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CONFEZIONI

- **meclon** *crema vaginale*
- **meclon** *ovuli*
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ALFA WASSERMANN

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Editorial

The New version of Italian Journal of Gynaecology and Obstetrics on WEB

P. Scollo

As SIGO President and Editor in Chief of the IJOG, I am proud to inform you that since the present issue of this officially historical SIGO magazine will be published on the web, we decided to preserve its characteristical format of the blue banner and SIGO Logo. This unique feature which is also on the printed version of the magazine has been familiar to all of us and has characterized it for so many years. The magazine will be on line and part of a website. This complete online transition to is due to the fact that we intend to make the Italian Journal more accessible, easier to read and consult not only for Italian readers but particularly for an International audience. The journal will bring the latest information in the field of Gynaecology and Obstetrics to Italian Gynaecologists and at the same time the best way to present Italian Gynaecology and Obstetrics to the world. Therefore, the first step in this project was to move from a traditional printed magazine to an online web issue through a web-site. At the same time, the Editorial Board has been completely renewed: two Editors (Prof. Herberth Valensise and Prof. Enrico Vizza) will coordinate the team of referees of both AOGOI and AGUI. The magazine has been registered by the Istituto Superiore di Sanità (ISS) and will soon be indexed. New sections will be created such as: Hot Topics, Case Reports, Reports from International Congresses and, News on International Guide-lines.

Many others measures will be taken in order to improve the diffusion of the Italian Journal. First of all, at the next SIGO Congress in Cagliari, the 10 best original presentations will be selected by the members of SIGO Board and the author will be invited to publish their work in the Italian Journal. In addition, every year a monographic number covering one of the Hot Topics on Ostetrics or Gynaecology with national and international expert in the field will be published.

This is an ambitious project aiming to transform our prestigious and historical Journal into a modern one, which is the perfect way for exchanging scientific knowledge between Italy and the rest of the World.

This will not be possible without your contribution.

President S.I.G.O.
Prof. Paolo Scollo

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Editorial

The gynecologist and the future, the future of the gynecologist: the importance of the medical culture

N. Surico

Our work is constantly evolving and only research and continuous updating can improve the quality of the healthcare. For this reason, the society's commitment to promote the updating is the continuous scientific research.

In the field of obstetrics the continuous renewal of the techniques of fetal chromosomal diagnosis through mother blood sample is radically changing the approach of the couples that call the obstetrician for an evaluation of the fetal well-being during pregnancy. Its effectiveness, in terms of sensitivity and specificity of true positives and true false, seems to be confirmed by the most recent scientific publications. However, while the scientific community proceeds carefully, discussing and questioning, looking for consolidated scientific certainty before opening up to new methods, the speed of direct information that internet and the websites allow is by far exceeding what societies can establish with difficulty through consensus and panel discussions. The couples go to the doctor and ask the doctor if the news found in forums are true or not, or if the reason is only of commercial interest. Doctors cannot be unprepared about the new requests of information and advice, and societies cannot be unprepared about evolution in knowledge that travel at unthinkable speeds for the slow 'rhythm' of our meetings, roundtables, and recommendations made.

Even in the gynecological field the evolution of the knowledge and the use of drugs for the treatment of benign diseases is changing significantly the need of updating. If we just think about the recent experience about the treatment of endometriosis or uterine fibroid therapy we can see that two cornerstones of laparoscopic and laparotomy surgery are tackled with other non-invasive methods, with more selectively medical therapy. The need to expand the case studies in international studies is certainly a duty before a final evaluation, but the ability to be able to assess the woman with the advantages and disadvantages of these new techniques of treatment and care is essential. Even in the gynecological field the slow pace of the society decisions is exceeded by the speed of information that the network gives to users, with the advantages and disadvantages of the uncritical information contained. The strength of the scientific information provided by a scientific society to its members is to argue scientifically against data collected superficially by the media tam tam.

