



Case Study

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EFFECT OF AYURVEDIC REGIMEN ON ELEVATED BETA-HCG LEVELS IN HYDATIDIFORM MOLE AFTER INDUCTION OF GARBHAPATA: A CASE STUDY

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ABSTRACT

The incidence of Molar pregnancy in India is one in 400 out of them 80% of the cases are uncomplicated and 20% are associated with an extensive list of perioperative complications, some of which may be of a critical nature. There is a wide variation in incidence reported worldwide which has been contributed by genetic, environmental and demographic and host related factors. We report a case of a 30-year old female with hydatidiform mole and elevated Beta-HCG level after D & C which was managed by *Ayurvedic* treatment regime. Implementation of an *Ayurvedic* approach with serum Beta-HCG levels, ultrasonographic help in success of this case without use of methotrexate.

Keywords: *Arbuhara kwatha*, Beta-HCG, Choriocarcinoma, hydatidiform mole, *Raktaja gulma*

INTRODUCTION

A molar pregnancy is a gestational trophoblastic disease¹ or hydatidiform mole (or hydatid mole, mola hydatidosa),² which grows into a mass in the uterus that has swollen chorionic villi. These villi grow in clusters that resemble grapes³. A molar pregnancy can develop when a fertilized egg does not contain an original maternal nucleus and do not develop in fetal tissue. It is categorized as partial moles or complete moles, with the word mole being used to denote simply a clump of growing tissue, or a growth.

More than 80% of hydatidiform moles are benign. The outcome after treatment is usually excellent. Close follow-up is essential to ensure that treatment has been successful.⁴ In 10 to 15% of cases, hydatidiform moles may develop into invasive moles. This condition is named persistent trophoblastic disease (PTD). The moles may intrude so far into the uterine wall that hemorrhage or other complications develop. In 2 to 3% of cases, hydatidiform moles may develop into choriocarcinoma, which is a malignant, rapidly growing, and metastatic (spreading) form of cancer.

Hydatidiform moles should be treated by evacuating the uterus by uterine suction or by surgical curettage as soon as possible after diagnosis, in order to avoid the risks of choriocarcinoma⁵. Patients are followed up until their serum human chorionic gonadotrophin (HCG) level has fallen to an undetectable level. HCG is excellent marker for continued trophoblastic activity. Invasive or metastatic moles (cancer) may require chemotherapy and often respond well to methotrexate.

According to *Ayurveda* molar pregnancy can be correlated with *Raktaja-gulma*. As per *Acharya Sushruta*, the treatment of *Raktaja gulma* is same as *Pittaja gulma* i.e. *Snehan* and *Madhur dravya Virechana*. He also mentioned a specific treatment for *Rakta-gulma* is *Rakta-vibhedana*. After *Rakta-vibhedana* treatment like *Raktapradara* should be done⁶.

According to *Acharya Charaka*, in each type of *Gulma*, the first line of treatment is *Vataghna* i.e. *Snehana – Swedana – Snigdha virechana*⁷. According to *Acharya Kashyapa* it is treated by *Niruha basti*⁸.

Case report

This is a case of a 30 year-old lady who visited the Prasuti Tantra and Stree Roga outpatient department (OPD) of National institute of *Ayurveda* hospital, Jaipur, on March 26, 2019 with the complaints of Nausea during menstruation, lower abdominal pain, White discharge per vagina, reduced appetite and sleep disturbances since 2 month with positive urine pregnancy test. She had her last menstrual period on 10th March 2019 with regular cycle with painless and clotted excessive flow, 4-5 pads per day and interval of 30-35 days, Obstetric history revealed 2 previous normal delivery of 2 male child ages 4 and 8 years. She had history of one induced abortion at Gestational age of 2 month 15 days in November 2018. Her histopathological report showed vesicular mole on 12/11/18.

On examination, the general condition of the patient appeared healthy. Blood pressure (BP) was 110/80 mmHg and pulse were 70 bpm, No pallor and edema were present, mild tenderness in lower abdomen was present during per- abdomen examination. Per- vaginal examination was withheld. Hematological, biochemical investigations were found within normal limit but her quantitative BHCG was 1212.65 mIU /ml on 1/4/2019, her uterus and adnexa USG were normal.

