African Journal of Health Issues
Open access
Original Research
eISSN: xxxx- xxxx

Gestational Trophoblastic Diseases: Alternatives to Biological Monitoring in Under-resourced Settings (Two clinical observations)

Joseph B. Nsambi [1], Olivier Mukuku [2], Xavier K. Kinenkinda [1], Jean-Baptiste S. Kakoma [1]

[1] *Département de Gynécologie-Obstétrique, Faculté de Médecine, Université de Lubumbashi, Lubumbashi, République Démocratique du Congo.*
[2] *Institut Supérieur des Techniques Médicales, Lubumbashi, République Démocratique du Congo.*

Abstract
Gestational trophoblastic disease (GTD) is a condition requiring regular monitoring of hormone human chorionic gonadotropin (HCG). The semi-quantitative method presented here is an alternative for monitoring in under-equipped environments. The illustration made from two clinical cases of GTD that we have followed shows that this method can be used in under-equipped settings and where the quantitative dosage is unavailable.
Keywords: *Gestational trophoblastic disease, Biological monitoring*

Maladie trophoblastique gravidique : alternative pour une surveillance biologique dans les milieux sous-équipés (illustration par deux observations cliniques)

Résumé
La maladie trophoblastique gravidique (MTG) est une affection qui nécessite une surveillance régulière de l'hormone chorionique gonadotrope humaine (HCG). La méthode semi-quantitative que nous présentons constitue une alternative pour une surveillance dans les milieux sous-équipés. L'illustration faite à partir de deux cas cliniques de MTG que nous avons suivi montre que cette méthode peut être utilisée dans les milieux sous-équipés et où le dosage quantitatif est indisponible.
Mots-clés : Maladie trophoblastique gravidique, Surveillance biologique.

Introduction

Gestational Trophoblastic Disease (GTD) includes a broad spectrum of pathologies ranging from benign pre-cancerous lesions (complete or partial hydatidiform mole) to malignant lesions (invasive mole, gestational chorio-carcinoma and tumor of the placental implantation site) [1]. The above mentioned malignant lesions are also known as gestational trophoblastic tumors (GTT); these can metastasize and be fatal if untreated [2,3]. All these forms of GTD have one common denominator, which is a hypersecretion of hormone human chorionic gonadotropin (HCG).

Hence, careful monitoring is essential in the treatment of GTD and requires regular monitoring of HCG to detect abnormal changes. HCG is the main marker in diagnosing and monitoring the evolution of GTD [4].

This work aims to propose alternatives to monitoring the evolution of GTD in under-equipped environments where the quantitative dosage is inaccessible.

Description of the method

The method presented here is a semi-quantitative method based on qualitative HCG assays of urine. We employed the qualitative method due to the excessive and prohibative costs of the laboratory equipment required to take quantitative (serum or urinary) in Lubumbashi. We conducted our study at the University Clinics of Lubumbashi in the Democratic Republic of Congo (DRC). Patient 1 was admitted in September 2012 and Patient 2 was admitted in March 2013.

Correspondence:
Joseph B. Nsambi, Département de Gynécologie-Obstétrique, Faculté de Médecine, Université de Lubumbashi, Dem. Rep. of the Congo.
Telephone: 00243971566607 - Email: josephnsambi@gmail.com
Manuscript received: 12-09-2017 **Accepted**: 25-10-2017
Published: 02-11-2017

Citation: Nsambi JB, Mukuku O, Kinenkinda XK, Kakoma JB. Gestational Trophoblastic Diseases: Alternatives to Biological Monitoring in Under-resourced Settings (two clinical observations). Afr J Health Issues. 2017 Nov 1; 1:4. DOI: https://doi.org/10.26875/ajhi112017iv

We used the pregnancy test strip, which is a rapid qualitative test (RQT), to selectively detect the presence of HCG in urine samples. This test has a sensitivity of 25 mIU/mL. At the sensitivity threshold indicated, the test strips show no cross-reaction with glycoproteins of related structure Follicle Stimulating Hormone (FSH), Luteinizing hormone (LH) and Thyroid Stimulating Hormone (TSH) [4].

Patients' urine was collected in a sterile container. We conducted a RQT in freshly collected urine (FCU). If the urine returned positive to presence of HCG, we switched to RQT in diluted urine. That is to say, we combined 1 mL of FCU with a very precise amount of solvent (tap water). The amount of solvent revealed which fraction of the solution the RQT is positive or negative. We commence by using 1 mL of FCU diluted in 100 mL of water (1/100). Depending on whether the RQT is positive or negative, we gradually increase or decrease the solvent to obtain the fraction by which the solution gives a negative RQT. To conclude, if a fraction is negated, three successive RQTs must be made for this fraction which will be the starting point for the next dosage.

We collected weekly doses of HCG levels until three successive negative tests are obtained, followed by six successive monthly negative tests indicating a good evolution.

