GYNEMEDIA

Information and Suggestions from GYNEMED
September edition 2020

FOREWORD

Dear Reader,

In this issue of Gynemedia we are very pleased to inform you that, since July of this year, Dr Julia Heinzmann has been the new managing director of Gynemedia alongside Dr Sell.

What is more, we have summarised two interesting publications from the virtual ESHRE for you.

The first one deals with the connection between early aging of the ovaries and an associated accelerated aging process in general.

The second deals with cerebral palsy and its connection with multiple pregnancy.

Finally, we report on a publication on sperm extraction in non-obstructive azoospermia (NOA) using GM501 Collagenase.

We remain, as ever,

Your Gynemed

Dr Julia Heinzmann appointed managing director

It has been official since July 2020. Dr. Julia Heinzmann will manage the business of Gynemed on equal terms with Dr. Fabian Sell.

Gynemed: Dr. Heinzmann, you have been working for Gynemed since 2015?

Dr Heinzmann: Exactly, up to now I have mainly been entrusted with medical and scientific issues. In addition to answering questions from customers, I was particularly involved in the support and further development of the GM501 media series, including scientific literature research, clinical evaluations and the evaluation of study results.

Gynemed: ... and in quality management!

Dr. Heinzmann: In quality management, which at Gynemed has always been and still is close to the overall management; I was mainly responsible for the maintenance of product documentation, but also for complaints management.

Gynemed: Do you have sales experience?

Dr. Heinzmann: Certainly not to the extent of Dr Sell and Mr Koch. But I have already contributed to supporting our sales staff by designing marketing materials and training distributors, dealers, employees and customers. In this respect, I have also got around a bit and have been able to really get to know the daily routine of IVF laboratories. Some of you may also know me from speaking on the telephone or at various conferences.

Gynemed: And what attracts you to the new position?

Dr. Julia Heinzmann

Dr. Heinzmann: As a biologist, you are only confronted with commercial issues to a limited extent during your studies and they're also not something I regularly encountered in my scientific work. The active design and further development of products and ideas also requires dealing with the financial side, I have found this very appealing for some time. Gynemed will also be able to achieve a lot in cooperation with our sister companies Hamilton Thorne (USA) and Planer (UK). I would like to take up this challenge. Dr. Sell and I have a great, innovative team, both at our location in Lensahn and with our young medical-technical sales force.

We have a great responsibility towards our customers and our employees, this is and has always been in line with the philosophy of Gynemed, as I have come to know it and would like to continue.

Gynemed: Dr. Heinzmann, we wish you good luck with this new challenge.

ESHRE Supplement

A study of almost 20,000 young women who had their first IVF cycle in Denmark between 1995 and 2014 shows that those who responded poorly to treatment and in whom only a few oocytes were obtained had a significantly increased risk of later age-associated diseases. The results, according to researcher Mette Wulf Christensen from the University of Aarhus in Denmark, suggest a "connection with early ageing of the ovaries and an accelerated ageing process in general." The results are consistent with what is known so far about early menopause. Several studies have already shown that they are associated with an increased risk of cardiovascular disease, osteoporosis and mortality. "Identifying women at risk of early menopause can therefore enable early health care initiatives to be taken with a view to a healthy lifestyle," says Christensen.

But this is the first time that the number of oocytes obtained in IVF as a measure of ovarian aging – and thus as a risk predictor for age-related diseases and mortality – has been investigated in a large-scale cohort study. The study was based on Denmark's national registry, in which each person has his or her own identification number, thus enabling networking between different health registries. In this specific case, women under 37 years of age who had their first IVF or ICSI cycle in Denmark between 1995 and 2014 were divided into one of two groups according to their response to ovarian stimulation: those in whom 5 or fewer oocytes could be punctured and were defined as "early aging of the ovaries". In contrast, those who responded "normally" to the therapy with at least eight oocytes. The number of oocytes was thus used as a marker for the ovarian reserve. There were 1,234 women in the former group and 18,614 in the latter.

During the average follow-up period of six years, the incidence of chronic disease in both groups was analysed using the networked registration data to obtain a real estimate of the risk of cardiovascular disease, osteoporosis, type 2 diabetes, cancer and all-cause mortality. The results showed that women in the early ovarian aging group had a 26% increased overall risk of all diseases compared to women with normal ovarian response. This higher risk was statistically significant and was seen in cardiovascular disease (39% higher) and osteoporosis (more than twice as high). The two groups were also matched against the "early retirement benefits" register, which also included the group with early aging of the ovaries with a higher probability. The risk of cancer, other age-related diseases and death from all causes was not significantly different.

