

Amsterdam Reproduction & Development

Thyroid function in neonates conceived after hysterosalpingography with iodinated contrast media

N. van Welie¹, M. Portela¹, I. Roest², J. van Rijswijk¹, H.R. Verhoeve³, A. Hoek⁴, P. Bourdrez⁵, J.P. de Bruin⁶, A.W. Nap⁷, M. Goddijn⁸, A.B. Hooker⁹, C.F. van Heteren¹⁰, C. Koks², C.B. Lambalk¹, K. Dreyer¹, B.W.J. Mol¹¹, M.J.J. Finken¹², V. Mijatovic¹

1. Amsterdam UMC, Vrije Universiteit Amsterdam, Department of Reproductive Medicine, Amsterdam, The Netherlands; 2. Maxima Medical Center, Department of Obstetrics and Gynaecology, Veldhoven/Eindhoven, The Netherlands; 3. OLVG, Department of Obstetrics and Gynaecology, Amsterdam, The Netherlands; 4. University Medical Centre Groningen, Department of Reproductive Medicine and Gynaecology, The Netherlands; 5. VieCuri Medical Centre, Department of Obstetrics and Gynaecology, Venlo, The Netherlands; 6. Jeroen Bosch Hospital, Department of Obstetrics and Gynaecology, 's Hertogenbosch, The Netherlands; 7. Rijnstate Hospital, Department of Obstetrics and Gynaecology, Arnhem, The Netherlands; 8. Amsterdam UMC, University of Amsterdam, Centre for Reproductive Medicine, Amsterdam, The Netherlands; 9. Zaans Medical Centre, Department of Obstetrics and Gynaecology, Zaandam, The Netherlands; 10. Canisius Wilhelmina Hospital, Department of Obstetrics and Gynaecology, Nijmegen, The Netherlands; 11. Monash University, Department of Obstetrics and Gynaecology, Melbourne, Australia; 12. Amsterdam UMC, Vrije Universiteit Amsterdam, Emma Children's Hospital, Department of Paediatric endocrinology, Amsterdam, The Netherlands

BACKGROUND

- Hysterosalpingography (HSG) is a standard tubal patency test during fertility work-up
- Oil- or water-based iodinated contrast medium is used
- Oil (480mg I/ml) contains more lodine than water (250mg I/ml)
- Previous Japanese study found ↑ risk of congenital hypothyroidism in neonates whose mothers were exposed to high amounts of oil-based contrast during HSG (Satoh et al. 2015)

STUDY QUESTION

Does exposure to preconceptional HSG with iodinated contrast (oil- or water-based) affect neonatal thyroid function?

- Retrospective study among children born from women randomized for HSG with oil- (n=557) or water-based contrast (n=562) (Dreyer et al. 2017)
- The RCT showed higher pregnancy rates ≤6 months after HSG with oil- as compared to water-based contrast
- Women who had a live born infant in the H2Oil trial were contacted for consent to collect data on their children
- Thyroid function tests were retrieved from the Dutch neonatal screening program for congenital hypothyroidism
 - All neonates had T4, followed by TSH if T4 ≤-0.8 Standard Deviation (SD) score (based on daily mean)
- Main outcome: thyroid function tests of neonates conceived after preconceptional HSG

FIGURE 1: FLOWCHART

1,119 women were randomised oil (n=557) vs. water (n=562) 369 women had a live birth oil (n=214) vs. water (n=155) 208 women consented to be approached for future research 138 parents consented to

FUNDING/CO This work was not funded. H.R.V. reports consultancy fees from Ferring. A.H. declares that the Department of Obstetrics and Gynaecology, University Medical Centre Groningen received an unrestricted research grant from Ferring Pharmaceuticals BV, the Netherlands. C.B.L. reports speakers fee from Ferring, and research grants from Ferring, Merck and Guerbet. K.D. reports consultancy for Guerbet. B.W.M. is supported by a NHMRC Practitioner Fellowship (GNT1082548). B.W.M. reports consultancy for ObsEva, Merck, Merck KGaA and Guerbet and travel and research support from ObsEva, Merck and Guerbet. V.M. reports receiving travel- and speakers fee as well as research grants from Guerbet. All other authors have nothing to declare

