Low Water Intake and Risk for New-Onset Hyperglycemia

Ronan Roussel, MD, PhD1,2,3,4
Leopold Fezeu, MD, PhD5
Naïde Boubry, PhD4,5,6
Beverley Balkau, PhD7,8
Olivier Lantier, MD, MPH9
François Alhenc-Gelas, MD, PhD4,5,6,10
Michel Marre, MD, PhD1,2,3
Lise Bankir, PhD3

For the D.E.S.I.R. Study Group*

OBJECTIVE—Water intake alters vasopressin secretion. Recent findings reveal an independent association between plasma copeptin, a surrogate for vasopressin, and risk of diabetes.

RESEARCH DESIGN AND METHODS—Participants were 3,615 middle-aged men and women, with normal baseline fasting glycemia (FG), who were recruited in a 9-year follow-up study. Odds ratios (ORs) and 95% CIs for the incidence of hyperglycemia (FG ≥7.0 mmol/L or treatment for diabetes) were calculated according to daily water intake classes based on a self-administered questionnaire.

RESULTS—During follow-up, there were 565 incident cases of hyperglycemia. After adjustment for confounding factors, ORs (95% CIs) for hyperglycemia associated with classes of water intake (<0.5 L, n = 677; 0.5 to <1.0 L, n = 1,754; and ≥1.0 L, n = 1,184) were 1.00, 0.68 (0.52–0.89), and 0.79 (0.59–1.05), respectively (P = 0.016).

CONCLUSIONS—Self-reported water intake was inversely and independently associated with the risk of developing hyperglycemia.

FROM THE 1Université Paris–Diderot, Paris 7, Paris, France; the 2Département d’Endocrinologie, Diabétologie et Nutrition, Assistance Publique-Hôpitaux de Paris, Hôpital Bichat, Paris, France; the 3INSERM U695, Paris, France; the 4INSERM Unité 872, Centre de Recherche des Cordeliers, Paris, France; the 5Université Pierre et Marie Curie, Paris, France; the 6Université Paris Descartes, Paris, France; the 7INSERM CESP Center for Research in Epidemiology and Population Health, U1018, Epidemiology of Diabetes, Obesity and Chronic Kidney Disease Over the Life Course, Villejuif, France; the 8Université Paris 11, UMRs 1018, Villejuif, France; the 9Institut Inter-Régional pour la Santé, La Riche, France; and the 10Département d’Hypertension Artérielle, Assistance Publique-Hôpitaux de Paris, Hôpital Évêque Georges Pompidou, Paris, France.

Corresponding author: Ronan Roussel, ronan.roussel@bch.aphp.fr.

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From the 1Université Paris–Diderot, Paris 7, Paris, France; the 2Département d’Endocrinologie, Diabétologie et Nutrition, Assistance Publique-Hôpitaux de Paris, Hôpital Bichat, Paris, France; the 3INSERM U695, Paris, France; the 4INSERM Unité 872, Centre de Recherche des Cordeliers, Paris, France; the 5Université Pierre et Marie Curie, Paris, France; the 6Université Paris Descartes, Paris, France; the 7INSERM CESP Center for Research in Epidemiology and Population Health, U1018, Epidemiology of Diabetes, Obesity and Chronic Kidney Disease Over the Life Course, Villejuif, France; the 8Université Paris 11, UMRs 1018, Villejuif, France; the 9Institut Inter-Régional pour la Santé, La Riche, France; and the 10Département d’Hypertension Artérielle, Assistance Publique-Hôpitaux de Paris, Hôpital Évêque Georges Pompidou, Paris, France.

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Table 1—Baseline characteristics of the study population and risk for new-onset hyperglycemia during follow-up, by classes of mean daily W-Intake