Finally an important role in the future of our scientific societies is to defend our members from regulatory aspects, insurance and legal protection point of view. The crux of compulsory insurance and insurance agencies 'cartel' that put insurance premiums ever higher, unattainable for anyone not only for our fellow neo specialist, can only be solved with a direct and immediate effect on parliament and parliamentary committees that need to legislate. The absence of remuneration limit for single harmful event that cannot depend from unpredictable judgment of single judges, makes this matter even more difficult and tricky. The recent strike action we made is the first act of protest needed to be heard by the Institution. Today, our voice, is even stronger for our Presidency in the Italian College of Surgeons, CIC, that counts more than 45,000 surgeons working in hospitals and universities.

In this perspective, SIGO continues to support the reorganization of the birth centers in an exclusive attempt to improve the quality of the work of its members and the safety of mothers and infants. A safe birth center with right organic for the amount of work to be performed and an appropriate structure is the first point of defense for the quality of work of the gynecologists and for their legal protection. In this sense, many birth centers were unified despite understandable local resistance, but unacceptable for a health system offered to the citizens to whom optimal security parameters must be given.

Similarly the SIGO commitment is to complete and continually update the ministerial regulations related to the availability of guidelines to follow in the clinical practice. Even the availability and

usability of these documents for everyone has, in ultimate end, the protection of quality of work and serenity of its members.

I spent three intense years at the SIGO chair with a very efficient Executive Board, who was leader in a very successful global event.

Surely we could have done more, but many things have been done on behalf of and for the cultural growth of the Italian gynecology.

In my opinion there has been a real renaissance of SIGO that is beginning to deliver, and while saying goodbye to you with warm greetings, I do hope that the new President Prof. Scollo will continue the journey begun in these years, and so clearly traced.

To him and to all the new Executive Board I wish a very good job.

Past President S.I.G.O.
Prof. Nicola Surico

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Planned pregnancy termination and secondary hysterectomy at 15 weeks for fetal anomaly in a previously untreated Uterine Arteriovenous Malformation
A case report

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ABSTRACT

BACKGROUND. uterine arteriovenous malformation (AVM) is a rare finding, typically evolving over time. Hormonal changes or trauma often stimulate its evolution. Pregnancy and related surgical procedures are two important evolving factors.

CASE. A 37 years old woman gravida 3-para 0, had to terminate her third pregnancy due to a fetal anomaly at 14 weeks and 5 days of gestation in 2013. In 2009 after a vaginal bleeding, RMN and TC had diagnosed an uterine AVM. She had previously received two dilatations and curettage for *spontaneous abortions and an operative hysteroscopy for septate uterus. Preoperative arterial selective embolization was performed, in order to avoid excessive blood loss during termination and a hysterectomy was performed according to patient's desire to avoid major complications and new pregnancy.

CONCLUSION. Fertile patient women affected by AVM should receive appropriate counseling and, treatment, when requested by the woman, should be envisioned before new conception.

Key-words: Uterine Arteriovenous Malformation – Pregnancy - Selective Embolization

RIASSUNTO

ANTEFATTO. Le malformazioni arterovenose (MAV) dell'utero sono reperti rari, che tipicamente progrediscono nel tempo. Modificazioni ormonali o traumatismi locali spesso inducono e stimolano l'evoluzione di tali lesioni. La gravidanza e le procedure chirurgiche ad essa collegate rappresentano due importanti fattori scatenanti.

CASO CLINICO. Nel 2013 una donna di 37 anni gravida 3, para 0, si trovò costretta ad interrompere la sua terza gravidanza per un severa anomalia fetale a 14 settimane + 5 giorni. Nel 2009 in occasione di un imponente evento meno-metrorragico, le era stata diagnosticata una malformazione arterovenosa dell'utero, tramite Risonanza Magnetica (RM) e Tomografia Assiale Computerizzata (TC). In precedenza la paziente era stata sottoposta a due isterosuzioni seguite da revisone della cavità uterina e ad una metroplastica isteroscopica per utero setto. Prima di procedere all'intervento è stata effettuata un'embolizzazione selettiva per limitare le perdite ematiche durante la procedura di interruzione e l'isterectomia programmata, in accordo con la paziente per evitare successive e più gravi complicanze in occasione di ulteriori gravidanze.

