

The Safety of Hormonal Contraceptive in Post Evacuation Hydatidiform Mole (Evidence - Based Case Report)

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Abstract:

Introduction: Hydatidiform mole is a self-healing disease, totally responded after clearance of the hydatidiform mole. Effective contraceptive is necessary during observing of human chorionic gonadotrophin (hCG) levels after uterine removal for hydatidiform mole

Objective: The point of this study was known the use of hormonal contraceptive influence the reduction of hCG level in postevacuation hydatidiform mole.

Method: To answer this question, we search the evidence from PubMed data base with the keywords: "hydatidiform mole" and "contraception". PubMed was used as the electronic database to find any relevant articles that have the same inclusion criteria. The inclusion criteria were articles published in English language with human population, and last 5 years published articles. The included studies were appraised for the validity, importance and applicability.

Result: From the searching literature, the titles of the filtered results from Pubmed was screened using the inclusion criteria. A second screening was conducted by reading the abstract, and read for 4 full text articles and finally 2 article were included to be appraised.

Conclusion: The use of hormonal contraceptive had no effect hCG normalization.

Keywords: Hormonal contraceptive, hydatidiform mole, hCG level

1. INTRODUCTION

Gestational trophoblastic diseases are infrequent disease come up from gestational products. They consist of: hydatidiform mole, complete or partial; invasive mole; choriocarcinoma developing from hydatidiform mole or, more infrequently, normal gestation; and the rarest, placental site trophoblastic tumor.¹⁻³

In several studies, hydatidiform mole is a self-healing disease, totally responded after clearance of the hydatidiform mole. Effective contraceptive is important during observing of human chorionic gonadotrophin (hCG) levels after uterine removal for hydatidiform

mole (HM), to differentiate an increase hCG related to process of gestational trophoblastic disease (GTD) and product from a new gestation.⁴⁻⁶

Several studies have escalated the hypothesis that the use of hormonal contraceptive, before gestation, may increase the incidence of gestational trophoblastic tumors. Therefore, monitoring by serial confirmation of quantitative hCG levels is important for the early detection and treatment of postmolar GTN.^{1, 7, 8}

We research this hypothesis in literatures. There have been only 2 journal that knows the use of hormonal contraceptive cause the normalization of hCG level in post hydatidiform mole removal. The question formulation in this case report study is hormonal contraceptive will effect the reduction of hCG level in post removal hydatidiform mole. To answer this question, we do the searching of literature study both systematic review or meta-analysis and studies in this case. We hope that this report could be useful for obstetric and gynaecologist specialists to do in their daily practice.

2. CASE DESCRIPTION

In this case, a 15 years old, patient with chief complaint vaginal bleeding since 18 hours before admission. Patient admitted 3 month of pregnancy. LMP ~ 11 +5 wga. ANC 1 time at obgyn said hydatidiform mole then came to Public health care to got referral to hospital. Physical examination was found within normal limit except abdomen was enlarged as high as navel (not appropriate with gestational age), no tenderness. Laboratory result was found within normal limit except Beta-HCG was 957.790 IU/L.





Figure 1. Ultrasound hydatidiform mole

Ultrasound was found uterus enlargement with vesicular mass avascular size 139x 54 mm correspond to hydropic degeneration. Stratum basalis regular, no signo finvation. Endocervix and portio wnl. Both tube and ovary within normal limit. No abnormal mass in both adnexal. Conclusion: hydatidiform mole (Figure 1).

Formulate the question

Is hormonal contraceptive will influence the reduction of hCG level in post evacuation hydatidiform mole?

3. METHODS

Searching the evidences

In order to answer the question above, we did a searching in PubMed site by using two key words using hydatidiform mole and contraception. PubMed was used as the electronic database to find any relevant articles that have the same inclusion criteria. Search results were filtered by the engine according to the following criteria: articles published in English language with human population, and past 5 years published article. The included studies were appraised for the validity, importance and applicability. Due to the limitation of systematic review or meta-analysis article as the highest level in the evidence based medicine, we accepted all studies related to the topic. Search technique, result, and the inclusion and exclusion criteria are appeared in the figure 2. Figure 2 showed the flowchart of selecting articles using in the EBCR.