| Daily W-Intake (L) | <0.5 | 0.5 to 1.0 | >1.0 | P for difference |
|--------------------|------|-----------|------|-----------------|
| General            |      |           |      |                 |
| n                  | 677  | 1,754     | 1,184|                 |
| Men (%)            | 48.6 | 47.9      | 45.4 | 0.31            |
| Age (years)        | 46.4 (9.9) | 47.3 (10.0) | 46.3 (9.9) | 0.001          |
| BMI (kg/m²)        | 24.1 (3.5) | 24.4 (3.5) | 24.7 (3.8) | 0.001          |
| Waist circumference (cm) | 81.6 (10.7) | 82.3 (11.0) | 82.7 (11.6) | 0.026          |
| Physical activity (%) |       |           |      | 0.0001          |
| Low                | 28.7 | 25.7      | 19.4 |                 |
| Medium             | 56.1 | 54.6      | 52.6 |                 |
| High               | 15.2 | 19.8      | 28.0 |                 |
| Tobacco smoking (%) |       |           |      | 0.0001          |
| Never smokers      | 47.7 | 55.9      | 57.8 |                 |
| Ex-smokers         | 26.3 | 26.6      | 24.1 |                 |
| Current smokers    | 26.0 | 17.5      | 18.2 |                 |
| Alcohol consumption (g/day) (%) |       |           |      | 0.0001          |
| Nonconsumers       | 22.0 | 23.0      | 30.7 |                 |
| 1–10               | 24.7 | 27.2      | 31.2 |                 |
| 10–20              | 8.1  | 8.4       | 6.7  |                 |
| >20                | 45.2 | 41.3      | 31.4 |                 |
| Creatininemia (μmol/L) | 81.2 (13.0) | 81.6 (13.0) | 81.0 (12.9) | 0.39          |
| C-reactive protein* | 1.00 (0.85–2.64) | 0.87 (0.85–2.00) | 0.85 (0.85–2.00) | 0.49 |
| Blood pressure     |      |           |      |                 |
| Systolic (mmHg)    | 129 (15) | 131 (15)  | 130 (15)  | 0.32          |
| Diastolic (mmHg)   | 79 (10)  | 80 (9)    | 79 (9)   | 0.21          |
| Hypertension (%)   | 32.5 | 34.3      | 32.4 | 0.50           |
| Treated THZD/Furo (%) | 3.7  | 2.2       | 3.2   | 0.07           |
| Metabolic data     |      |           |      |                 |
| Family history diabetes (%) | 20.6 | 19.0      | 19.3 | 0.67           |
| Fasting plasma glucose (mmol/L) | 5.21 (0.45) | 5.22 (0.44) | 5.17 (0.44) | 0.72 |
| Fasting insulinaemia (pmol/L) | 42.7 (23.3) | 45.0 (24.7) | 44.1 (27.6) | 0.08 |
| HOMA-IR            | 1.40 (0.80) | 1.48 (0.87) | 1.43 (0.96) | 0.10          |
| HOMA-B             | 63 (46–89) | 66 (46–92) | 65 (47–91) | 0.15          |
| Total cholesterol (mmol/L) | 5.76 (0.97) | 5.72 (0.97) | 5.66 (0.98) | 0.007          |
| Triglycerides (mmol/L) | 1.14 (0.85) | 1.09 (0.66) | 1.09 (0.65) | 0.15          |
| HDL cholesterol (mmol/L)** | 1.64 (0.41) | 1.66 (0.43) | 1.64 (0.44) | 0.44          |
| LDL cholesterol (mmol/L)** | 3.39 (0.83) | 3.35 (0.89) | 3.32 (0.90) | 0.032          |
| Other drinks       |      |           |      |                 |
| Mean volume of sweet drinks (L) (%) |       |           |      | 0.0001          |
| <0.5               | 92.0 | 95.5      | 97.0 |                 |
| 0.5 to 1.0         | 6.9  | 4.3       | 1.9  |                 |
| >1.0               | 1.0  | 0.2       | 1.1  |                 |
| Mean volume of wine/day (L) (%) |       |           |      | 0.0001          |
| <0.5               | 89.1 | 93.9      | 96.4 |                 |
| 0.5 to 1.0         | 9.9  | 6.1       | 3.6  |                 |
| >1.0               | 1.0  | 0.0       | 0.1  |                 |
| Mean volume of beer or cider (L) (%) |       |           |      | 0.056           |
| <0.5               | 96.9 | 98.1      | 98.7 |                 |
| 0.5 to 1.0         | 2.7  | 1.8       | 1.1  |                 |
| Urine              |      |           |      |                 |
| Urine density (× 1,000) | 1,019.6 (8.0) | 1,019.3 (9.1) | 1,017.9 (9.6) | 0.0001 |
| ORs for new-onset hyperglycemia |       |           |      |                 |
| Model 1            | 1.00 (reference) | 0.64 (0.49–0.83) | 0.73 (0.55–0.97) | 0.003 |
| Model 2            | 1.00 (reference) | 0.68 (0.52–0.89) | 0.79 (0.59–1.05) | 0.016 |