CONCLUSIONI. Al momento della diagnosi di una MAV uterina, le pazienti in età fertile dovrebbero ricevere un adeguato counseling ed un appropriato trattamento prima di rimanere nuovamente in stato di gravidanza.

Parole chiave: Malformazione Arterovenosa Uterina – Gravidanza – Embolizzazione Selettiva

INTRODUCTION

Uterine Arteriovenous Malformations (AVM) may be either congenital or acquired. Congenital AVM are very sporadic, but some mutations have been identified in systemic vascular malformations syndrome, such as Hereditary Hemorrhagic Telangectasia (ALK-1 and endoglin)[1,2,3]. Acquired AVM are usually post instrumental such as diagnostic curettage or curettage for abortion or post partum procedures, caesarian delivery, surgical trauma but also are linked to gestational trophoblastic disease, diethylstilbestrol exposure, endometrial, cervical cancer and conservative procedures such as embolization for placenta percreta[4,5,6]. An AVM consists of supplying arteries bypassing the capillary bed and draining veins. Typically lesions start with minimal shunting but time and traumatic or hormonal stimulation make it evolve to active shunting with venous engorgement and venous hypertension. Extensive vaginal bleeding with negative beta-H CGC along with a history of any uterine instrumentation are strongly evocative of a uterine AVM. Also post partum or

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post abortion hemorrhages, typically worsened by curettage, could be signs of a hidden uterine AVM. Trans-vaginal color Doppler US shows dilated vascular channels within the myometrium characterized by high velocity, low resistance and multidirectional flow. MR and TC can show these vascular anomalies perfectly. MR angiography and angio-TC with 3D reconstructions are useful in demonstrating the extension and vascular anatomy of the lesions[7]. As angiography has been the gold standard for the diagnosis of AVM for a long time, this procedure now has to be considered as the first step of a therapeutic embolization, avoiding two endovascular approaches. Embolization has gained increasing acceptance as first line treatment option, and is preferred to more invasive solutions like selective uterine artery ligation or hysterectomy. Also expectant management or medical therapies are available alternatives. Management of uterine AVM should be individualized, depending on hemodynamic stability and the patient's desire to preserve fertility. This report describes complications which occurred in a pregnant woman with a previously diagnosed untreated symptomatic uterine AVM.

CASE REPORT

In February 2013, a 37 years old woman, gravida 3-para 0 had to terminate her pregnancy for an serious fetal malformation diagnosed at the end of the first trimester. In 2002 and 2004 she had received two dilations and curettage for spontaneous abortions. In September 2008, an operative hysteroscopy was carried out to treat her septate uterus. In December 2008, the patient was hospitalized for two days in an intensive care unit, for massive menorrhagia, requiring uterine tamponade, bladder catheterization with compressive balloon and blood transfusions. As ultrasonography showed vascular malformation of myometrium, medical therapy with Gn-RH analogues was started.