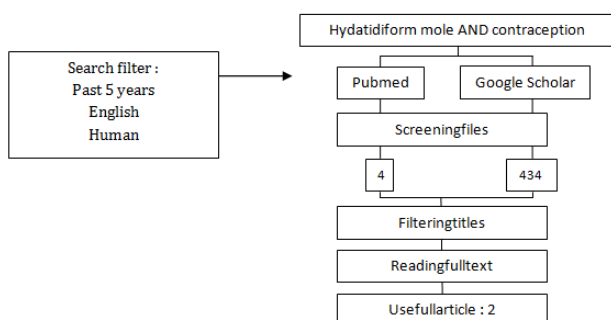


Figure 2. Flow chart of selecting articles using in EBCR

Selection

The titles of the filtered results from Pubmed was screened using the inclusion criteria. A second screening was conducted by reading the abstract, and read for four full text articles and finally 2 article were included to be appraised.

Critical appraisal

Braga A, Maesta I, Short D, Savage P, Harvey R, Secki MJ. Hormonal contraceptive use before hCG remission does not increase the risk of gestational trophoblastic neoplasia following complete hydatidiform mole: an historical database review. An international Journal of Obstetrics and Gynecology, 2016; 123: 1330-5 (Table 1).

Dantas PRS, Maestá I, Filho JR, Junior JA, Elias KM, Howoritz N, et al. Does hormonal contraception during molar pregnancy followup influence the risk and clinical aggressiveness of gestational trophoblastic neoplasia after controlling for risk factor. Gynecol Oncol. 2017;147(2):364-70 (Table 1)

Table 1. Critical appraisal

	Questions	Remark	
		Braga A. et al	Dantas PRS. et al
Validity	<ul style="list-style-type: none"> Was the diagnostic test evaluated in a representative spectrum of patients? Was the reference standard applied regardless if the index test result? Was there an independent, blind comparison between the index test and a appropriate reference (gold) standard of diagnosis? 	Yes Yes Yes	Yes Yes Yes
Importancy	What were the result?	Hormonal contraceptives is not related to development of postmolar GTN or delayedhCG remission	HC during postmolar follow-up does not show increasing the risk of GTN or its severity and does not put off the reduction of hCG levels.
Applicability	Will the result affect our management and help our patient?	Yes	Yes

4. DISCUSSION

Based on Braga research, a total of 2777 women with complete hydatidiform mole were registered during the research period; of these, postmolar hCG recovery curve information was available for 2509, the remainder already having a normal hCG as their first value following complete hydatidiform mole removal. Information about the use of hormonal contraceptive was available for 2423 (154 HC users, 2269 non-HC users), and so these were included in the following observation.⁷

Median patient age was 30 years (range 15–56). GTN needed chemotherapy, it was found in 409 women (17%), divided into low risk, 378 patient (92%) and high risk, 31 patient (8%) as previously represent and define. The proportion of patients using the all kind of hormonal preparations was as follows: combined oral contraceptive pill in 65% (100), progestogen - only pill in 28% (43), progestogen - only injectable contraceptive in 7% (11).⁷

Other demonstrates that no connection was monitored between use of hormonal contraceptive and any of the following: meanwhile to hCG remission (HC users: 12 weeks versus HC nonusers: 12 weeks, $P = 0.19$); post-CHM GTN development (HC users: 20.1% versus HC nonusers: 16.7%, $P = 0.26$); and high-risk FIGO score (HC users: 0% versus HC nonusers: 8%, $P = 0.15$).⁷

The risk of developing GTN after complete hydatidiform mole increased 3% for every 1-year increase in patient age (OR = 1.03, 95% CI = 1.02–1.04, $P < 0.001$). However, no relationship between hormonal contraceptive and GTN development was found, even when an age-adjusted model was used (OR = 1.37, 95% CI = 0.91–2.08, $P = 0.13$).⁷

The use of hormonal contraceptive had no effect on time to hCG normalization. From this literature, it give information that after 8-12 weeks hCG will reach normal level in post evacuation hydatidiform mole. The most vital finding to develop from this research is that Hormonal contraceptive use was not related to the event of postmolar GTN, a result comparable to other studies.^{1,5} Otherwise, the original Stone et al. paper, assessing the effect of the high combined oral dose of hormonal contraceptive on the post molar observation, appeared the opposite. Why is there such a distinction? The argument that Stone et al used to justify a better event of GTN in users of Hormonal contraceptive was that these contraceptive methods advanced a down regulation in the immun respond of the receptor against trophoblastic disease, producing in exacerbated cell proliferation.^{4,7,9} In any case, placental tissue and trophoblastic tumours do express estrogen receptor beta and progesterone receptors and others have appeared mitogenic effects of sex steroid hormones on

these tissues.^{2,6,10} Interestingly, recent work appears that estrogen receptor alpha (ERa) is not nuclear in GTD tissues proposing that the receptor might not be important for tumour biology.^{1,3,8} However, ERa can use tumourigenic impact in the cytoplasm and the paper did not examine estrogen receptor beta, which may also play a role in tumour biology.^{4,7,9}

