

# Sugar-Sweetened Drinks Tied to Blood Pressure

BY FRANCES CORREA

FROM HYPERTENSION

High consumption of sugar-sweetened beverages appeared to adversely affect blood pressure levels in a population-based study involving more than 2,600 people living in the United Kingdom and the United States.

The findings should help shore up the message to patients that consumption of soda and fruit juice needs to be limited for a healthy diet.

"If individuals want to drink sugar

**For each serving of a sugar-sweetened beverage consumed per day, systolic blood pressure increased by 1.6 mm Hg. Diastolic blood pressure rose by 0.8 mm Hg.**

sweetened beverages, we suggest they do so only in moderation [fewer than three 12-ounce cans per week]," the study's lead investigator, Ian Brown, Ph.D., said in an interview.

The International Study of Macro/Micronutrients and Blood Pressure (INTERMAP) involved 2,696 people aged 40-59 years recruited from 10 population samples in the United Kingdom and United States.

In addition to providing answers to questions about the intake of beverages sweetened by fructose, glucose, and sucrose, participants were asked about their consumption of diet beverages and alcohol.

Each participant also provided two 24-hour urine collection samples, according to Dr. Brown of the department of epidemiology and biostatistics at Imperial College of London, and his colleagues.

Multiple regression analyses showed

that for each serving of a sugar-sweetened beverage consumed per day, systolic blood pressure increased by 1.6 mm Hg. Diastolic blood pressure rose by 0.8 mm Hg, according to the investigators.

A direct association also was observed between the intake of fructose-sweetened beverages and blood pressure, they noted.

Fructose intake that was higher by 2

standard derivations was associated with a 3.4-mm Hg increase in systolic blood pressure and a 2.5-mm Hg increase in diastolic blood pressure, according to the findings (J. Hypertens. 2011 Feb. 28[doi: 10.1161/hypertension.aha.110.165456]).

These associations between sugared beverage intake and blood pressure were strongest among individuals with higher urinary sodium excretion, the re-

searchers added. The results remained statistically significant after the investigators accounted for differences in body mass.

Dr. Brown and his coinvestigators concluded that higher blood pressure is associated with high consumption of glucose and fructose, as well as with higher levels of dietary sugar and sodium.

There was no significant correlation

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\*saxagliptin

#### Indication and Important Limitations of Use

KOMBIGLYZE XR is indicated as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment with both saxagliptin and metformin is appropriate. KOMBIGLYZE XR should not be used for the treatment of type 1 diabetes mellitus or diabetic ketoacidosis.

KOMBIGLYZE XR has not been studied in combination with insulin.

#### Important Safety Information

##### WARNING: LACTIC ACIDOSIS

Lactic acidosis is a rare, but serious, complication that can occur due to metformin accumulation. The risk increases with conditions such as sepsis, dehydration, excess alcohol intake, hepatic impairment, renal impairment, and acute congestive heart failure.

The onset of lactic acidosis is often subtle, accompanied only by nonspecific symptoms such as malaise, myalgias, respiratory distress, increasing somnolence, and nonspecific abdominal distress.

Laboratory abnormalities include low pH, increased anion gap, and elevated blood lactate.

If acidosis is suspected, KOMBIGLYZE XR should be discontinued and the patient hospitalized immediately.

[See Warnings and Precautions]

#### Contraindications

- Renal impairment (e.g., serum creatinine levels  $\geq 1.5$  mg/dL for men,  $\geq 1.4$  mg/dL for women, or abnormal creatinine clearance)
- Hypersensitivity to metformin hydrochloride
- Acute or chronic metabolic acidosis, including diabetic ketoacidosis
- KOMBIGLYZE XR should be temporarily discontinued in patients undergoing radiologic studies involving intravascular administration of iodinated contrast materials because use of such products may result in acute alteration of renal function.

#### Warnings and Precautions

- The reported incidence of lactic acidosis in patients receiving metformin is very low (approximately 0.03 cases/1000 patient-years). When it occurs, it is fatal in approximately 50% of cases. Reported cases of lactic acidosis have occurred primarily in diabetic patients with significant renal insufficiency.
- Patients with congestive heart failure requiring pharmacologic management, in particular those with unstable or acute congestive heart failure who are at risk of hypoperfusion and hypoxemia, are at increased risk of lactic acidosis.
- Lactic acidosis risk increases with the degree of renal dysfunction and patient age. The risk may be significantly decreased by use of minimum effective dose of metformin and regular monitoring of renal function. Careful renal monitoring is particularly important in the elderly. KOMBIGLYZE XR should not be initiated in patients  $\geq 80$  years of age unless measurement of creatinine clearance demonstrates that renal function is not reduced.
- Withhold KOMBIGLYZE XR in the presence of any condition associated with hypoxemia, dehydration, or sepsis.
- Before initiation of KOMBIGLYZE XR, and at least annually thereafter, renal function should be assessed and verified as normal.
- KOMBIGLYZE XR is not recommended in patients with hepatic impairment.
- Metformin may lower vitamin B12 levels. Measure hematological parameters annually.
- Warn patients against excessive alcohol intake.
- KOMBIGLYZE XR should be suspended for any surgical procedure (except minor procedures not associated with restricted intake of food and fluids), and should not be restarted until patient's oral intake has resumed and renal function is normal.
- Use of saxagliptin or metformin with medications known to cause hypoglycemia
  - Saxagliptin: Insulin secretagogues, such as sulfonylureas, cause hypoglycemia. Therefore, a lower dose of the insulin secretagogue may be required to reduce the risk of hypoglycemia if used in combination with KOMBIGLYZE XR.