An MRI and a CT in February and September 2009 confirmed the diagnosis, showing a vascular arteriovenous malformation within the right, anterior and fundic myometrial wall, reaching the endometrium and involving ipsilateral uterine vessels (Figure 1). In November 2012, she spontaneously achieved a twin pregnancy. Since uterine AVM was still present, the mother was counseled about risks related to both pregnancy and delivery. Initially, she wanted to go on with pregnancy but first one twin vanished and then a large omphalocele was found in the surviving fetus, at 13 weeks of gestation. Angio-CT was repeated showing evolution of uterine AVM (Figure 2). Before terminating pregnancy, after informed consent was obtained, angiographic selective catheterization and embolization of the right ovarian artery and the right uterine artery was performed in order to avoid hemorrhagic complication during surgical procedures. A large vascular anomaly was seen during caesarean delivery in right large ligament. As previously planned with the patient, after fetal and placental removal, a subtotal hysterectomy, with conservation of both, andrexa was performed. Histological examination of the uterus showed chorionic villi deeply cleaving the right uterine wall near the tubal ostium and numerous vessels in the right myometrium and surrounding tissues. Placenta was characterized by maturational and morphostructural changes. Autopsy confirmed severe fetal malformation.

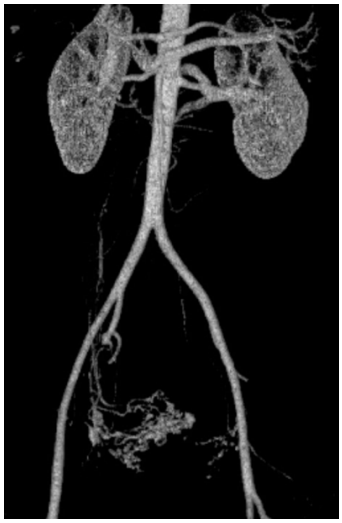
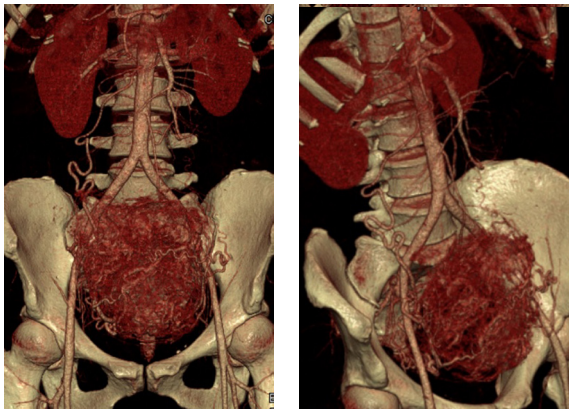


Figure 1.
3D-angio CT reconstruction of an performed in 2009 in non-pregnant condition, shows uterine AVM originating from the right uterine and ovary arteries.



Figures 2a-b.
3D-angioCT reconstruction at the 14th week of gestation in the same patient shows the evolution of the uterine AVM and typical vascularization in pregnant condition.

DISCUSSION

Uterine AVM's true incidence is unknown. These rare vascular anomalies have been reported in both adolescence and in menopause, but they predominantly occur in women of reproductive age. As in the present case, its most frequent clinical presentation is menorrhagia or menometrorrhagia, requiring blood transfusion in 30% of reported cases[8].

Curettage is the most frequent cause of an acquired uterine AVM 4, even if any uterine trauma could lead to this pathology. In particular, in the present case, operative hysteroscopy could induce AVM since inset of menorrhagia was reported two months after hysteroscopic procedure.

To date, few cases of uterine AVMs in pregnant women have been described.

Most of these were related to primary or secondary post-partum hemorrhages, either from term deliveries[9,10,11, 12], or after procedures for second trimester termination of pregnancies [13, 14].

Also massive uterine bleeding at 8 gestational weeks, requiring hysterectomy with bilateral salpingo-oophorectomy has been described[15].

In 1995 Simpson reported an acute abdomen secondary to a rupture of a uterine AVM in the peritoneal cavity, with severe fetal distress at 38 weeks. Both mother and neonate survived[16].

A recurrence of a previously treated uterine AVM was reported in a pregnancy with pre-term labor and forceps vaginal delivery of a healthy child at 34 weeks of gestation[17].

In two cases of uterine AVMs, one congenital[3] and the other acquired[18], conservative management of pregnancy ended in both good fetal and maternal outcomes.