Treatment protocol

Considering the fact that she is the follow up case of vesicular mole, she was advised to admission in the Prasuti tantra and Stree Roga inpatient department. Her uterine curettage was done, and endometrium was sent for biopsy. Histopathological examination

showed increased glands to stroma ratio suggestive of interval endometrium on 3/4/2019.

She was advised to take light diet. Cap *Giloy*, Cap *Neem* was started as two times per day and Kalka of 2-3 *Sadabahar* leaf in early morning at empty stomach, *Avipatikara Churna* 3 gm two times per day 15 min before meal. Again, quantitative Beta-HCG

was done on 4/4/2019 which was same as earlier 1212.65 mIU/ml and repeated in every 15 days which was very fluctuating. From her next LMP which was on 29/4/19 Tab ovulac-LD OCP was also started. In 21 May 2019 beta-HCG value was 865.28 mIU/ml which were same as in April.

Table 1: Sequential changes in the clinical and biochemical parameters and treatment plan

Day	Date	Complaints	serum Beta-hCG value in mIU/ml	Treatment given
Day 0	26.3.19	Nausea during menses, Lower abdominal pain White discharge per vagina, UPT Positive H/O D & C in November 2018 Histopathological report shows vesicular mole		<i>Avipatikara churna</i> -3 gm <i>Pittantaka churna</i> -3 gm 15 min before meal
Day 5	1.4.19	Weakness, USG- Ut and Ad shows no gestational sac, Normal study	1212.65 mIU/ml	Planned for D&C D & C done on 2.4.19
Day 7	3.4.19	Histopathological examination shows increased glands to stroma ratio suggestive of interval endometrium on 3/4/2019		Kalka of 2-3 <i>Sadabahar</i> leaf in early morning empty stomach. Cap <i>Giloy</i> , Cap <i>Neem</i> 2 b. d., <i>Avipatikara Churna</i> 3 gm b. d 15 min before meal, light diet.
Day 8	4.4.19	Pain in lower abdomen Burning sensation in urine	1212.65 mIU/ml	<i>Gokshura churna</i> 3gm three times a day
Day 15	11.4.19	Relief in previous complaints	991.94 mIU/ml	<i>Gokshura churna</i> Stop, continue remaining treatment as it.
Day 27	23.4.19		865.28 mIU/ml	
Day 33	29.4.19	LMP 25.4.19		Tab ovulac LD OCP for contraception started
Day 38	4.5.19		1166.53 mIU/ml	
Day 44	11.5.19	Spotting p/v sometime Pain in lower abdomen		<i>Nagkesara churna</i> 3 gm <i>Sphatika bhasma</i> 500 mg b. d
Day 48	15.5.19	Relief in previous complaints		Stop <i>Nagkesara churna</i> & <i>Sphatika bhasma</i> Continue rest treatment as it
Day 54	21.5.19	Relief in previous complaint	865.75 mIU/ml	Continue same treatment
Day 74	10.6.19	LMP 28.5.19 stop in 5 days Pad 2/ day	572.56 mIU/ml	<i>Arbudhara kwatha</i> 10 gm orally in <i>kwatha</i> form <i>Raktaprasadaka him</i> 10 gm O.D At Approx 10 am
Day 100	6.7.19	LMP 23.6.19	408.47 mIU/ml	<i>yoga basti</i> with <i>Dashmoola taila</i> 60 ml for <i>Anuvasana basti</i> and <i>jwarahara kwatha</i> for <i>Asthapana basti</i> from 11.7.19 to 19.7.19
Day 120	27.7.19	LMP 21.7.19 Nausea, Lower abdominal pain sometimes		Tab containing herbomineral drugs 1 tab b. d after meal and <i>yoni pichu</i> with <i>apamarga kshara taila</i> in 2 alternate days
Day 147	23.8.19	LMP 19.8.19 No fresh complaint	295.80 mIU/ml	Continue same treatment
Day 166	12.9.19	LMP	13.20 mIU/ml	Continue same treatment
Day 205	21.10.19	LMP 18.10.19	364.00 mIU/ml	<i>yoga basti</i> start from 29 November 2019 with <i>triphala taila</i> 60 ml for <i>Anuvasana basti</i> and <i>Arbudhara kwatha</i> for <i>Asthapana basti</i> <i>Nidana Parivarjana</i> and <i>Prakritivighata</i> was strictly advised to stop non vegetarian diet and advised to take fresh green leafy vegetables like <i>Patol</i> , <i>methi</i> , <i>palak</i> , <i>Karela</i> , <i>moong dal</i> and <i>Barley daliya</i> or any Preparation of <i>Barley</i>
Day 230	16.11.19	LMP 5.11.19	83.17 mIU/ml	Again, <i>yoga basti</i> start from 29.11.19 to 6.12.19 with <i>triphala taila</i> 60 ml for <i>Anuvasana basti</i> and <i>Arbudhara kwatha</i> for <i>Asthapana basti</i>
Day 255	11.12.19	LMP 7.12.19	1.20 mIU/ml UPT Negative	Finally, BHCG was found to be less than 1.20 mIU/ml In follow up same treatment continue for 2 months

