An Ayurvedic treatment protocol to improve anti-mullerian hormone: A prerequisite for assisted reproductive technique- A case report

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Abstract

Anti-Mullerian hormone (AMH) produced by granulosa cells of preantral and antral follicles acts as a potential marker for ovarian reserve useful in predicting ovarian response to controlled ovarian stimulation. A woman undergoing *in vitro* fertilization (IVF) with low AMH has poor success rate and ultimately the couple is left with the only option of IVF with a donor egg. The signs and symptoms of a patient with low AMH level can be compared to *Dhatukshayajanya Vandhyata*. The present case report documents the efficacy of an Ayurvedic treatment protocol in improving the AMH value, which is a prerequisite for assisted reproductive technique (ART) without a donor egg. The patient with low AMH level was subjected to Ayurvedic management protocol including *Shamana* for 3 months and *Shodhana* procedure for 21 days. The follow-up was done for 3 months. A marked improvement in the AMH level was noted in the first 3 months and also after the follow-up period, thus making her eligible for ART with her own egg.

Keywords: Anti-Mullerian hormone, Ayurveda, case report, infertility, Vandhyata

Introduction

Infertility though not a physically disabling disorder has far reaching psychological and social consequences.[1] The advent of medical science treatments, especially intra-cytoplasmic sperm injection (ICSI) in the field of assisted reproductive techniques (ART), has been devised to overcome the conditions pertaining to severe male factor infertility, oligoasthenoteratozoospermia (OAT).[2] The success rates of in vitro fertilization (IVF) techniques depend largely on the ovarian response at the time of oocyte retrieval which eventually reflects on the ovarian reserve.[3] The term "ovarian reserve" describes the number and the quality of the remaining oocytes in the ovaries. Anti-Mullerian hormone (AMH) is a promising marker of ovarian reserve that is produced by the granulosa cells of preantral and antral follicles.[4] After production, AMH is released into the circulation from the granulosa cells and can be measured in plasma. AMH has the potential to predict future reproductive lifespan and is therefore considered to be the best endocrine marker for assessing age-related decline of ovarian pool in healthy women. Since AMH level is indicative of ovarian response, its measurement becomes an inevitable

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criteria before IVF. [5] Considering the high cost and possible complications of ART procedures, [6] the unavoidable role of AMH as a superior candidate predicting ovarian reserve [7,8] has been explored in various studies. Therefore, uncertainty in the ART procedure outcome can be minimized to a greater extent. Reports suggest that patients with a diminished ovarian reserve have the only option of IVF with a donor egg. [9] The clinical symptoms observed in the present case report resembles to *Dhatukshayajanya Vandhyata* (infertility due to depletion of body tissues), that has been already explained in Ayurveda. The role of an effective Ayurvedic treatment protocol to improve the AMH level to a satisfactory level to have a better response to ovarian stimulation for IVF has to be validated, thereby opening a scope of an integrated medical approach. The present case report is an attempt on the same.

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Case Report

Presenting concerns

The case of this report is a 36-year-old married, nonsmoking, non-alcoholic female with primary infertility since 9 years of married life undergoing continuous interventions and repeated ART. Previous specialized evaluations include hormonal assays such as follicle-stimulating hormone, luteinizing hormone, estradiol, thyroid function test and AMH; ultrasonography (USG); and karyotyping. Investigations into the male factor revealed OAT. She underwent three courses of intrauterine insemination (IUI) and three courses of ICSI which were unsuccessful. AMH value before fourth ICSI was very low after which she was advised for an ICSI with a donor ovum.

