significant difference in the effect of alcohol reduction on BP between trials with a longer or shorter duration of follow-up. The pooled effect size of -3.24 and -2.22 mm Hg for systolic and diastolic BP in the 5 trials with the longest duration (≥12 weeks) suggests that the reduction in BP can be maintained over periods that are relevant in clinical and public health practices. Our study also suggests that both low-alcohol beer substitute and counseling intervention significantly lower BP and that their effects on BP reduction do not differ. Therefore, both approaches can be used to lower BP in heavy alcohol drinkers.

In summary, our findings indicate that a reduction in alcohol intake among heavy drinkers significantly reduces systolic and diastolic BP. Furthermore, our study suggests that alcohol reduction should be recommended as an important component of lifestyle modification for the prevention and treatment of hypertension among heavy drinkers.

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