ScienceDirect

Journal of Reproductive Immunology

Volume 133, June 2019, Pages 1-6

Oral sex is associated with reduced incidence of recurrent miscarriage

T. Meuleman [a], N. Baden [a], G.W. Haasnoot [b], M.M. Wagner [a], O.M. Dekkers [c], S. le Cessie [c d], C. Picavet [e], J.M.M. van Lith [a], F.H.J. Claas [b], K.W.M. Bloemenkamp [a f]

Show more

https://doi.org/10.1016/j.jri.2019.03.005

Get rights and content

Abstract

A possible way of immunomodulation of the maternal immune system before pregnancy would be exposure to paternal antigens via seminal fluid to oral mucosa. We hypothesized that women with recurrent miscarriage have had less oral sex compared to women with uneventful pregnancy.

In a matched case control study, 97 women with at least three unexplained consecutive miscarriages prior to the 20th week of gestation with the same partner were included. Cases were younger than 36 years at time of the third miscarriage. The control group included 137 matched women with an uneventful pregnancy. The association between oral sex and recurrent miscarriage was assessed with conditional logistic regression, odds ratios (ORs) were estimated. Missing data were imputed using Imputation by Chained Equations.

In the matched analysis, 41 out of 72 women with recurrent miscarriage had have oral sex, whereas 70 out of 96 matched controls answered positive to this question (56.9% vs. 72.9%, OR 0.50 95%CI 0.25–0.97, p = 0.04). After imputation of missing exposure data (51.7%), the association became weaker (OR 0.67, 95%CI 0.36–1.24, p = 0.21).

In conclusion, this study suggests a possible protective role of oral sex in the occurrence of recurrent miscarriage in a proportion of the cases. Future studies in women with recurrent miscarriage explained by immune abnormalities should reveal whether oral exposure to seminal plasma indeed modifies the maternal immune system, resulting in more live births.

Introduction

About 1% of all couples trying to conceive, are confronted with recurrent miscarriage, which is often defined as three or more consecutive pregnancies losses prior to the 20th week of gestation (Coulam, 1991). Possible etiologic factors include uterine anomalies, endocrine disorders, maternal inherited and acquired thrombophilia, and parental chromosomal abnormalities (Branch et al., 2010; Larsen et al., 2013). However, in only about 25–50% of the couples an underlying cause for recurrent miscarriage can actually be identified (Rai and Regan, 2006; Branch et al., 2010).

Most research into the immunology of recurrent miscarriage focused on the maternal immune system, leaving paternal factors aside. However, males seems to be capable to affect the female immune system prior to conception (Robertson and Sharkey, 2001). Studies in mice have shown that during copulation, thus before implantation, fetus specific maternal tolerance toward paternal antigens is induced (Moldenhauer et al., 2009).

A well-known route to induce immune tolerance is via oral exposure, possibly because the gut has the most adequate absorption in the absence of an inflammatory environment (Sosroseno, 1995; Brandtzaeg, 1996). In transplantation models of rats, oral administration of MHC molecules diminishes the occurrence of allograft rejection (Hancock et al., 1993). In addition, Clark et al showed that direct seminal plasma antigen presentation to a mouse model of NK-cell mediated recurrent miscarriage may prevent the rejection of embryos (Clark et al., 2013).

Koelman et al hypothesized that a potent way of inducing tolerance towards paternal HLA antigens of the fetus in pregnancy would be exposure of these antigens to oral mucosa (Koelman et al., 2000). To support this theory, they showed that both oral sex and swallowing sperm reduced the incidence of preeclampsia (Koelman et al., 2000). Another study showed that the pattern of oral sex practice was similar in 66 women with two miscarriages and a control population (N = 110), but 44.5% women in the control group swallowed sperm compared to 24.2% of the women with recurrent miscarriage (Mattar et al., 2005). Here we describe the outcome of a matched case control study to assess the effect of oral sex on the occurrence of recurrent miscarriage in a well-characterized population.

Section snippets

Case group

From 433 women who visited the recurrent miscarriage clinic of the department of Obstetrics and Reproductive Medicine at the Leiden University Medical Centre (LUMC), a tertiary referral center in the Netherlands, between 2000 and 2014, 273 women were eligible and invited to participate in this study.

Eligible cases were women who had three or more consecutive miscarriages prior to the 20th week of gestation with the same partner, and who were younger than 36 years at time of their third…

Baseline characteristics

In total, 97 women with recurrent miscarriage were included and 137 matched controls (Fig. 1). Table 1 shows the baseline characteristics of the study population.