Table 2: Ingredients of *Arbudhara kwatha*

S. No.	Name of Drug	Latin name	Part used	Quantity
1	<i>Shigru twak</i>	<i>Moringa Oleifera</i>	Bark	1 part
2.	<i>Varun twak</i>	<i>Crataeva nurvala</i>	Bark	1 part
3.	<i>Kanchnar twak</i>	<i>Bauhinia variegata</i> Linn.	Bark	1 part
4.	<i>Haridra kanda</i>	<i>Curcuma longa</i>	root	1 part

Table 3: Ingredients of *Raktaprasadaka him*

S. No.	Name of Drug	Latin name	Part used	Quantity
1	<i>Sariva kanda</i>	<i>Hemidesmus indicus</i>	Bark	1 part
2.	<i>Manjistha kanda</i>	<i>Rubia cordifolia</i> Linn	Bark	1 part
3.	<i>Kakmachi Sarvanga</i>	<i>Solanum nigrum</i> Linn	Whole plant	1 part
4.	<i>Bhumiamalaki Sarvanga</i>	<i>Phyllanthus urinaria</i>	Whole plant	1 part
5.	<i>Usheer mula</i>	<i>Vitiveria zizanioides</i> Linn	Root	1 part

Then she had complained of occasional spotting through vagina and pain in lower abdomen. So, we added *yoga basti* with *Dashmoola taila* 60 ml for *Anuvasana basti* and *Jwarahara kwatha* for *Asthapana basti* for 2 cycles in July and August. Meanwhile Beta-HCG was reducing significantly however it was raised at two or three occasion. Then treatment was changed and *Raktaprasadaka hima* 10 gm was given in empty stomach, Tab containing herbomineral drugs (*Kanchnar guggulu*, *Shweta mushali*, *Ark bhasma*, *Lavang*, *Rasa Karpura*, *Suvarna bhasma*, *Ras sindura*, *Abhraka bhasma*, *Panna bhasma*, *Hiraka bhasma*, *Tulsi*) 1 tab two times per day after meal and *yoni pichu* with *apamarga kshara taila* in 2 alternate days. Her Beta-HCG value was 13.20 mIU /ml on 12 September 2019 and 226.77 on 5 October 2019.

Then *Nidana Parivarjana* and *Prakritivighata* was done and she was strictly advised to stop non vegetarian diet, intake of fresh green leafy vegetables like *Patol*, *methi*, *palak*, *Karela*, *moong dal* and *Barley daliya* or any preparation of *Barley*. Finally, we planned for *yoga basti* on 29 November 2019 with *Triphala taila* 60 ml for *Anuvasana basti* and *Arbudhara kwatha* for *Asthapana basti*. Now Beta-HCG was finally reduced to 1.20 mIU /ml on 11/12/2019 and UPT was negative and patient got complete relief. Her follow up were taken for consecutive 3 month and Beta-HCG was found to be less than 1.20 mIU /ml and UPT was also negative.

Basti procedure

Triphala oil for *Anuvasana Basti* (60 ml) and *Arbudhara kwatha* decoction for *Niruha Basti* (350 ml), honey (30 ml), *Saindhava Lavana* (rock salt) (5 g), *Triphala* oil (60 ml), *Shatpushpa* powder (20 g).

