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Review

Is salivary gland function altered in noninsulin-dependent diabetes mellitus and obesity–insulin resistance?

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ABSTRACT

Salivary gland dysfunction in several systemic diseases has been shown to decrease the quality of life in patients. In non-insulin dependent diabetes mellitus (NIDDM), inadequate salivary gland function has been evidenced to closely associate with this abnormal glycemic control condition. Although several studies demonstrated that NIDDM has a positive correlation with impaired salivary gland function, including decreased salivary flow rate, some studies demonstrated contradictory findings. Moreover, the changes of the salivary gland function in pre-diabetic stage known as insulin resistance are still unclear. The aim of this review is to comprehensively summarize the current evidence from *in vitro*,*in vivo* and *clinical* studies regarding the relationship between NIDDM and salivary gland function, as well as the correlation between obesity and salivary gland function. Consistent findings as well as controversial reports and the mechanistic insights regarding the effect of NIDDM and obesity–insulin resistance on salivary gland function are also presented and discussed.

Contents

1. Introduction

The salivary glands are important organs in the oral cavity and are responsible for the secretion of saliva into the oral and pharyngeal cavity. The main functions of saliva are to maintain oral mucosa integrity, prevent oral infection and to promote appetite (Hayward & Shea, 2009), resulting in a comfortable quality of life (Amerongen & Veerman, 2002). The acinar cells of the salivary glands are the secretory units that synthesize and secrete proteins, while water and electrolytes can be pass though the acinar cells *via* variety of mechanism (Proctor & Carpenter, 2007). Therefore, saliva is mainly composed of 99% water and only a small portion of 1% proteins. The activity of salivary glands is regulated by the sympathetic and parasympathetic innervations (Garrett & Kidd, 1993). The activation of parasympathetic innervations in the

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Table 1
The evidence of salivary flow rate in NIDDM from *clinical studies*.

Model (all human)	Age	Method	Major findings	Interpretation	Ref.

• Obese with NIDDM
  • Female: 11
  • Male: 9
• Non-obese with NIDDM
  • Female: 10
  • Male: 10
• Healthy subject
  • Female: 12
  • Male: 10
	38–66 years	• Fasting and unstimulated saliva levels 5 min or 5 mL
		• No medication details of patients'
			No change in salivary flow rate in all groups	NIDDM had no effect on the salivary flow rate	Aydin (2007)

• NIDDM[a] with hypoglycemic, anti-hypertensive and anti-cholesterol medication
  • Female: 12
  • Male: 33
• Healthy subjects
  • Female: 23
  • Male: 13
	20–65 years	• Each patient attended an out-patient diabetes educational program
		• Fasting blood glucose (FBS)
		• Unstimulated whole saliva and citric acid-stimulated parotid saliva
			• NIDDM: Fasting blood sugar (FBS) ↑
			• No difference in unstimulated and stimulated salivary flow rate between all groups
				• NIDDM without xerogenic medication had no influence on salivary output
				• Salivary flow rate was not changed following the change of FBS
				• The glycemic control program did not affect the salivary flow rate
					Dodds and Dodds (1997)

Men
• Study A
  • Impaired glucose tolerance (IGT): 10
  • NIDDM: 10
  • Control: 12
• Study B
  • NIDDM patients
  • Insulin treatment:15
  • Anti-diabetic drugs: 9
• Control:12
	59–77 years	• Citric acid-stimulated parotid saliva collection at 0, 15, 30, 45, 60 and 120 min (interval 0.5–1 min)
		• Patients in study A were not on any medication
		• OGTT was used to determine NIDDM and IGT in study A
		• HbA1C was used to determine treatment, either insulin or anti-diabetic drug treatment, for the patients in study B
			• In study A, there was no change in salivary flow rate.
			• In study B, there was no change in salivary flow rate between insulin-treated NIDDM patients and medication-treated NIDDM patients
				• NIDDM had no effect on stimulated salivary flow rates	(Borg Andersson et al., 1998)

• NIDDM: 45
• Female: 13
• HbA1C: 9.2 ± 2.2
  • Male: 32
• HbA1C: 8.2 ± 1.9
• Control: 86
  • Female: 45
  • Male: 32
	59–79 years	• The medication use in NIDDM and control subjects was recorded
		• Unstimulated saliva was collected at 1 h after meal for 5 min
		• Paraffin wax-stimulated whole saliva was collected for 5 min
		• Deep breathing test (expiratory to inspiratory (E/I) ratio),
		  • E/I ≤ 1.10 indicates parasympathetic neuropathy
		  • Orthostatic test (systolic blood pressure change)
		  • SBP decreased more than 30 mmHg: indicates sympathetic neuropathy
			• Parasympathetic and sympathetic neuropathies were significantly higher in NIDDM patients
			• No difference in unstimulated and stimulated salivary flow rate among groups
			• An increase in the number of drugs used daily resulted in a decrease in both resting and stimulated flow rate in the control subjects, but not in NIDDM patients
				• The resting and stimulated saliva secretions were not different between the NIDDM patients and the control subjects
				• NIDDM did not seem to affect salivary flow
					Meurman et al., (1998)

• Non-NIDDM: 38
  • Female: 20
  • Male: 18
• NIDDM:35
  • Female: 17
  • Male: 18
	43–45 ± 13 years	• Unstimulated whole saliva for 10 min
		  • Flow rate (mL/min)
		  • Salivary resistin (ng/mL)
			• No difference in salivary flow rate between groups	NIDDM had no effect on the salivary flow rate	Yin et al. (2012)

• Non-NIDDM
  • Female: 14
  • Male: 9
• Well-controlled NIDDM
  • Female: 3
  • Male: 8
• Poor-controlled NIDDM (HbA1C > 9%)
  • Female: 10
  • Male: 8
	54–90 years	• OGTT, HbA_{1c}
		• Unstimulated whole saliva collection
		• Unstimulated parotid saliva collection using Carlson-Crittenden cup
		• Stimulated parotid saliva collection
		• All current medication use were recorded
			• No differences in salivary flow rate between well-controlled NIDDM and non-NIDDM.
			• Poor-controlled DM:
			• ↓ salivary flow rate
			• Taking xerostomia medication in well-controlled and poor-controlled NIDDM: ↓ salivary flow rate
				• Poorly-controlled DM could be associated with salivary dysfunction
				• Xerogenic medication accelerated a decrease in salivary flow rate in NIDDM
					Chavez et al., (2000)