In the case group, 63 women (64.9%) had primary recurrent miscarriage and 34 (35.1%) secondary recurrent miscarriage. A total of 65 women had 4 or more consecutive miscarriages (67.0%), and 39 women (40.2%) had 5 or more miscarriages. A total of 6 (6.2%) cases had hereditary thrombophilia, i.e, factor V Leiden (n = 4), prothrombin gene …

Discussion

This matched case control study suggests that women with recurrent miscarriage had less oral sex compared to women with uneventful pregnancy. This is in line with the hypothesis that the gut has the most adequate absorption in the absence of an inflammatory environment (Sosroseno, 1995; Brandtzaeg, 1996), and seminal fluid contains soluble HLA antigens which can already induce maternal immune tolerance towards inherited paternal antigens of the fetus before implantation.

The strength of this…

Acknowledgements

The authors would like to thank R. Wolterbeek for his help with the power analysis.…

References (31)

I. Athanassakis
Detection of soluble hla-g levels in maternal serum can be predictive for a successful pregnancy
Transplant. Proc. (1999)

D.A. Clark
Seminal plasma peptides may determine maternal immune response that alters success or failure of pregnancy in the abortion-prone cbaxdba/2 model
J. Reprod. Immunol. (2013)

E.M. Kho
Duration of sexual relationship and its effect on preeclampsia and small for gestational age perinatal outcome
J. Reprod. Immunol. (2009)

C.A. Koelman
Correlation between oral sex and a low incidence of preeclampsia: a role for soluble hla in seminal fluid?
J. Reprod. Immunol. (2000)

R. Mattar
Sexual behavior and recurrent spontaneous abortion

Int. J. Gynecol. Obstet. (2005)

K.A. Pfeiffer
Soluble hla levels in early pregnancy after in vitro fertilization
Hum. Immunol. (2000)

R. Rai *et al.*
Recurrent miscarriage
Lancet (2006)

S.A. Robertson *et al.*
The role of semen in induction of maternal immune tolerance to pregnancy
Semin. Immunol. (2001)

P.Y. Robillard *et al.*
Association of pregnancy-induced-hypertension, pre-eclampsia, and eclampsia with duration of sexual cohabitation before conception
Lancet (1996)

I. Zidi
Shla-g1 and hla-g5 levels are decreased in tunisian women with multiple abortion
Hum. Immunol. (2016)

View more references

Cited by (6)

Reply to: Responsibility of scientific community in claiming to have found an association with recurrent pregnancy loss
2019, Journal of Reproductive Immunology

Responsibility of scientific community in claiming to have found an association with recurrent pregnancy loss
2019, Journal of Reproductive Immunology

Oral tolerance and the materno-fetal relationship
2019, Journal of Reproductive Immunology

Show abstract

The Health Benefits of Sexual Expression
2023, Midwifery and Sexuality

Framing and understanding the whole aspect of oral sex from social and health perspectives: A narrative review ↗

2022, F1000Research

Regulatory T Cells in Pregnancy: It Is Not All About FoxP3 ↗

2020, Frontiers in Immunology

Recommended articles (6)

Research article

Reciprocal HLA-DR allogenicity between mother and child affects pregnancy outcome parameters

Journal of Reproductive Immunology, Volume 133, 2019, pp. 15-17

Show abstract

Research article

Exposure to systemic and intrauterine inflammation leads to decreased pup survival via different placental mechanisms

Journal of Reproductive Immunology, Volume 133, 2019, pp. 52-62

Show abstract

Research article

Lower frequency of the HLA-G UTR-4 haplotype in women with unexplained recurrent miscarriage

Journal of Reproductive Immunology, Volume 126, 2018, pp. 46-52

Show abstract

Research article

Epigenetic signatures in phospholipase A2 receptor genes predict cancer initiation and therapeutic progression

Phospholipases in Physiology and Pathology, Volume 4, 2023, pp. 443-451

Show abstract

Research article

The immunomodulating effect of seminal plasma on T cells

Journal of Reproductive Immunology, Volume 110, 2015, pp. 109-116

Show abstract

Research article

Perceived physical strength in men is attractive to women but may come at a cost to ejaculate quality

Animal Behaviour, Volume 142, 2018, pp. 191-197

Show abstract

View full text