Commenting on the implications of the results, Ms Christensen said that although the common biological mechanisms for ovarian ageing and general ageing are "somewhat unclear", the data from this study show that young women with early ovarian ageing – defined as low ovarian production after FSH stimulation – have an increased risk of age-related morbidity and possibly mortality "and strongly support the hypothesis that low ovarian reserve could be a useful marker for later health problem". Advising this group of patients in fertility clinics is therefore "important in introducing preventive measures such as lifestyle changes or the use of HRT to reduce the adverse health risks after early menopause."

(Abstract O-238, Wednesday 8 July 2020: Early ovarian ageing and long-term health consequences: Is number of oocytes harvested in ART associated to an earlier and increased risk of age-related diseases?)

Risk rate now comparable

Fifteen years ago, a large population study from Denmark showed a significantly increased risk of cerebral palsy in infants born as a result of assisted reproduction. Although the absolute risk was low, such studies at that time led to the conclusion that cerebral palsy was the greatest risk of birth defects associated with IVF.

Another large-scale population study using data from birth cohorts in Denmark, Finland and Sweden has shown that the risk of cerebral palsy in IVF children has decreased by more than 50% over the last two decades, largely because the rate of twins has dropped significantly, said study leader Dr Anne Lærke Spangmose from Rigshospitalet at Copenhagen University Hospital at the ESHRE online annual meeting.

The study included three national IVF birth cohorts, the first in Denmark from 1990 to 2010, the second in Finland from 1990 to 2010 and the third in Sweden from 1990 to 2014, with a total of 111,844

children. These births were then divided into six groups: those born in 1990-1993, 1994-1998, 1999-2002, 2003-2006, 2007-2010 and 2011-2014. The national health records of these children were tracked until 2014 for Denmark and Finland and until 2018 for Sweden and compared with the records of almost 5 million naturally conceived children.

The risk of cerebral palsy was still evident in the study results, but the overall prevalence decreased steadily over the six periods – from 12.5 cases per 1000 live births between 1990 and 1993 to 3.4 per 1000 in 2011-2014. In contrast, the prevalence decreased only slightly throughout the period – from 4.3 to 2.1 per 1000 naturally conceived children, but for IVF-born single offspring the prevalence of cerebral palsy decreased from 8.5 per 1000 (1990-1993) to the background population rate of 2.8 (2011-2014), but remained stable at 10.9 per 1000 for IVF twins.

The results, Dr Spangmose said, provide strong evidence that reducing the number of twins born after IVF treatment has reduced the risk of cerebral palsy in the IVF population to levels comparable to those conceived naturally. "Multiple embryo transfer is still standard practice in many countries," she warns, "Our results underline that single embryo transfer and single births should be encouraged worldwide.

It also noted that over the last two decades, twin birth rates after IVF treatment have fallen significantly, particularly in Europe and the Nordic countries, where IVF twin rates have fallen from almost 25% in the 1990s to less than 5% today. Not much different from the 2% twin rate in the background population of naturally conceived pregnancies.

This reduction in the rate of multiple births in IVF has also led to a reduction in the rate of premature births (the highest risk of multiple births in obstetrics), which is also known to increase the risk of cerebral palsy. While the exact cause of cerebral palsy is largely unknown, preterm births, low birth weight and twin births are known to be the main risk factors. The prevalence of cerebral palsy increases exponentially with the number of foetuses in a pregnancy, mainly due to an increased risk of premature birth and low birth weight.

Large registration studies have now shown that the risk of cerebral palsy in IVF children born in the Nordic countries has practically disappeared after a policy of transferring individual embryos was introduced in the early 2000s. According to Dr Spangmose, the strength of this study lies in the large sample – with almost 112,000 IVF children born over 24 years in Denmark, Finland and Sweden. "The inclusion of full IVF and naturally conceived birth cohorts makes our data robust," she adds, "and has allowed an assessment of the real risk of cerebral palsy in IVF and its decline over time."

(Abstract 0-144, Tuesday 7 July 2020: The risk of cerebral palsy in ART children has more than halved over two decades – a Nordic collaborative study on 55,233 live born children)

GM501 Collagenase

O-126 The added value of enzymatic digestion to mechanical minicing in testicular sperm retrieval in non-obstructive azoospermia.

Veerle Vroeberghs (UZ Brussels, Belgium) presented in the virtual ESHRE 2020 an optimised method for sperm extraction in non-obstructive azoospermia (NOA) using GM501 collagenase.

NOA continues to pose a major challenge in the context of fertility treatments. First of all, a testicular biopsy (TESE) is performed. In the second step, ICSI, the success rate (fertilisation, embryo development, pregnancy) is lower with NOA than with obstructive azoospermia.

Although there is growing evidence that the surgical technique in NOA has little impact on the outcome as long as multiple biopsies are taken, this discussion continues. The important role played by the laboratory and the methods used have only been investigated in a few studies to date. This was emphasised by Veerle Vroeberghs in her presentation. Research in this area is additionally influenced by the heterogeneity of NOA diagnosis or the selection of the study population.

