Saliva insulin as an innovative method of risk assessment for caries, pre-diabetes and obesity: A randomized controlled trial

Mimansa Cholera, BDS, DDS, MPH[1], Rowena Cape[2] , Thomas Tanbonliong, DDS[1] , Jodi Stookey, PhD[2]

1. Division of Pediatric Dentistry, University of California, San Francisco
2. Maternal, Child And Adolescent Health, San Francisco Department of Public Health

UCSF School of Dentistry

Introduction

- San Francisco has **gaps** in public health monitoring for preventable conditions related to **elevated insulin (obesity, pre-diabetes, and caries)**, affecting >20% of children, and causing health disparities.
- ***Hyperinsulinemia*** is a **SILENT DISEASE**, a sign of pre-diabetes or early onset type 2 diabetes. **Insulin resistance** is common in obese individuals. It is a symptom of insufficient hydration and osmotic stress which causes **xerostomia** which increases caries risk. Insulin increases in response to exposure to carbohydrates which is the chief dietary factor responsible for caries.
- In the US recent trends have shown increase in diabetes and obesity at a much younger age. Diabetes prevalence in <20 years old has **doubled** in last decade. One in 6 youth are obese. Caries is the most common chronic childhood disease.
- Saliva insulin, which can 1) be measured **painlessly** without provoking anxiety in outpatient settings 2) **track risk** of obesity, pre-diabetes, and caries, 3) be regularly included in **routine school-based oral health screenings,** MIGHT fill gaps in monitoring IF ACTIONABLE or sensitive to intervention, such as drinking water promotion.

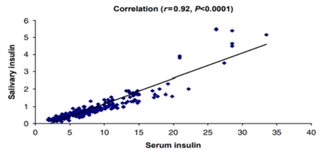


Figure 1: Correlation between saliva Insulin and serum insulin (1)

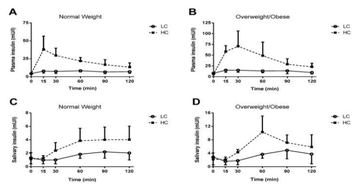


Figure 2: Saliva Insulin levels peak at 60 minutes after low and high carbohydrate meals and covaries with plasma insulin (2)

- **Drinking water intervention** to reduce risks related to elevated insulin is recommended by health authorities but hampered by lack of monitoring data for planning and evaluation.

Aims

- Determine if drinking water instead of juice or no drink **significantly lowers risk of elevated insulin** (>170 pg/mL) within 45-60 minutes.
- Determine if, in line with lower saliva insulin, drinking water instead of juice or no drink **significantly reduces risk of caries (indexed by IgA, IgG, amylase, buffering capacity, pH, osmolality).**

Methods

- Randomized controlled trial: Randomization with equal probability
- Stratified by weight status
  - Normal weight: BMI 5th to 84th percentile
  - Overweight or Obesity: >85th percentile
- Three randomly assigned groups
  - **500 ml drinking water (W)**
  - **200 ml apple juice (AJ)**
  - **No drink (ND)**
- Non-fasting saliva
- Survey on dietary habits, exercise was given to each patient.
- Analyzed for Insulin, IgA, IgG, and amylase by Salimetrics, San Diego
- Analyses with STATA SE 15.1
- Intention-to-treat test for reduced risk using logistic regression.
- Test for relationship between quantile change in saliva insulin and change in oral health risk factors using OLS linear regression.

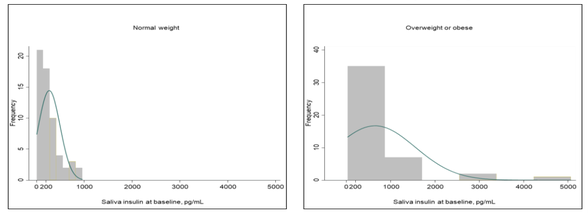
Recruitment & Enrollment

Results

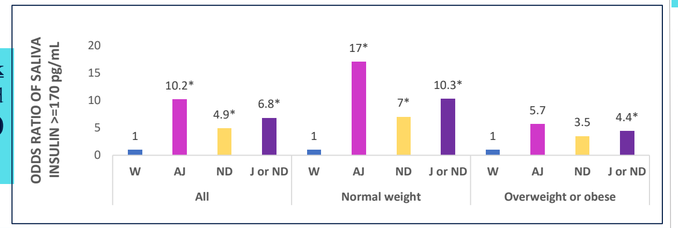
Demographics

- Selected to align with SFUSD oral health screening programs
- UCSF IRB approval (June 2022 - 2024)
- Data Collection (Oct 2022 – June 2023)
- Residents of San Francisco Bay Area
- 5- to 10 y/o patients of UCSF Pediatric dental clinic
- Healthy, ASA 1
- 30% Hispanic, 5% Black or AA, 52% Asian, 8% Multi-racial
- 100% Denti-Cal insurance
- 83% High caries risk population

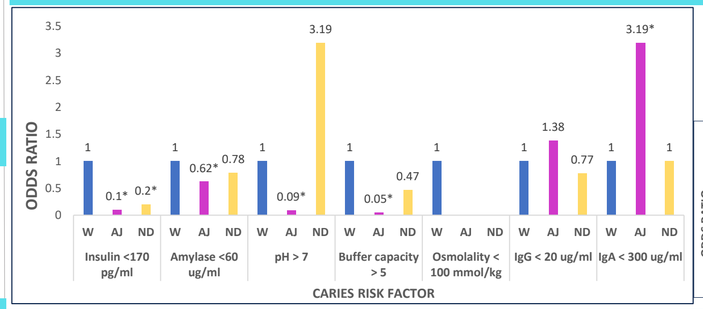
Distribution of saliva insulin at baseline by weight status