One bilateral uterine artery embolization, during an ongoing pregnancy of 20 weeks of gestation has been described. At 35 weeks a repeat cesarean delivery was performed without any complications[19].

Although literature suggests that Uterine AVMs' behavior is unpredictable during pregnancy, potentially life-threatening conditions are frequently reported. The hormonal changes during pregnancy seem to make the lesion evolve[20]. Therefore when diagnosed, spontaneous or therapeutic resolution of the lesion is advocated before pregnancy.

In our case, placentation was strictly connected to vascular lesion, as shown by histological examination. This could represent a negative prognosis factor for uterine AVM evolution during gestation and for failure of conservative management. Castro et al, in their case report described "always normal myometrium between the AVM and placenta".

If diagnosed in asymptomatic women, uterine AVM resolves spontaneously in a high percentage of cases, so in stable women, especially if asymptomatic, expectant management may have a role[21].

If bleeding is not severe, long term medical management with methilergonovine, estrogen and progestin or Gn-RH agonist[22], could stop the bleeding and make the AVM disappear, with possible subsequent pregnancies[23, 24, 25].

In the presence of recurrent or severe bleedings, or instable hemodynamic conditions, angiographic arterial embolization is currently the treatment of choice, with several cases of successful deliveries[26, 27, 28, 29, 30, 31, 32].

In the present case, after acute treatment in December 2008, medical therapy with Gn-RH analogues stopped bleedings, but did not induce regression of AVM. Also three years of expectant management did not work. This lesion most probably worsened during this pregnancy, as at its beginning in November 2012, it was certainly present. Considering the motherhood desire of this woman, even in the absence of clinical manifestations, an angiographic selective embolization before pregnancy should have been attempted.

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Sulphadoxine-Pyrimethamine and the prevalence of malaria (in blood and placenta) among booked women who have completed intermittent preventive treatment in Zaria, northern Nigeria

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ABSTRACT

INTRODUCTION. Malaria is currently regarded as the most common and potentially the most serious infection occurring in pregnancy in sub Sahara African countries.

OBJECTIVE. The objective of this study was to look at Sulphadoxine pyrimethamine and the prevalence of malaria (in blood and placenta) among booked women who had completed intermittent preventive treatment in Zaria, Nigeria. To determine the prevalence of malaria at booking, peripheral blood & placenta parasitaemia of those who had completed Intermittent Preventive Therapy and compare the sensitivity of placental tissue biopsy and peripheral blood smear method for the diagnosis of malaria infection at delivery.

METHOD. The study took place in ABUTH Zaria. It was a longitudinal study of 108 consecutive mother-baby pair who had antenatal care and delivered during the study period of seven months. Participants were enrolled from the booking clinic of ABUTH Zaria. A structured questionnaire was administered to obtain information about the socio-demographic factors and other relevant information about the participants. Base line packed cell volume as well as blood film for malaria parasite was done at booking. They received 2 adult doses of SP orally as direct observation therapy (DOT) during clinic visits. They also received routine haematinics and continued with their routine antenatal visits. At delivery, blood smear for malaria parasites was prepared from maternal peripheral blood and Placental biopsy was examined for malaria pigments and parasites. Gestational ages at delivery as well as the weight of the infants were recorded. The packed cell volume of the parturient was determined at delivery.

RESULTS. The prevalence of malaria parasitaemia at booking was 36.1%. The prevalence of malaria parasitaemia after completion of IPT with SP was 25.9% and 16.6% in peripheral blood and placenta tissue biopsy respectively. By simple proportion, peripheral blood smears method was more sensitive than placental tissue biopsy in the diagnosis of malaria infection at delivery.

There was no significant difference in peripheral parasitaemia before and after administration of IPT with SP. The prevalence of maternal anaemia (pcv<30%) was 8.3%, while that of preterm delivery (GA<37weeks) was 3.7%. No infant was born with a birth weight of less than 2500g.

