

Is Adiponectin Related to Orofacial Clefts?

Dear Editor,

Orofacial clefts are the most common congenital anomalies of the head and neck and its incidence ranges from 1/500 to 1/2000 live births, depending on populations.¹ Etiology of these anomalies is multifactorial and includes both environmental and genetic factors. Many teratogenic agents and factors in pregnancy are claimed to cause clefting, such as maternal smoking and hypoxia² and diabetes mellitus.^{3,4} The pivotal role of diabetes mellitus and maternal obesity on the incidence of orofacial clefts has been discussed previously.⁵

Adiponectin is 244-amino acid collagen-like polypeptide that is secreted by adipocytes and acts as an anti-inflammatory hormone and insulin sensitizer.⁶ Adiponectin exists in at least two forms, low molecular weight oligomer that is hexamers (two trimers) and high molecular weight oligomer consisting of four to six trimers.⁷ Plasma concentration of this polypeptide in human blood ranges from 3 to 30 µg/ml and accounts for 0.05% of total plasma protein.⁸

Findings from animal studies and metabolic studies in human suggests that adiponectin has different properties, such as suppression of hepatic gluconeogenesis, stimulation of fatty acid oxidation in the liver, glucose uptake in skeletal muscle and stimulation of insulin secretion.^{8,9} According to most of the studies in different populations, higher adiponectin level is associated with a lower risk of diabetes¹⁰ and low plasma level of adiponectin is associated with increased insulin resistance both in children and adults.¹¹

As we know, diabetes mellitus is one of the major risk factors of orofacial clefts.³ So it is suggested that lower adiponectin levels in diabetic pregnant women takes part as a risk factor for orofacial clefts. This

hypothesis could be assessed by screening pregnant women with diabetes mellitus for serum adiponectin level, and then investigating the incidence of cleft lip and/or palate in their children in comparison to control group.

According to our knowledge, diabetes mellitus is one of the important risk factors of orofacial clefts.³ Adiponectin is secreted by adipocytes and increases insulin sensitivity. Higher levels of adiponectin are associated with lower risk of diabetes mellitus and the dose-response relation is consistent. If the association between adiponectin level and orofacial clefts in pregnant mothers can be verified, then one of the major risk factors of orofacial clefts could be achieved. These evidences suggest adiponectin level can be used as a screening marker for early diagnosis of obesity related abnormalities.

Keywords: Cleft lip and palate; Diabetes mellitus; Adiponectin

Conflict of interest: None declared.

S Khazaei¹, Sh Kazemi¹, M Khazaei^{2*}

¹Dental Student, Student Research Committee, School of Dentistry, Isfahan University of Medical Sciences, Isfahan, Iran ²Fertility and Infertility Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran

*Correspondence: Mozafar Khazaei, PhD, Fertility and Infertility Research Center, Kermanshah University of Medical Sciences, Kermanshah, Iran. Tel: +98-831-4281563, Fax: +98-831-4281563, e-mail: mkhazaei1345@yahoo.com
Received: May 12, 2011 Accepted: August 10, 2011

References

- Cooper ME, Ratay JS, Marazita ML. Asian oral-facial cleft birth prevalence. *Cleft Palate Craniofac J* 2006;**43**:580-9. [16986997] [http://dx.doi.org/10.1597/05-167]
- Källén B, Harris J, Robert E. The epidemiology of orofacial clefts. 2. Associated malformations. *J Craniofac Genet Dev Biol* 1996;**16**:242-8. [8897214]
- Spilson SV, Kim HJ, Chung KC. Association between maternal diabetes mellitus and newborn oral cleft. *Ann Plast Surg* 2001;**47**:477-81. [11716256] [http://dx.doi.org/10.1097/00000637-200111000-00001]
- Mohammadzadeh G, Zarghami N. Hypoadiponectinemia in obese subjects with type II diabetes: A close association with central obesity indices. *J Res Med Sci* 2011;**16**:713-23. [22091299]
- Stothard KJ, Tennant PW, Bell R, Rankin J. Maternal overweight and obesity and the risk of congenital anomalies: a systematic review and meta-analysis. *JAMA* 2009;**301**:636-50. [19211471] [http://dx.doi.org/10.1001/jama.2009.113]
- Kadowaki T, Yamauchi T, Kubota N,

- Hara K, Ueki K, Tobe K. Adiponectin and adiponectin receptors in insulin resistance, diabetes, and the metabolic syndrome. *J Clin Invest* 2006;**116**:1784-92. [16823476] [<http://dx.doi.org/10.1172/JCI29126>]
- 7 Kelesidis I, Kelesidis T, Mantzoros CS. Adiponectin and cancer: a systematic review. *Br J Cancer* 2006;**94**:1221-5. [16570048] [<http://dx.doi.org/10.1038/sj.bjc.6603051>]
- 8 Chandran M, Phillips SA, Ciaraldi T, Henry RR. Adiponectin: more than just another fat cell hormone? *Diabetes Care* 2003;**26**:2442-50. [12882876] [<http://dx.doi.org/10.2337/diacare.26.8.2442>]
- 9 Rabe K, Lehrke M, Parhofer KG, Broedl UC. Adipokines and insulin resistance. *Mol Med* 2008;**14**:741-51. [19009016] [<http://dx.doi.org/10.2119/2008-00058.Rabe>]
- 10 Li S, Shin HJ, Ding EL, van Dam RM. Adiponectin levels and risk of type 2 diabetes: a systematic review and meta-analysis. *JAMA* 2009;**302**:179-88. [19584347] [<http://dx.doi.org/10.1001/jama.2009.976>]
- 11 Gil-Campos M, Cañete RR, Gil A. Adiponectin, the missing link in insulin resistance and obesity. *Clin Nutr* 2004;**23**:963-74. [15380884] [<http://dx.doi.org/10.1016/j.clnu.2004.04.010>]