collect data on 140 neonates

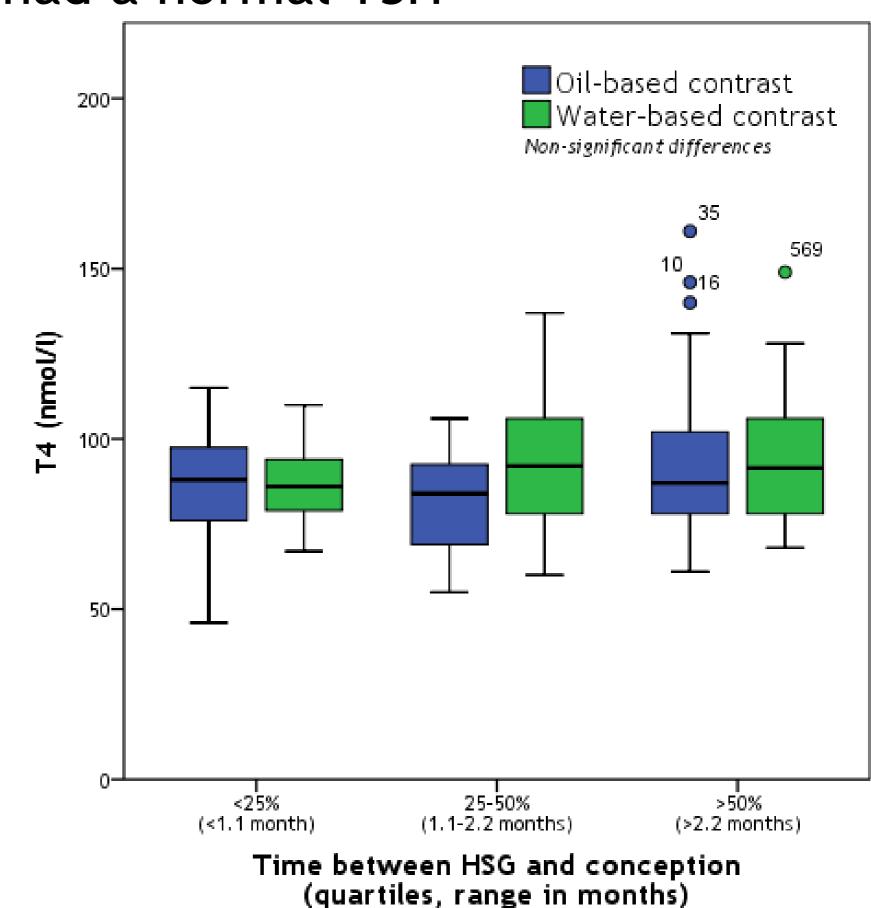
RESULTS

None of the 140 neonates had a positive screening result for congenital hypothyroidism

Neonates conceived after HSG with		
Oil contrast (480mg lodine/ml)	Water contrast (250mg lodine/ml)	P-value
n=76	n=64	
39.7 [39.0-40.9]	39.6 [38.6-40.7]	0.27
3470 [3115-3855]	3460 [3065-3721]	0.67
0 (0.0)	0 (0.0)	-
87.0 [76.0-96.0]	90.0 [78.0-106.0]	0.13
-0.05 [-0.5-0.5]	0.2 [-0.3-0.9]	0.12
9.0 [6.0-11.8]	10.0 [7.5-14.0]	0.43
2.3 [1.1-4.3]	2.1 [1.1-4.0]	0.83
	Oil contrast (480mg lodine/ml) n=76 39.7 [39.0-40.9] 3470 [3115-3855] 0 (0.0) 87.0 [76.0-96.0] -0.05 [-0.5-0.5] 9.0 [6.0-11.8]	Oil contrast (480mg lodine/ml) Water contrast (250mg lodine/ml) n=76 n=64 39.7 [39.0-40.9] 39.6 [38.6-40.7] 3470 [3115-3855] 3460 [3065-3721] 0 (0.0) 0 (0.0) 87.0 [76.0-96.0] 90.0 [78.0-106.0] -0.05 [-0.5-0.5] 0.2 [-0.3-0.9] 9.0 [6.0-11.8] 10.0 [7.5-14.0]

Data presented as median [IQR] or number of neonates (%). a Birthweight was missing in one neonate in the water group. b Neonatal screening result was missing in 1 neonate, due to neonatal screening abroad. c The concentration of T4 is expressed as standard deviation (SD) score and is compared with the daily mean. d Amount of contrast was missing in 32 versus 39 women.

• 13 children (oil contrast) had a T4 ≤-0.8SD score versus 7 children (water contrast) (RR, 1.5; 95%CI 0.7 to 3.6, P-value $0.32) \rightarrow \text{all had a normal TSH}$



CONCLUSION

- Preconceptional HSG with iodinated contrast (oil- and waterbased) did not result in decreased neonatal thyroid function
- Due to lack of information on the maternal thyroid function after HSG, we recommend keeping the amount of contrast as low as possible and further evaluation of the impact on offspring neurodevelopment is needed

ACKNOWLEDGEMENTS The employees of the Dutch National Institute for Public Health and Environment (in Dutch: Rijksinstituut voor Volksgezondheid en Milieu (RIVM)) are gratefully acknowledged for all the efforts made to send us the data of all included neonates.

Nienke van Welie, n.vanwelie@amsterdamumc.nl Amsterdam UMC, Vrlje Universiteit Amsterdam, Department of Reproductive Medicine