Data are means (SD) or medians (25th–75th percentiles) for continuous variables and percentages of patients for categorical variables. THZD, thiazidic diuretics; Furo, furosemide; HOMA-IR, homeostatic model assessment index of insulin resistance; HOMA-B, homeostatic model assessment index of insulin secretion. Hypertension was defined as systolic or diastolic blood pressure >140 or 90, respectively, or treated with antihypertensive drugs. ORs (95% CIs) for the association between daily W-Intake at baseline and the risk of incident hyperglycemia (fasting plasma glucose ≥6.1 mmol/L or treatment for diabetes) are presented according to two statistical models; variables for adjustment were either known risk factors for type 2 diabetes or factors associated (P < 0.10) with hyperglycemia and W-Intake in our population. Model 1: Adjusted for age, sex, BMI, baseline FG, physical activity, smoking status, triglycerides, HOMA-IR, and total cholesterol. Model 2: Further adjusted on self-reported intake of other fluids (i.e., volumes of beer or cider, sweet drinks, and wine consumed per day). Significant P values (<0.05) are in boldface.

*The C-reactive protein was available for only 181, 466, and 333 subjects in the three classes of W-Intake, respectively. **HDL cholesterol and LDL cholesterol were not available for 28 and 26 subjects, respectively.
are presented according to their class of W-Intake (Table 1). Among them, during follow-up, 565 subjects became hyperglycemic and 202 developed diabetes. The daily W-Intake was negatively associated with the risk of new-onset hyperglycemia, even after adjustment for multiple metabolic risk factors. Compared with daily W-Intake of <0.5 L, ORs were 0.64 (95% CI 0.49–0.83) and 0.73 (0.55–0.97) for classes of 0.5–1.0 L and >1.0 L, respectively (P = 0.003). After further adjustments for intake of other beverages, the ORs were slightly attenuated: 0.68 (0.52–0.89) and 0.79 (0.59–1.05) for classes of 0.5–1.0 L and >1.0 L, respectively (P = 0.016) (Table 1). The relation was not linear (data not shown).

With the two upper classes combined, the OR was 0.72 (0.56–0.92) (Supplementary Fig. 1). There was no interaction with sex and age (Supplementary Table 1). The same trend, although nonsignificant, was observed for the association with new-onset diabetes: compared with participants with a daily W-Intake of <0.5 L, ORs were 0.68 (95% CI 0.41–1.15) and 0.75 (0.43–1.32), respectively, P = 0.36.

CONCLUSIONS—Risk for hyperglycemia was negatively and independently related with self-reported W-Intake in normoglycemic middle-aged individuals from the French general population. This observational study does not establish causality. However, the association was moderately attenuated when important metabolic risk factors and potential confounders were introduced as covariables in the analysis, including intake of other classes of beverages with known adverse long-term effects (sweet and alcohol-containing drinks). Our data support the novel idea that vasopressin as a possible risk factor for hyperglycemia and diabetes until a recent report of an association between copetin and the incidence of diabetes (1,4,5,14). Our study extends this observation, drawing attention to a low W-Intake as a possible new risk factor for impaired glycemia. It suggests that an increase in W-Intake, an easy and costless intervention, could prevent or delay the onset of hyperglycemia and subsequent diabetes. Hopefully, our study will serve as a benchmark to design appropriate clinical trials testing the efficacy of this intervention in people who report drinking <0.5 L of water per day, as did almost 20% of the participants in this cohort.

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APPENDIX—Members of the D.E.S.I.R. Study Group: INSERM CESP U1018: B. Balkau, P. Ducimetière, and E. Escève; INSERM U367: F. Alhenc-Gelas; CHU D’Angers: Y. Gallois and A. Girault; Bichat Hospital: F. Fumeron, M. Marre, and R. Roussel; CHU de Rennes: F. Bonnet; CNRS UMR8090, LILLE: P. Froqgel; Centres d’Examens de Santé: Alençon, Angers, Blois, Caen, Chartres, Chateauroux, Cholet, Le Mans, Orleans, and Tours; Institut de Recherche Médecine Générale: J. Cognneau; General practitioners of the region; and Institute inter-Regional pour la Santé: C. Born, E. Cacas, M. Cailleau, J.G. Moreau, O. Lantieri, F. Rakotozafy, J. Tichet, and S. Vol.

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