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RIASSUNTO

INTRODUZIONE. La malaria è attualmente considerata come l'infezione più comune e potenzialmente più grave che si verifica in gravidanza nei paesi africani subsahariani.

OBIETTIVO. L'obiettivo di questo studio era di esaminare la Sulphadoxine pirimetamina e la prevalenza della malaria (nel sangue e nella placenta) tra le donne reclutate che avevano completato il trattamento preventivo intermittente a Zaria, Nigeria. Per determinare la prevalenza della malaria al momento del reclutamento, sangue periferico e parassitemia placentare di coloro che avevano completato la Terapia Preventiva Intermittente e confrontare la sensibilità della biopsia del tessuto placentare e del metodo di striscio di sangue periferico per la diagnosi di infezione da malaria al momento del parto.

METODO. Lo studio ha avuto luogo in ABUTH Zaria. E' stato uno studio longitudinale di 108 coppie consecutive madre-bambino sottoposte a cure prenatali e che hanno partorito durante il periodo di studio durato sette mesi. I partecipanti sono stati arruolati dall'ospedale di ABUTH Zaria. Un questionario è stato somministrato per ottenere informazioni sui fattori socio-demografici e altre informazioni pertinenti sui partecipanti. L'ematocrito di base così come per la ricerca del parassita della malaria sullo striscio di sangue è stato fatto al momento del reclutamento. Hanno ricevuto 2 dosi per adulti di SP per via orale come terapia osservazionale diretta (DOT) durante le visite cliniche. Hanno inoltre ricevuto ematinici di routine e hanno continuato con le loro visite prenatali di routine. Al parto, la ricerca del parassita della malaria sullo striscio di sangue è stato effettuato da sangue periferico materno e la biopsia placentare è stata esaminata per i pigmenti e i parassiti della malaria. Età gestazionale al parto e peso dei neonati sono stati registrati. L'ematocrito della partoriente è stato determinato al momento del parto.

RISULTATI. La prevalenza della parassitemia malarica al reclutamento era del 36,1%. La prevalenza della parassitemia malarica dopo il completamento della IPT con SP è stata del 25,9% e del 16,6% rispettivamente nel sangue periferico e nella biopsia dei tessuti della placenta. Con una semplice proporzione, la ricerca del parassita sullo striscio di sangue periferico è risultata essere una metodica più sensibile della biopsia del tessuto placentare nel diagnosticare l'infezione malarica al momento del parto.

Non vi era alcuna differenza significativa nella parassitemia periferica prima e dopo la somministrazione di IPT con SP. La prevalenza di anemia materna (PCV <30%) è stata del 8,3%, mentre quella da parto pretermine (GA <37 settimane) è stato del 3,7%. Nessun bambino è nato con un peso alla nascita inferiore a 2500g.

CONCLUSIONE

IPT con SP riduce la prevalenza di parassitemia periferica e

CONCLUSION. IPT with SP reduces the prevalence of peripheral and placental parasitaemia and improves pregnancy outcome. However, this is based on simple proportions, it was statistically insignificant.

Key-words: sulphadoxine-pyrimethamine, malaria, placenta, blood, parsitaemia, prevalence.

placentare e migliora l'esito della gravidanza. Tuttavia ciò è basato su semplici proporzioni ed è stato statisticamente insignificante.

Parole chiave: sulphadoxine-pirimetamina, malaria, placenta, sangue, parassitemia e prevalenza.