The advantages of this method compared to the quantitative method are mostly in terms of efficiency since the majority of the population in DRC lives below the poverty line and thus it is difficult to obtain quality care:

- It may be practiced by any medical personnel.
- It can be carried out in any environment (rural or urban).
- This method costs less than 2 USD (for 5-10 RQT), while the price of a quantitative assay varies between 25 and 50 USD (prices given by three laboratories where this dosage is possible in the city of Lubumbashi).

Clinical observations

Patient 1

Mrs. C.K, aged 19, (P0G2A2, two spontaneous abortions) consulted the Gynecology-Obstetrics Department as she was in a state of genital haemorrhage. Clinical features (amenorrhea, exacerbation of parasympathetic signs, and increase of uterine volume) and paraclinic (positive HCG assay and ultrasound) led us to conclude a complete hydatidiform mole. We used evacuating curettage and subjected the patient to methotrexate and folic acid. Before treatment, we conducted a RQT that had negated at a fraction of 1/30. After initiating treatment, we began with the weekly beta-HCG control by the method we have described (fractional dilution of urine). One week after the first RQT, the second RQT was negative at 1/17. The details are shown in *figure 1*.

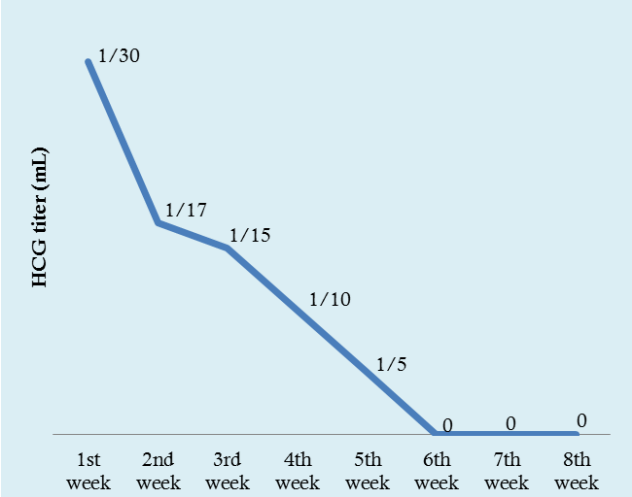

Figure 1: Urinary Assay for Patient 1

Patient 2

Mrs. F.M, aged 38, (P4G5A1D0), had a history of a complete hydatidiform mole (dating back 15 months). The post-molar sequences were marked by a negative beta-HCG assay after curettage administered with methotrexate. The patient had not been followed-up after hospitalization. She consulted after 24 hours of pain. After a full clinical examination (rapid positive pregnancy test and liquid effusion on ultrasound), we concluded that it was ruptured ectopic pregnancy and an emergency exploratory laparotomy was performed. This procedure revealed a haemoperitoneum, ruptured spleen and the presence of a small fleshy mass in the left iliac fossa covered in blood. A splenectomy was performed and the anatomopathological analysis of the surgical specimens (spleen and fleshy mass) concluded a metastatic choriocarcinoma.

Afterwards, we performed a uterine biopsy curettage, the pathological examination of which revealed the existence of a gestational choriocarcinoma. The patient was treated with methotrexate and folic acid. Weekly biological monitoring by the beta-HCG urine assay was initiated and showed a perfect regression curve as soon as treatment was initiated *(figure 2)*.

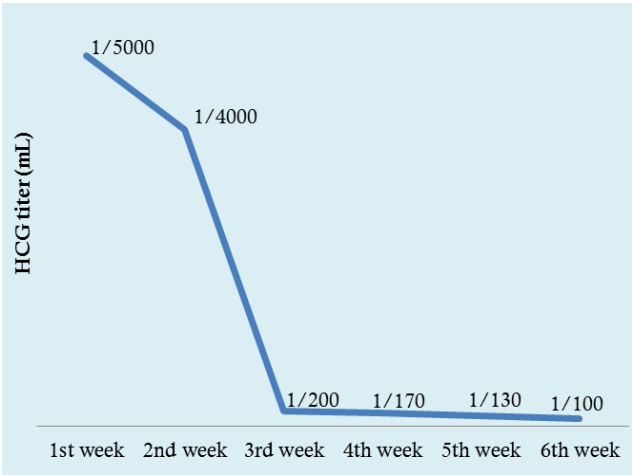

Figure 2: Urinary Assay for Patient 2

African Journal of Health Issues Afr. J. Health Issues. 2017; 1(1): 4. DOI: https://doi.org/10.26875/ajhi112017iv

Comments

Gestational trophoblastic tumors (GTT) result from abnormal proliferation of different types of trophoblastic cells. All trophoblastic tumors, benign or malignant, secrete the beta-fraction of hormone human chorionic gonadotrophin (beta-HCG), whose plasma or urine level is proportional to the tumor volume. This rate constitutes the basis for the biological monitoring of these diseases [4,5].

HCG evolves in the same way as blood and urine; the free beta chain evolves in blood like HCG. In the case of molar pregnancy, the evolution of serum concentrations of HCG is anarchic with values five to 10 times higher than expected, or even higher in some cases (in the case of a complete mole, the values may be greater than 1 million mIU/mL). The total HCG and the beta-HCG subunit are elevated, with the beta-HCG/HCG ratio increasing in proportion to the invasiveness of the tumor. The percentage of beta-HCG is between 0.05 and 1% during normal pregnancies; it varies from 1 to 5% in the case of molar pregnancy (benign mole) and exceeds 5% in the case of choriocarcinoma [5].

