News from here and there

Multicentre randomized study suggests oil-based hysterosalpingography may be therapeutic rather than only diagnostic

The New England Journal of Medicine published a Dutch study conducted across 27 hospitals in the Netherlands in May 2017. In the study, 1119 women were randomly assigned to hysterosalpingography with oil contrast (557 women) or water contrast (562 women) in 4 academic, 12 teaching and 11 non-teaching hospitals. Inclusion criteria were women between 18 and 39 years of age with spontaneous menstrual cycles, and who had been trying to conceive for at least 1 year, with an indication for evaluation of tubal patency by means of hysterosalpingography. This Water versus Oil (H_2Oil) trial was approved by the ethics committee and institutional review board of the Academic Medical Center, Amsterdam, and by the board of directors of all participating hospitals.

The trial was more than twice as large as the largest previous trial and had a very low rate of loss to follow-up (1%). The primary outcome, ongoing pregnancy, occurred in 220 of 554 women (39.7%) randomly assigned to oil contrast and in 161 of 554 women (29.1%) randomly assigned to water contrast. Of the 220 ongoing pregnancies in the oil group, 162 (73.6%) were naturally conceived, 15 (6.8%) were conceived after intrauterine insemination without mild ovarian hyperstimulation, 39 (17.7%) were conceived after intrauterine insemination with mild ovarian hyperstimulation, and 4 (1.8%) were conceived after embryo transfer following *in vitro* fertilization (IVF) or intracytoplasmic sperm injection (ICSI). The rates of ongoing pregnancy within 6 months after randomization and the subsequent live-birth rate were significantly higher among infertile women who underwent hysterosalpingography with oil contrast as compared to women who underwent this procedure with the use of water contrast.

The authors of this study suggest that although underlying mechanisms by which oil contrast might enhance fertility are unclear, testing of tubal patency with an oily medium may flush debris and dislodge mucus plugs from undamaged tubes. They advocate the use of tubal flushing with oil-based hysterosalpingography during a fertility work-up as a minimally invasive and inexpensive procedure, in comparison with IVF. Further research on newer outpatient ultrasound-based tubal testing methods using oil-based contrast has also been recommended by this study.

When contacted for a quote on the topic by this correspondent, Dr Ravi Ramakantan, Director, Department of Radiology, Kokilaben Dhirubhai Ambani Hospital, Mumbai and former Professor and Head, Department of Radiology, Seth G.S. Medical College and King Edward Memorial Hospital, Mumbai said: 'I must have seen at least a few thousands of lipiodol hysterosalpingographies in my time and what I say is based on my experience alone as I do not have any hard data or longitudinal study to justify this. First of all, there is no risk of clinically significant embolization with lipiodol. This is also borne out by our experience with lipiodol-based lymphangiography where much larger (20 ml) volumes of contrast are used. Though lipiodol is seen in the lungs as oil embolization, this has never been symptomatic. Regarding its therapeutic effect, we have had anecdotal cases where this has happened with both lipiodol- and water-based contrast material. Also, in many instances of attempted interventional procedures for recannalization of the tubes by hysterosalpingography, just flushing the tubes has resulted in immediate recanalization. I am unable to say if this results in the "cure" of infertility or not as I do not have follow-up data. The numbers quoted by the study group are small for a robust comparison between the two contrast materials. The other practical issue is that lipiodol is not easily available in India and is quite expensive in comparison with water-based contrast materials. The Indian Council of Medical Research should institute a randomized, blinded, multicentre trial on this subject in India to arrive at incontrovertible data.'

MAHARRA HUSSAIN, *Dubai, United Arab Emirates*

Increase in thyroid cancer incidence in Kerala: Real or artificial?

There appears to be an increase in the incidence of thyroid carcinoma in Kerala, report Indu Mathew and Aju Mathew in the May 2017 issue of the *Journal of the Endocrine Society*.

The authors studied the population cancer registries of Thiruvananthapuram, Kerala as well as of Mumbai, Chennai and Bengaluru for the years 2006, 2009 and 2012 and found a drastic increase in the numbers of thyroid cancers in Kerala, but not in the other registries.

Much of the increase was in women below 40 years of age.

The authors hypothesize that increase in the number of cases does not reflect a real increase or an epidemic of thyroid cancer; rather, it suggests an overdiagnosis of the disease. Differentiated thyroid cancers are the most common type of thyroid cancers, and are notorious for inter-observer differences in opinion because of the subjectivity of microscopic features for their diagnosis. (As a pathologist, I am well aware of this!) Indeed, in 2016, the Endocrine Pathology Society Working Group reclassified the encapsulated follicular variant of papillary thyroid carcinoma as 'Noninvasive follicular thyroid neoplasms with papillary-like nuclear features'. The authors of that study pointed out that while most differentiated thyroid cancers relapsed within the first decade, the tumours which had now been reclassified had had a 1% recurrence at 15 years after surgery.

The Kerala study showed almost a doubling of the incidence of thyroid carcinoma among women in the Thiruvananthapuram registry over the 6-year period. Correct diagnosis is essential because patients with papillary carcinoma, the most common form of thyroid carcinoma are treated with radioactive iodine after surgery.

There have been fears that the thorium-rich monazite sands of Kerala may lead to increased background radiation and result in thyroid cancer. However, there is no evidence to support this fear. Rather, the fact that Kerala has a better socioeconomic status than most parts of India and has better health facilities

may have led to this 'epidemic'. Better access to healthcare combined with subjectivity of diagnosis of differentiated thyroid cancer may have resulted in increasing numbers of patients with 'thyroid carcinoma'.

However, not all are convinced that overdiagnosis is the only problem. Dr K.P. Aravindan (Professor of Pathology, Calicut Medical College), stated in an email: 'There may be a trend for a slight increase of thyroid cancer cases all over the world, as smaller tumours are picked up and treated. This is not to be confused with overdiagnosis, in the sense of clinically undetectable and prognostically uncertain cases being picked by active surveillance and imaging technologies. Such a thing, which may have partly explained the increased incidence in South Korea is not relevant for Kerala, where no such active surveillance is in place. The vast majority of thyroid cancers diagnosed here are clinically significant lesions and there has been a definite trend of increase of these lesions in recent times. Moreover, the increase in thyroid papillary cancer has been accompanied by a concomitant rise in the prevalence of lymphocytic thyroiditis and thyroid autoantibodies. The simultaneous increase of thyroiditis and papillary cancer is similar to what has been reported from China and elsewhere after the introduction of salt iodization programmes. It is not background radiation that one should be asking about, but whether the levels of iodization has to be brought down at least in iodine-sufficient populations.'

SANJAY A. PAI, *Bengaluru, Karnataka*

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