Clinical findings

The patient got married in the year 2005 at the age of 27 years. Investigations carried out on both partners after 2 years of married life revealed OAT. After correcting the sperm count with oral medications, she underwent three cycles of IUI in 2010 which was unsuccessful. Due to OAT and failed IUIs, she was subjected for ICSI after necessary hematological evaluation and hormonal assays which came out to be normal. AMH value was 2.5 ng/mL before first ICSI on November 3, 2011. Six eggs were retrieved and one embryo was transferred, but there was no rise in human chorionic gonadotropin (hCG) value. Second ICSI was on May 10, 2012, in which three eggs were retrieved and three matured embryos were transferred. hCG value raised to >1500 mIU/ml on May 31, 2012, but had tubal abortion on June 3, 2012. Third ICSI was on July 21, 2013 and three embryos were transferred from five retrieved eggs. She had threatened abortion on August 19, 2013, and USG on August 20, 2013, showed single intrauterine gestational sac with subchorionic hematoma and a repeated scan on September 3, 2013, revealed an empty endometrial cavity. Routine investigations carried out on January 2, 2014, before fourth ICSI revealed very low AMH value (0.07 ng/mL). She was advised for undergoing next ICSI with a donor ovum due to the low AMH value. As the couple was not willing to accept a donor egg, they visited our outpatient department (OPD) on February 1, 2014 in the hope of undergoing ICSI with her own ova by improving the AMH value with Ayurvedic treatment. Her medication includes Eltroxin 50 mcg for hypothyroidism since 2010. Her history was relevant only for chickenpox in 2005 and jaundice in 2012. Family history was negative for any premature ovarian failure or low AMH. Her personal history revealed a regular bowel habit and sound sleep. Her appetite was apparently normal and the tongue was uncoated. She attained menarche at the age of 12 years with 2-3 days' duration in 26-28 days' interval. The amount was scanty with noticeable vaginal dryness since 3 months. Her obstetric history was gravida 2 abortion 2 ectopic pregnancy 1 (G2A2E1). On examination, she was calm and pain free. Her blood pressure was 120/80 mmHg, pulse rate 70/min and body mass index 23 kg/m². She is of Vata Kapha Prakriti with Madhyama Satva (moderate mental strength) and Madhyama

Koshtha (moderate bowel). Her physical examination and examination of external genitalia did not revealed any abnormal findings. Per speculum examination showed a healthy nulliparous cervix without any significant abnormality. Bimanual examination revealed an anteverted mobile uterus with a negative cervical motion tenderness. Medical history of the patient is detailed in Table 1.

Diagnostic focus and assessment

In the view of symptoms of *Artava Kshaya* (hypomenorrhea), the present case was diagnosed as *Dhatukshayajanya Vandhyata* (infertility due to depletion of body tissues). The assessment was done by comparing baseline AMH value with repeated evaluation after 3 months of *Shamana* (oral medication) and *Shodhana* treatment (purification therapy). Baseline AMH value was 0.07 ng/ml (reference range: 2–6.80).

Therapeutic focus and assessment

The therapeutic plan was to administer *Shamana Chikitsa* (oral medication) followed by Shodhana Chikitsa (purification therapy). Shamana Chikitsa was done for 3 months with Vaishavanara Churna and Mahanarayana Taila. As her clinical symptoms and AMH value after Samana Chikitsa showed satisfactory improvement, she was subjected to Shodhana Chikitsa. Initially, her Agni was corrected by Dipana-Pachana (improving digestion) with Vaishavanara Churna as a Purvakarma (preparation) of Shodhana. She attained Nirama Lakshana (signs of digestion of Ama) by 2 days after which Accha Snehapana (intake of oil) was started with Mahanarayana Taila. Samyak Snigdha Laksana (signs of proper oleation) was observed after 6 days of Snehapāna. Mridu Virechana (mild purgation) was performed on the administration of Trivritlehya. After Virechana, she was subjected to Yoga Basti and Uttara Basti (medicated enema). After completion of Shodhana therapy, she was discharged from the hospital [Table 2].

Follow-up and outcomes

After 3 months, the patient was advised to have a follow-up in the OPD with a reassessment of AMH value. It was observed that there was a marked improvement in the AMH value as shown in Table 3.

Table 1: Timeline of medical history			
Year	Clinical events and interventions		
2007	Diagnosed OAT		
2010	Underwent 3 IUI's which was failure		
November 3, 2011	First ICSI-failure		
May 10, 2012	Second ICSI-tubal abortion		
June 21, 2013	Third ICSI-got aborted		
January 2014	Suggested donor egg for fourth ICSI as AMH value was very low		
February 1, 2014	Started taking Ayurvedic treatment		

OAT: Oligoasthenoteratozoospermia, IUI: Intrauterine insemination, ICSI: Intracytoplasmic sperm injection, AMH: Anti-Mullerian hormone