Poorvakarma

Preparation of the patient

On each day, patient was subjected to lower part body massage with *Tila taila* for 25–30 min followed by mild fomentation for 5–10 min for 8 days. After recording the vitals, the patients were advised to lie comfortably in the left lateral position on table.

Preparation of Basti Dravya

Anuvasana Basti

Shatpushpa powder and rock salt (*Saindhava Lavana*) each 1 g is mix with lukewarm *Triphala* oil (60 ml) and is filled in syringe after that with the help of rubber tube catheter no.8 *basti* is given.

Niruha Basti

In round bowl Honey (30 ml) and rock salt (*Saindhava Lavana*) (5 g) was mixed up to disappearance of sound. Lukewarm *Triphala* oil (60 ml) was mix in it and continuous triturating done till homogenous mixture was formed.

Then, *Shatpushpa Kalka* (paste 20 g) was mixed properly in it. Afterward, lukewarm *Arbudhara kwatha* decoction (350 ml) was added in it and mix well until homogenous mixture was formed. Then filled into *Basti Putaka* (enema pot)

Pradhanakarma

Method of administration of Basti Dravya

Catheter fitted with syringe (in *Anuvasana basti*) or enema pot (in *Niruha basti*) was inserted into the anus after lubricating it with oil. Oil was pushed into the rectum when piston of the syringe was pressed slowly. Patient was advised to take deep breath until the procedure is completed. Then, the patient was advised to lie down in the supine position with hand and legs freely spread over the table. After *basti* the legs of the patient were raised for three times; the buttocks were gently tapped, simultaneously taps were given on the soles and palm also. During course of *Basti* procedure, patient was advised to take lukewarm water, avoid heavy and oily food items traveling or, heavy exercise and suppression of natural urges.

Outcome

Beta HCG was decreasing consequently and within normal range after treatment. Urine pregnancy test was also negative; relief in previous symptoms of pain in lower abdomen, Nausea, weakness. In follow up period for consecutive 3 month and Beta-HCG was found to be less than 1.20 mIU. (Table 1)

DISCUSSION

Methotrexate (MTX), formerly known as amethopterin, is a chemotherapeutic and immuno suppressant agent. It is used to treat cancer, autoimmune diseases, ectopic pregnancy and for medical abortions⁹. Common side effects include nausea, feeling tired, fever, increased risk of infection, low white blood cell counts and breakdown of the skin inside the mouth. Other side effects may include liver disease, lung disease, lymphoma and severe skin rashes¹⁰. It acts by blocking the body's use of folic acid. Although patient was explained for prognosis and advised to take methotrexate therapy, but Patient and his close family denied pursuing methotrexate, instead of that, they opted for *Ayurvedic* treatment and we started the planned treatment protocol after proper consent of patient and their family members.

Even though patient was advised to avoid sexual contact but OCP Tablet Ovuloc LD (Desogestrel (0.15 mg) + Ethinyl Estradiol (0.02 mg) was started for contraception. It is a very small dose contraceptive.

As the patient is coming with complaint of raised beta-HCG after D & C; so, she we planned for D & C again which was the line of treatment in this case. But after that procedure also beta-HCG levels not reduce. So, we manage patient with *Ayurvedic* treatment.

On the basis of symptomatology, Hydatidiform mole may resemble with *Raktaja gulma*. To keep the fact that it is a follow up case of Hydatidiform mole (*Raktaja gulma*) with the vitiation of *Pitta dosha* along with *vata* and *kapha*. We had planned *Tridosha hara* treatment protocol.

Avipatikara Churna has fourteen different ingredients which are: *Shunthi* (*Zingiber officinale* Roxb), *Maricha* (*Piper nigrum* Linn), *Pippali* (*Piper longum* Linn), *Haritaki* (*Terminalia chebula* Retz), *Vibhitaki* (*Terminalia bellerica* Roxb), *Amalaki* (*Emblica officinalis* Gaerth), *Musta* (*Cyprus rotundus* Linn), *Salt* (*Vida lavana*), *Vidanga* (*Embelia ribes* Burmf), *Ela* (*Elettaria cardamomum* Maton), *Patra* (*Cinnamomum tamala* Nees and Eberm) *Lavanga* (*Syzygium aromaticum* Linn), *Trivita* (*Operculina turpethum* Linn) and *Sharkara* (Sugar candy)¹¹. They are *Ushna* and *laghu*. They are also known to be *Pitta kapha Shamaka*. They are *Agnidipak* and *Amapachak*. It also works as *Mridu Virechan* which helps in *Rakta Shodhan* as acharya indicated laxative in *Rakta gulma*¹².