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between diet soda intake and blood pressure levels.

The study was the first in people to suggest that there is an association between high sodium intake and high sugar-sweetened beverage intake and the overall effect on blood pressure, Dr. Brown said in an interview.

"It has been suggested by other scientists that consumption of high levels of sugars and salt may lead to sodium retention in the kidneys and/or volume expansion (i.e., an increased level of fluid in the body), which could lead to higher blood pressure," Dr. Brown said.

The findings also suggest that people who

consume more than one sugar-sweetened beverage daily tend to consume less of other types of nutrients including starch, fiber, protein (animal and vegetable), and polyunsaturated and monounsaturated fatty acids, the researchers noted.

But critics of the study emphasized that the "level of blood pressure changes noted by the authors are inconsequential and well within standard measurement error," according to a statement by the American Beverage Association.

In addition, "The results of [the analysis] obfuscate other important variables that are linked to high blood pressure." ■

## VITALS

**Major Finding:** For each serving of a sugar-sweetened beverage consumed per day, systolic blood pressure increased by 1.6 mm Hg. Diastolic blood pressure rose by 0.8 mm Hg.

**Data Source:** The International Study of Macro/Micronutrients and Blood Pressure (INTERMAP) involving 2,696 participants, aged 40-59, who were surveyed about their consumption of sugar-sweetened and diet beverages and who provided urine samples for analysis.

**Disclosures:** The investigators reported having no conflicts of interest. Dr. Brown's analysis was supported by a U.K. Medical Research Council studentship. The INTERMAP Study as a whole was supported by a grant from the National Heart, Lung, and Blood Institute, the Chicago Health Resource Foundation, and national agencies in China, Japan and the United Kingdom.

control in your adult patients with type 2 diabetes when treatment with both saxagliptin and metformin is appropriate



# A dynamic duo

Combining complementary mechanisms  
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—Metformin: Hypoglycemia does not occur in patients receiving metformin alone under usual circumstances of use, but could occur when caloric intake is deficient, when strenuous exercise is not compensated by caloric supplementation, during concomitant use with other glucose-lowering agents (such as sulfonylureas or insulin), or with use of ethanol. Elderly, debilitated, or malnourished patients and those with adrenal or pituitary insufficiency or alcohol intoxication are particularly susceptible to hypoglycemic effects.

- Intravascular contrast studies with iodinated materials can lead to acute alteration of renal function and have been associated with lactic acidosis in patients receiving metformin. KOMBIGLYZE XR should be temporarily discontinued at the time of or prior to the procedure, and withheld for 48 hours after the procedure and reinstated only after renal function is normal.
- There have been no clinical studies establishing conclusive evidence of macrovascular risk reduction with KOMBIGLYZE XR or any other anti-diabetic drug.

#### Adverse Reactions

- Adverse reactions reported in >5% of patients treated with metformin extended-release and more commonly than in patients treated with placebo were: diarrhea (9.6% vs 2.6%) and nausea/vomiting (6.5% vs 1.5%).

- Adverse reactions reported in ≥5% of patients treated with saxagliptin and more commonly than in patients treated with placebo were: upper respiratory tract infection (7.7% vs 7.6%), urinary tract infection (6.8% vs 6.1%), and headache (6.5% vs 5.9%).
- Adverse reactions reported in ≥5% of treatment-naive patients treated with coadministered saxagliptin and metformin immediate-release (IR) and more commonly than in patients treated with metformin IR alone were: headache (7.5% vs 5.2%) and nasopharyngitis (6.9% vs 4.0%).

**Drug Interactions:** Because ketoconazole, a strong CYP3A4/5 inhibitor, increased saxagliptin exposure, limit KOMBIGLYZE XR to 2.5 mg/1000 mg once daily when coadministered with a strong CYP3A4/5 inhibitor (e.g., atazanavir, clarithromycin, indinavir, itraconazole, ketoconazole, nefazodone, nelfinavir, ritonavir, saquinavir, and telithromycin).

#### Use in Specific Populations

- **Pregnant and Nursing Women:** There are no adequate and well-controlled studies in pregnant women. KOMBIGLYZE XR should be used during pregnancy only if clearly needed. It is not known whether saxagliptin or metformin are secreted in human milk. Because many drugs are secreted in human milk, caution should be exercised when KOMBIGLYZE XR is administered to a nursing woman.
- **Pediatric Patients:** Safety and effectiveness of KOMBIGLYZE XR in pediatric patients have not been established.

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