GTD are less frequent, but potentially devastating diseases, occurring in women of childbearing age. GTD management involves uterine evacuation with chemotherapy and regular monitoring of serum and/or urinary levels of HCG [6, 7]. After uterine evacuation, the level of HCG decreases gradually to negative in less than 12 weeks [8]. Surveillance is initially performed by weekly dosing up to the negativity of three normal successive dosages, then monthly for one year and quarterly for the second year. A significant increase in HCG levels leads to the malignant degeneration of a mole or the occurrence of metastases in the case of choriocarcinoma [8].

This biological monitoring in GTDs is performed with the quantitative determination of beta-HCG, which is expensive and not available in DRC. Thus, we have been able to use the semi-quantitative method which is an alternative for under-equipped environments. This method, which is performed regularly, gives an evolutionary curve *(figures 1 and 2)* showing the elevation or fall of the HCG level during a treatment of GTD and makes it possible to conclude whether it is a good or bad evolution.

The purpose of regular monitoring during GTD is to confirm the success or failure of the treatment, but also to identify women with persistent GTD who may require adjuvant chemotherapy or surgery. Although it is semi-quantitative, the method makes it possible to use the criteria based on the HCG assay established by the International Federation of Gynecologists and Obstetricians (FIGO) to diagnose a persistent GTD [9]:

• A plateau of HCG level of four values ± 10% recorded over a period of 3 weeks (days 1, 7, 14 and 21).

An HCG level increasing by more than 10% of three values recorded over a period of two weeks (days 1, 7 and 14).

• HCG persistence detectable for more than six months after molar evacuation.

But it will be necessary to emphasize the importance of associating with this biological surveillance, clinical and medical imaging (ultrasound) because the positivity of the tests of the HCG can also be found outside a pregnancy context (end-stage renal failure) [10].

Conclusion

This semi-quantitative method is a simple and less costly way to monitor GTD. Using this method in under-equipped settings would allow better biological monitoring of patients and reduce mortality associated with GTD in developing countries.

Competing interests

The authors do not declare any competing interests.

Author contributions

All authors participated in the design of the study, data acquisition, analysis and interpretation of results, in the review of the literature and editing of the manuscript.

List of Acronyms

DRC	: Democratic Republic of the Congo
FCU	: freshly collected urine
GTD	: Gestational Trophoblastic Disease
GTT	: Gestational Trophoblastic Tumors
HCG	: hormone human chorionic gonadotropin
IU	: international unit
mL	: milliliters
RQT	: rapid qualitative test

References

1. Shanbhogue AK, Lalwani N, Menias CO. Gestational trophoblastic disease. Radiologic Clinics 2013; 51(6): 1023-1034. PubMed | Google Scholar
2. Directives cliniques de la SOGC. Maladie trophoblastique gravidique. J Obstet Gynaecol Can 2002; 24(5):441-6. . PubMed | Google Scholar
3. World Health Organization. Gestational trophoblastic diseases. Technical Report Series 692. Geneva: WHO, 1983. . Google Scholar
4. Vuong PN, Guillet JL, Houissa-Vuong S, Lhomme C, Proust A, Cristalli B. Pathologie des tumeurs trophoblastiques gestationnelles Gynécologie obstétrique & fertilité 2000; 28 (12): 913-926. Google Scholar | Crossref
5. Brown J, Naumann RW, Seckl MJ, Schink J. 15 years of progress in gestational trophoblastic disease: Scoring, standardization, and salvage. Gynecologic Oncology 2017; 144: 200–207. PubMed | Google Scholar | Crossref

6. Hanna RK, Soper JT. The Role of Surgery and Radiation Therapy in the Management of Gestational Trophoblastic Disease. The Oncologist 2010; 15: 593–600. PMC | Google Scholar | Crossref

7. Tse KY, Chan KKL, Tam KF, Ngan HYS. Current management of gestational trophoblastic disease. Obstetrics, Gynaecology and Reproductive Medicine 2014; 25:1. Google Scholar | Crossref

8. Khabouze S, Erchidi IE, Bouchikhi C, Chahtane A, Kharbach A, Chaoui A. Les maladies gestationnelles trophoblastiques : à propos de 105 cas. Gynécol Obstét Fertil 2002; 30: 42-9. PubMed | Google Scholar | Crossref

9. Kohorn EI. The new FIGO 2000 staging and risk factor scoring system for gestational trophoblastic disease: description and clinical assessment. Int J Gynecol Cancer. 2001; 11: 73-7. PubMed | Google Scholar

10. De Backer B, Goffin F, Nisolle M, Minon JM. Élévation faible d'hCG en dehors d'un contexte gravidique: à propos de deux cas et revue de la littérature. Ann de Biol Clin (Paris). 2013; 71 (4): 496-502. PubMed | Google Scholar | Crossref