The effect of increased sodium intake with a carbohydrate-rich meal on glucose homeostasis in subjects without diabetes after bariatric surgery: A proof-of-concept, randomised, open-label, crossover study (The SALT Study).

• Who carried out the research? (Including details of sponsor, funding and any competing interests)

This study was funded by the Novo Nordisk UK Research Foundation and the National Institute for Health and Care Research (NIHR) Biomedical Research Centre. The University of Leicester sponsored the study.

• Where and when the study took place:

The study was carried out in the Leicester Diabetes Centre, Leicester General Hospital.

• Why was the research needed?

People without diabetes who have undergone weight loss surgery can sometimes experience low blood sugar (glucose) levels a few hours after eating a meal high in carbohydrates (like sugars and starches). This condition is called post-bariatric hypoglycaemia. It happens because, after surgery, food can move too quickly from the stomach to the intestines, causing carbohydrates to be absorbed too fast. As a result, the body releases too much insulin, a hormone that helps manage blood sugar levels and this leads to a sudden drop in blood sugar levels few hours later.

Symptoms of post-bariatric hypoglycaemia can include dizziness, sweating, shaking, hunger, and drowsiness. Current treatments are limited and may include following long-term a low in carbohydrates diet, or even reversing the surgery in more serious cases. There are also very few medical treatments for this condition which are not always well tolerated and some of them are very expensive. Because of the lack of effective treatments, more research is needed to find better solutions for this condition.

Previous studies in animals (mini-pigs) that have undergone weight loss surgery suggested that adding salt to a carbohydrate-rich meal might help modify how sugar is absorbed in the gut and overall modify blood glucose levels after a meal. If this is the case also in humans, it could mean that adding salt might have the potential to improve post-bariatric hypoglycaemia.

In this study we investigated the effect of adding salt to a carbohydrate-rich meal to see if this improves glucose levels after the meal in people who have had weight loss surgery (gastric bypass).

• Who participated in the study?

Eleven adults (four male, seven female) who have had weight loss surgery (Roux-en-Y-gastric bypass) were included in the final analysis. They met the following key criteria to take part in the study:

 \cdot they had weight loss surgery one year or longer prior to joining the study.

- they did not have a diagnosis of post-bariatric hypoglycaemia or diabetes.
- What treatments or interventions did the participants take/receive?

All participants received the same meals, but the order of the meals (with or without added salt) was different depending on the group they were randomly placed in. The groups were:

• Group one: participants ate a meal with two grams of added salt first, followed by a meal without added salt one week after.

• Group two: participants ate a meal without added salt first, followed by a meal with two grams of added salt one week after.

Each meal took place in fasting state. Blood sugar, insulin and appetite hormones were measured at fasting state (before meal consumption) and for three hours after the meal to see if the added salt affected the levels of these markers. The researchers were particularly interested in the lowest point of blood sugar in participants (known as nadir glucose) after the meal.

• What were the results of the study?

We found that when the participants had a meal with salt, their highest blood sugar reading (peak glucose) was lower compared to when they did not have salt added in their meal. The added salt made no difference to their nadir glucose levels or average glucose during the three-hour period after the meal was consumed. There was no difference in the levels of insulin and appetite hormones between the two treatments.

• How has this study helped patients and researchers?

The study results suggest that while adding salt may slightly reduce the peak blood sugar after a meal, it does not significantly impact overall blood sugar control or insulin levels in people who have had gastric bypass surgery. More research is needed to see if adding salt to a meal could be helpful for those with established post-bariatric hypoglycaemia.

• Where can I learn more about this study?

The study has been completed now, but an overview of the study is provided at the link below:

https://www.leicesterdiabetescentre.org.uk/research-blog/salt