Gynemed
GM501 Collagenase

In the presented retrospective study from one centre, all patients were included in whom the first diagnostic or therapeutic TESE using open biopsy was performed between 2004 and 2017. All patients were genetically normal and the

NOA diagnosis was histologically confirmed. Patients with previous TESE or hypospermatogenesis were excluded. The primary outcome was the collection of sperm for cryopreservation or ICSI. Up to 6 biopsies were taken per testis. If no sperm could be found after 30 minutes' search after mechanical processing, the remaining tissue pieces were enzymatically digested with collagenase IV (GM501 Collagenase).

The results were classified according to treatment intention (diagnostic / therapeutic). In order to assess which factors influence sperm extraction, a multivariable regression analysis was performed, taking into account the factors age, FSH level, testicular volume and histology.

425 patients participated in the study. In 69/425 (16.2%) sperm could be found after mechanical processing. In 115/356 (32.3%) patients, in whom no sperm were found after mechanical processing, sperm could be isolated after enzymatic treatment.

In order to exclude a possible bias in the results of sperm isolation, TESE treatments on the day of ICSI (therapeutic / 109 patients) and TESE in the context of treatment planning (diagnostic / 316 patients) were considered separately. The patient groups did not differ significantly in age, testicular volume and histological diagnosis. The FSH level was significantly higher in the diagnostic group than in the therapeutic group (22.3 vs. 18.5 IU/L). Sperm retrieval was significantly higher in the therapeutic group than in the diagnostic group, both after mechanical processing (24.8% vs. 13.9%) and after enzymatic digestion (43.1% vs. 21.5%). Multivariable regression analysis showed that enzymatic digestion is a significant predictor of spermatogenesis.

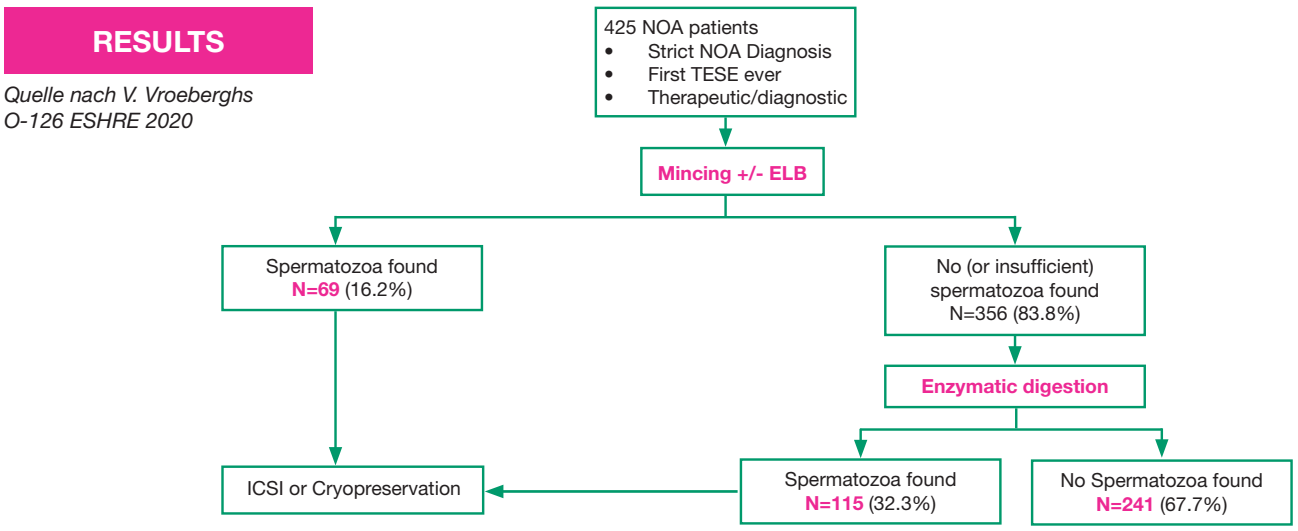
In conclusion, it can be said that the enzymatic digestion of testicular tissue after TESE, in addition to the mechanical preparation in NOA, improves sperm extraction in both diagnostic and therapeutic TESE.

In the final round of questions during the session, the question arose whether a CE-certified product was available and which is used in Veerle Vroeberghs' laboratory, she answered: GM501 Collagenase from Gynemed.

If you are interested or have questions about the product GM501 Collagenase, please contact us!

RESULTS

Quelle nach V. Vroeberghs
O-126 ESHRE 2020



Sperm retrieval after mechanical and enzymatic digestion = 69 + 115/425 = 43.3%

LEGAL NOTE

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