Table 2: Treatment protocol			
Treatment procedure	Method of administration	Treatment duration	
Dipana, Pachana with Vaisvanara Churna	10 g twice daily before food with warm water	Day 1-2	
Snehapana with Mahanarayana Taila	Arohana Krama after assessing the Agni and Koshtha	Day 3-8	
Snehana and Svedana	Sarvanga Abhyanga with Dhanvantara Taila followed by Nadi Sveda	Day 9-11	
Mriduvirecana with Trivritlehya	30 g given at 7 am	Day 12	
Yoga Basti	Niruha Basti with 750 ml of Mustadiyapana Basti and Anuvasana Basti with 150 ml of Mahanarayana Taila	Day 14-21	
Uttara Basti	With 3 ml Mahanarayana Taila into the uterine cavity on the day of Anuvasana Basti		

Table 3: Results of baseline and follow-up assessment of anti-Mullerian hormone value

Date of test	AMH value in ng/mL	Ref. range
January 2, 2014	0.07 ng/mL	2.00-6.80 ng/mL
May 24, 2014	1.64 ng/mL	2.00-7.00 ng/mL
September 18, 2014	2.11 ng/mL	2.00-7.00 ng/mL

AMH: Anti-Mullerian hormone

Discussion

The psychosocial stigma related to infertility has provoked the need for an ART in spite of the time-consuming, expensive, and stressful strategies. ICSI has now created a new opening in the treatment of previously untreated cases of severe male factor infertility. The value of AMH in detecting the ovarian reserve for an IVF cycle has begun to be better understood in the recent years. It is so unfortunate that donor egg IVF would be the last option of them who have a low AMH value with poor ovarian reserve. Lack of awareness regarding the efficacy of an integrated approach to medical intervention in such cases to proceed with a donor egg IVF technique has grown up as a great challenge to the physicians as well as patients. To satisfy the needs of the present situation, there should be a better understanding regarding the importance of Garbha Samagri^[10] (essential elements for healthy conception), thereby generating better treatment options. Although the Ayurvedic approach to Dhatukshayajanya Vandhyata[11] in terms of low level of AMH is gaining importance, the lacuna of effective research works based on the integrated medical approach still exists. The present disease entity with a close resemblance to Dhatukshayajanya Vandhyata can be traced out as an attributing female factor in association with the male factor for infertility. The case presents with a Vata Dosha Vikriti (alteration of Dosha) progressing toward a Dhatu kṣhaya, thereby affecting Artava Upadhatu which was evident from the Artavakshaya Lakshana^[12] of the patient. The treatment protocol aims for a Shamana of Vata Dosha and correction of Agni, thereby creating equilibrium of Doshas in the Madhyama Vaya (middle age) Avastha. The Dhatu Pushti itself can be attributed for the physiology of Artava. Oral administration of Vaishvanara Churna[13] having Dipana and Pachana properties helps in Agni Vardhana (enhancing digestive fire), of Dhatu). Oral administration of Mahanarayana Taila[14]

owing to its *Vatahara*, *Dhatuvardhaka*, *Vandhyatvahari*, *Balya* and *Brimhana* properties helps in the improvement of *Artavaksaya* through *Dhatupusti*, thus creating a satisfactory improvement in the AMH value. Furthermore, *Mahanarayana Taila* used for *Snehapana* imparts a synergistic effect on *Dhatu Pushti*. *Virechana* helps in attaining *Agni Dipti* and *Sroto Vishuddhi* (purification of channels) and hence supports the proper *Dhatu Parinama*. [15]

Pathogenesis of gynecological disorders always involves *Vata Dosha*. [16] Hence, *Basti Karma*, which is the best therapy for *Vata Shamana*, was administered after *Mrdu Shodhana*. In Ayurveda, *Mustadiyapana Basti*^[17] is indicated for infertility as it is *Balajanana*. *Uttara Basti* is indicated for all gynecological disorders, especially in *Puspanasa* (destruction of ovum). [18] Notable improvement in the symptoms of *Artavaksaya* (scanty menstruation and vaginal dryness) was observed after the *Shodhana Karma*. The value of AMH after the treatment was considerably improved on a much satisfactory level, so that the option of egg donation IVF could be discarded.

Conclusion

This Ayurvedic treatment protocol including a combination of both *Shamana* and *Shodhana* therapies were helpful in improving the AMH value to a satisfactory level. Hence, this was helpful for the patient to undergo an IVF treatment with her own eggs that was not possible earlier due to low AMH level. Therefore, this approach can be considered in patients with low AMH values and for further research in integrative medicine.

Patient perspective

The patient was satisfied with the treatment as she had considerable improvement in the AMH value that made her eligible for an ICSI with her own ovum.

Patient consent

The patient provided written permission for publication of this case report.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published

and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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