INTRODUCTION

Falciparun malaria in pregnancy is an important cause of maternal and perinatal morbidity and mortality in areas where malaria is endemic. Pregnant women in malaria endemic areas may experience a variety of adverse consequences from malaria including anaemia and accumulation of parasites in the placenta. The outcomes of placental invasion by parasites, inflammatory cells and cytokines include: abortion, premature labour, small-for-date babies, congenital malaria and foetal/maternal death in some instances. This unfavourable pregnancy outcomes in the mother and in her baby[(1)] is the reason why this condition need to be treated and prevented as a matter of routine in all women at risk of infection[(2)]. Because of the consequences of Plasmodium Falciparum infection during pregnancy, the world health organization (WHO) recommends that women living in malarious areas receive chemoprophylaxis during pregnancy[(3)]. Since, Schultz and colleagues[(4)] demonstrated the efficacy of SP in decreasing placental malaria, SP is still the drug of choice for prophylaxis in pregnancy. IPT for preventing malaria reduces the incidence of maternal anaemia, spontaneous abortion, preterm birth, still birth and low birth weight. The aim of this study was to look at SP and the prevalence of malaria parasitaemia (in blood and placenta) of booked women who had completed intermittent preventive therapy in Zaria, Nigeria.

This study was carried out at Ahmadu Bello University Teaching Hospital Zaria.

Zaria is one of the major cities in Kaduna state of Nigeria. The ABUTH Zaria serves as a tertiary/ referral health facility for Zaria and its environs.

SUBJECTS AND METHODS

Participants were enrolled from the booking clinic of ABUTH Zaria. Booked women in their index pregnancy who were between 16 and 24 weeks gestation were enrolled, those excluded from the study included those with sickle cell anaemia, HIV positive women, previous adverse reaction (hypersensitivity) to Sulphonamides, multiple gestations and those who did not give their consent.

Eligible participants were required to give informed verbal consent after explanation of study procedures. Enrolled participants completed the routine ANC measurements, examinations and investigations. Gestational age was ascertained by last menstrual period and abdominal palpation. A questionnaire was administered to collect information about the socio-demographic factors and other relevant information about the participants. A finger stick blood sample was drawn for packed cell volume and malaria thick blood smear. They received 2 adult doses of SP orally by (DOT) during clinic visits administered by the supervision of midwives and recorded in subjects ANC case notes and signed. Antenatal records of subject were stamped for easy identification during delivery and the use of SP was confirmed from it. The first dose of SP was given in the second trimester and the second dose was given in the third trimester at least four weeks apart up to 34 weeks gestation. All participants of this group received Sulphadoxine Pyrimethamine obtained from the hospital pharmacy. The same batch was used. Each dose of SP consists of 3 tablets containing 500mg of sulphadoxine and 25mg of pyrimethamine per tablet. They also received prescription for folic acid and iron supplements and continued with their routine antenatal visits. Participants who developed malaria during the study period were treated with Artemisinin/ Lumefantrine combinations and noted. Case definition of malaria in this study was defined as the participants who develop fever, headaches, joint pains, nausea/vomiting in the absence of other causes of the above symptoms with or without peripheral malarial parasitaemia. At delivery, thick and thin film for malaria parasites was prepared from maternal peripheral blood and placental impression smear (within 1 hour of delivery). Placental biopsy was examined for malaria pigments and parasites. Gestational age at delivery as well as the weight of the baby was recorded. The packed cell volume of the parturient was determined again. Babies were weighed to the nearest gram using a weighing scale (Way Master, made in England.) and for the purpose of this

study; LBW was defined as neonatal birth weight less than 2,500 g. Babies born before 37 weeks of gestation were considered pre-term while those born after 37 weeks of gestation and above were considered term, while a packed cell volume reading of <30% in the parturient was considered as anaemia.

LABORATORY PROCEDURE

Maternal peripheral venous blood (2 ml) was collected by venopuncture within 24 hours of parturition and used to prepare thick blood films. Immediately following delivery, the placenta was obtained and a small piece of placental tissue (2 by 2 by 1 cm) was excised from the centre of the placenta and fixed in 10% neutral buffered formalin for histopathological studies. Fixed placental biopsies was processed, embedded in paraffin wax and sectioned onto slides by standard techniques. Sections were stained later with haematoxylin-eosin stain for analysis. Microscopic examination of blood smears was done under oil immersion for parasite detection. When no parasite was found, 200 high power fields were examined before the smear was considered negative. Parasites were counted against 200 leucocytes assuming an average leukocyte count of 8,000 per microlitre of blood[5]. Placental histological sections were examined by a Histopathologist without knowledge of the blood film microscopy results. One thousand intervillous cells (IVS) were counted to determine the level of parasitaemia in placenta tissue sections. Past infection was defined as the presence of malaria pigment in fibrin or monocyte/macrophage without malaria parasites[6]. Sections were observed under light microscopy to assess the presence of malaria pigment[7].