The active principles from *T. cordifolia* enhance host immune system by increasing immunoglobulin. It has *Tikta kashaya rasa* (Bitter, Astringent), *laghu, guru, snigdha guna*, (Light, Heavy, Unctuous), *ushna veerya* (Hot potency), *Madhura Vipaka, vishaghna* (Anti-toxic)¹³. It has *vata-pitta- kapha nashaka, agnideepan* properties¹⁴.

Earlier studies on *Neem* (*Azadirachta indica*) reported that plants and their constituents show inhibitory effects on the growth of malignant cells via modulation of cellular proliferation, apoptosis, tumour suppressor gene and various other molecular pathways¹⁵. *Nimbolide* a limonoid from *Azadirachta indica* inhibits proliferation and induces apoptosis of human choriocarcinoma (BeWo) cells¹⁶. Its properties are *Tikta rasa, Ruksha guna, Sheeta virya, katu vipaka, grahi* and *pittanasaka*¹⁷.

Vincaloblastine, an alkaloid originally derived from *Vinca rosea* by Cutts, Beer and Noble^{18,19} has a remarkable inhibitory effect upon the growth of human choriocarcinoma maintained in heterologous transplant in the hamster cheek pouch. *Vincaloblastine* has suppressed tumor growth and activity in five of eight women with methotrexate-resistant, metastatic trophoblastic disease²⁰. *Vinca rosea* has *laghu, ruksha guna, kashaya tikta rasa, katu vipaka, ushna virya* properties. In *Ayurvedic* classics, *sariva* (*Hemidesmus indicus*), *Manjishtha* (*Rubia cordifolia*), *bhumi amalaki* (*Phyllanthus niruri*), etc. has been reported for skin care, hepato-protective as well as cognitive enhancer. All these drugs have property of *rakta shodhana*.

Arbudhara kwatha is the preparation of NIA Pharmacy itself. It is used as antitumor and anticancer drug. (Table 4), (Table 5)

Table 4: Pharmacodynamics properties of *Arbudhara kwatha*

S. No.	Drugs	Rasa	Guna	Virya	Vipaka	Dosha karma
1.	<i>Shigru twaka</i> ²¹	<i>Madhura, Katu (Kshariya), Tikta.</i>	<i>Laghu, Ruksha, Tikshna.</i>	<i>Ushna</i>	<i>Katu</i>	<i>Kaphavata shamaka</i>
2.	<i>Varun twaka</i> ²²	<i>Tikta, kashaya</i>	<i>Laghu, Ruksha</i>	<i>Ushna</i>	<i>Katu</i>	<i>Vatashleshma hara</i>
3.	<i>Kanchnar twak</i> ²³	<i>Kashaya</i>	<i>Laghu, Ruksha</i>	<i>Sheeta</i>	<i>Katu</i>	<i>Tridosahara</i>
4.	<i>Haridra kanda</i> ²⁴	<i>Katu, Tikta</i>	<i>Ruksha</i>	<i>Ushna</i>	<i>Katu</i>	<i>Kaphapitta hara</i>

Table 5: Properties and pharmacological action of the drugs in *Arbudhara kwatha*