Patricia Rangel Sobral Dantas research, a total 2828 patients included in this study, 95% used hormonal contraceptive and 5% used barrier methods. The use of hormonal contraceptive did not necessary effect the incident of GTN ($p=0.060$), consists of: progesterone-only ($p = 0.060$) or combined oral contraception (COC) ($p = 0.60$) or with different dosages of ethinyl estradiol: 15 mcg ($p = 0.288$), 20 mcg ($p = 0.901$), 30 mcg ($p = 0.437$) or 35 mcg ($p = 0.386$). Time to hCG reduction ≥ 10 weeks ($p = 0.071$) or time to remission with chemotherapy ≥ 14 weeks ($p=0.067$) did not necessary differ among hormonal contraceptive users when compared to patients using barrier methods.¹

To avoid undesirable gestation during therapy, patients should use contraceptive advice. The use of Hormonal contraception is enable for patients with molar gestation and must be began soon after evacuation. Because about 12–23% of the patients found new gestation through chemotherapy. This study shows that the rates of new gestation among women using barrier methods are numerously higher than those using hormonal contraceptive, explicitly showing the benefits of hormonal contraceptive for patients with molar pregnancy and postmolar GTN.¹

5. CONCLUSION

Hormonal contraceptive is not related to development of postmolar GTN or delayed time to hCG reduction. The use of Hormonal contraceptive had no effect on time to hCG normalization. Because of this, hormonal contraceptive can be safely used for hydatidiform mole regardless of hCG level.

REFERENCES

- [1] Dantas PRS, Maestá I, Filho JR, Junior JA, Elias KM, Howoritz N, et al. Does hormonal contraception during molar pregnancy follow-up influence the risk and clinical aggressiveness of gestational trophoblastic neoplasia after controlling for risk factors? *Gynecol Oncol.* 2017;147(2):364-70.
- [2] López CL, Lopes VGS, Resende FR, Steim JL, Padrón L, Sun SY, et al. Gestational Trophoblastic Neoplasia after Ectopic Molar Pregnancy: Clinical, Diagnostic, and Therapeutic Aspects. *Rev Bras Gynecol Obstet.* 2018;40(5):294-9.
- [3] Simon DA, Smith AL, Holzhauser JR. Case Report of an Ectopic Molar Pregnancy in the Presence of an Intrauterine Device. *WMJ.* 2017;116(4):215-7.

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- [4] Royal college of obstetricians and gynaecologists. The management of gestational trophoblastic disease. Green-top guideline no 38. 2010.
- [5] Çekmez Y, Haberal ET, Ulu L, Gülşen S. Hormonal contraceptive use before hCG remission does not increase the risk of gestational trophoblastic neoplasia following a complete hydatidiform mole: a historical database review. BJOG. 2016;123(10):1706.
- [6] Joneborg U, Folkvaljon Y, Papadogiannakis N, Lambe M, Marions L. Temporal trends in incidence and outcome of hydatidiform mole: a retrospective cohort study. Acta Oncol. 2018;16:1-6.
- [7] Braga A, Maesta I, Short D, Savage P, Harvey R, Secki MJ. Hormonal contraceptive use before hCG remission does not increase the risk of gestational trophoblastic neoplasia following complete hydatidiform mole: a historical database review. An international Journal of Obstetrics and Gynecology. 2016;123:1330-5.
- [8] Coyle C, Short D, Jackson L, Sebire NJ, Kaur B, Harvey R, et al. What is the optimal duration of human chorionic gonadotrophin surveillance following evacuation of a molar pregnancy? A retrospective analysis on over 20,000 consecutive patients. Gynecol Oncol. 2018;148(2):254-7.
- [9] Hardman S. Use of hormonal contraception after hydatidiform mole. An international Journal of Obstetrics and Gynecology. 2016.
- [10] Mulisya O, Roberts DJ, Sengupta ES, Agaba E, Laffita D, Tobias T, et al. Prevalence and Factors Associated with Hydatidiform Mole among Patients Undergoing Uterine Evacuation at Mbarara Regional Referral Hospital. Obstet Gynecol Int. 2018;1(9561413).