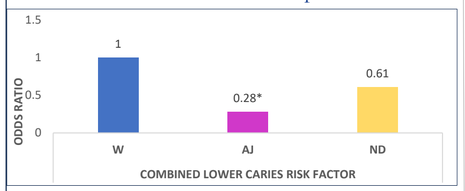
At 45-60 minutes, **drinking juice or no drink** instead of water was **significantly** associated with **elevated saliva insulin >170 pg/ml**, regardless of weight status * p <0.05



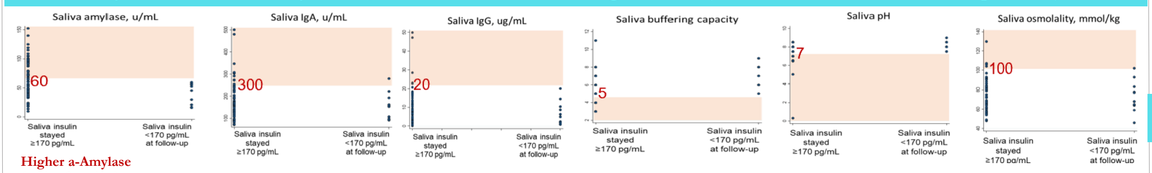
At 45-60 minutes, **drinking water** instead of juice was **significantly associated with reduction of multiple caries risk factors: Insulin <170 pg/ml, amylase<60, pH above 7, buffering above 5.** (p<0.05).



At 45-60 minutes, drinking water instead of juice was significantly associated with **combined caries risk factor reduction** * p <0.05



People with an **incident decrease in insulin below 170 pg/mL** were **10 times** more likely than people whose insulin remained above 170 pg/mL to have **statistically significant reduction in multiple caries risk factors IgG<20, IgA<300, amylase<60, osmolality<100, pH above 7, and buffering above 5** (OR, 95%CI: 10.1, 4.94-20-45, p<0.001).



Higher a-Amylase (caries favoring):
It binds to bacteria in plaque and may facilitate dietary starch hydrolysis to provide additional glucose for metabolism by plaque microorganisms close to the tooth surface.

Salivary IgA and IgG (caries protective factors):
IgA inhibits the process of bacterial adhesion to the tooth surface, neutralizes certain enzymes and bacterial toxins of cariogenic bacteria.
Higher IgA for caries active patients

Higher buffer capacity (caries protective):
Saliva buffer capacity controls the pH of mouth environment

Buffering Ability
0 - 5 Very Low
6 - 9 Low
10 - 12 Normal

Higher Alkaline pH is caries protective:
The low salivary pH provides an acidogenic environment for the growth of aciduric bacteria leading to dental caries which again further lowers the salivary pH leading to a vicious cycle

Lower salivary Osmolality (caries protective):
Lower the osmolality, less viscous the saliva, more the cleansing effect of saliva, less the caries risk

Conclusion

- **Saliva insulin covaried with caries risk factors:** carbohydrate intake (from apple juice), lower pH, lower buffering, higher IgA and higher amylase.
- Saliva insulin was **sensitive** to immediate caries risk reduction by drinking water intervention in children eligible for school-based oral health screenings and public health services in San Francisco.
- Saliva insulin monitoring is **ACTIONABLE** for public health.

Key takeaways:

- Clinicians can cite RCT data to back recommendations to ***"Drink water!! Avoid Juice!"***
- Clinicians can use elevated saliva insulin to ***detect early risk*** of caries before caries develop and cause irreversible damage.
- Clinicians can ***track saliva insulin*** to see if patient's follow their advice and reduce carbohydrate intake.
- Recommendation for ***USDA*** to discontinue providing juice with school meals.

Innovations:

- A ***non-invasive*** test to measure insulin and detect risk of diabetes, obesity and caries risk at a much younger age.
- More ***reliable*** way to measure caries risk than current measures that rely on patient responses and manifested disease.
- An easy ***inexpensive intervention*** of drinking water to reduce the risks of these chronic diseases.
- ***Novel preventive approach*** to reduce health disparities at large scale in public health setting.
- ***One biomarker*** to map risk of multiple chronic diseases.
- Potential for a ***chairside test*** to measure risk, improvement, and get timely treatment.

Next Steps

- Given small sample size, convenience study population, the clinical setting, and short-term follow-up, saliva insulin data from representative groups of SFUSD students are needed to estimate how many children have elevated insulin and confirm that saliva insulin monitoring can track longer-term change in risk.

Acknowledgments

We are grateful to the wonderful institutions for supporting us with a total of $40000 funding

California Society Pediatric Dentistry
Drinking Water Research Foundation
UCSF CTSI Lab Grant #UL1 TR001872
San Francisco Public Health Foundation

References

1. Measurement of fasting salivary insulin and its relationship with serum insulin in children Article in Endocrine Connections · November 2012 DOI: 10.1530/EC-12-0024 · Source: PubMed
2. Myette-Côté É, Baba K, Brar R, Little JP. Detection of Salivary Insulin Following Low versus High Carbohydrate Meals in Humans. Nutrients. 2017 Nov 2;9(11):1204. doi: 10.3390/nu9111204. PMID: 29099048; PMCID: PMC5707676.