S. No.	Drugs	Properties	Pharmacological action
1.	<i>Shigru twak</i>	<i>Shophaghna, Sukarala, Chakshushya, Dipana, Hrdya, Rochana, Samgrahi, Vishaghna, Vataghna</i> ²⁵	Anti-histaminic, abortifacient, anthelmintic, antiseptic, aphrodisiac, astringent, cardiogenic, carminative, stomachic and tonic. It is used in general anasarca, cancerous growth, glandular diseases, intermittent fever
2.	<i>Varun twak</i>	<i>Bhedi, Dipana, Gulma hara</i>	Stomachic, laxative, antilithic, anthelmintic, bechic, expectorants; antipyretic, sedative and tonic ²⁶ .
3.	<i>Kanchnar twak</i>	<i>Dipana, Grahi, Krimighna, Kushthaghna, Gandamala nashaka, Vranaropaka, Mehaghna and Raktapitta Shamaka, Gandamala, Apachi, Vridhdihara</i> ²⁷	Anti-diabetic, anti-ulcer, antioxidant, nephroprotective, anti-cancer, hepatoprotective, anti-inflammatory, immunomodulatory, anti-microbial, anti-bacterial ²⁸ .
4.	<i>Haridra kanda</i>	<i>Krimighana, Kushthaghna, vishaghna, varnya, pramehna</i>	anti-inflammatory, antioxidant, anti-mutagenic, anti-diabetic, antibacterial, hepatoprotective, expectorant and anticancerous ²⁹

Arbudhara kwatha has *katu, tikta rasa, laghu ruksha guna, katu vipaka* and *Tridosha hara* property. It also exhibits *Amapachana, Shroto-Shodhana* and *Vatanulomana* activity which plays important role in *Samprapti-Bhanga* (to break the pathogenesis). *Katu Rasa* is formed by *Vayu* and *Agni Mahabhuta*,³⁰ and *Tikta rasa* is a combination of *Vayu* and *Akasha Mahabhuta*³¹ respectively having properties of *Deepan, Pachan, Lekhana, Kleda, Meda, Vasa, Pitta* and *Kapha shoshna*³² *Shothaghana, Kandughna* and *Upachaya-Abhishyanda-Kleda-Sneha Upahanti, Masam Vilikhati* properties³³. *Laghu, Ruksha Guna* pacifies vitiated *Kapha* and *Kleda* and supports the function of the other Rasas. *Ushna virya* directly effect on *Jatharagni* and *Dhatwagni*.

By these properties it decreases *Meda dhatu* and also prevents condition of endometrial hyperplasia; as, Beta HCG is secreted by trophoblast, so our main aim is the formation of normal endometrium and removal of trophoblast. *Lekhana* and *Arbudhara* property of *Kashaya* helps in formation of normal endometrium and thus results in reducing Beta HCG.

As *Arbudhara kwatha* possess Antitumor and Anticancer activities. It has been found that niazimicin, a thiocarbamate from *Moringa oleifera*, exhibits inhibition of tumor promote-induced Epstein-Barr virus activation³⁴. The methanol fraction of *Moringa oleifera* leaf showed hepatoprotective and anticoagulant

effect in rats. Roots have also been reported to have hepatoprotective activities³⁵. *In vitro* and animal studies indicate that the leaf, seed and root extracts of *Moringa oleifera* have anticancer, hepatoprotective, hypoglycemic, anti-inflammatory, antibacterial, antifungal and antiviral, help lower cholesterol level and promote wound healing³⁶. *Crataeva nurvala* is highly effective in lymph adenitis (*Gandamala nasan*) and immature wound healing (*Apakva Vidradhi*) etc. It has diuretic, anti-malarial, antipyretic, sedative and hepato-protective, anti-diabetic and anti-ulcer activity. *In vitro* study revealed that *Bauhinia variegata* extract showed anti-cancer activity by inhibiting the growth of these cell lines³⁷ *curcumin* affects a variety of growth factor receptors and cell adhesion molecules involved in tumor growth, angiogenesis and metastasis³⁸. *Curcumin* is known for its synergic effect as anti-cancer agent.

CONCLUSION

Management for follow up case of vesicular mole appears to be a possible, high-risk alternative to methotrexate and should only be in those women who refuse standard management of taking methotrexate. Therefore, strict patient selection is of paramount importance since it may be associated with a higher risk of morbidity. Sequential changes in serum beta-HCG and ultrasonography can be used as combined methods for the follow-up of such type of cases. *Ayurvedic* treatment regimens which possess Antitumor and Anticancer activities like *Arbudhara kwatha* are helpful in managing such type of cases. Also, there is possibility to avoid second time D & C, if we start *Ayurvedic* management soon after first D & C in such type of cases. This will also help us to avoid complication originated by invasive procedures.

Patient consent

Written consent for publication of this case study was obtained from the patient.

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