The packed cell volume (PCV) was determined using blood collected into heparinized capillary tubes and spun with a Hawksley micro-hematocrit centrifuge for 5 minutes and read using the heamatocrit reader. Haemoglobin concentration was calculated from PCV values as described by Topley[8].

STATISTICAL ANALYSIS

Data obtained were analyzed using SPSS version 15.0. Frequencies and percentages were presented in tables and charts, statistical significance of differences between qualitative variables was tested using Chi Square and level of significance was set at $p < 0.05$. P. falciparum infection was defined as the presence of malaria parasites as detected in thick peripheral blood or placental tissue sections. Malaria infection on placental tissue section was defined as positive, only when active infection was found (presence of infected erythrocyte in the intervillous space).

RESULTS

During the period of the study, a total of 150 participants who fulfilled the inclusion criteria were recruited. Out of these, 22 (14.6%) did not come for delivery, placenta biopsy was not taken in 12 (8%) clients and the other 8 (5.3%) has no blood sample taken for malaria parasitaemia. Only 108 results were analysed. All the infant birth weight were 2500g and above. One client had intra-uterine foetal death at term. She had a positive malaria parasite at booking but negative at delivery both in the peripheral blood and placenta. The birth weight was 2500g. One hundred and five (97.3%) delivered after 37 weeks gestation while 3 (2.7%) delivered below 37 weeks gestation.

Table I shows the socio-demographic profile of the client. They were between ages 19 and 41 years with a mean age of 27.75 years. primigravidae were 35.2%, multipara constituted 40.7% and grandmultips 11.1% percent.

Figure 1.
PCV at Booking and at Delivery.

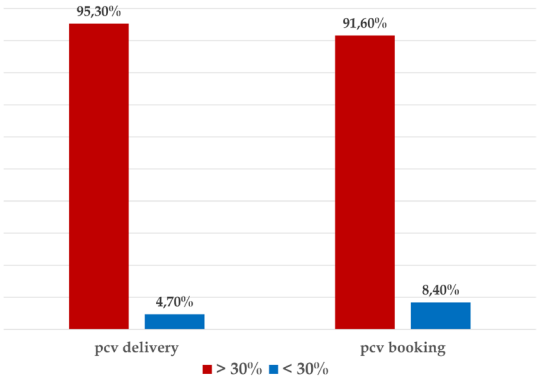

Table II shows symptomatic malaria among clients at booking. During the first visit, 2 client (1.9%) compliant of headache/fever, 1 (0.9%) compliant of dizziness/weakness and another 1 (0.9%) had joint pains and 2 (1.9%) were pale. These patients were treated with Artemisinin/ Lumefantrine combination and they had their 2 doses of SP at the scheduled intervals. Only one

Table I.
Socio demographic profile of clients.

Characteristic	Frequency	Percentage
Age		
<20	4	3.7
20-29	62	61.4
30-39	39	36.1
>40	3	2.8
Parity		
0	38	35.2
1	14	13.0
2-4	44	40.7
≥ 5	12	11.1
Marital Status		
Single	6	5.6
Married	102	94.4
Educational Status		
Quranic	3	2.8
Primary	8	7.4
Secondary	37	34.3
Tertiary	60	55.6
Occupation		
House Wife	56	51.9
Business	13	12.0
Civil Servant	27	25.0
Religion		
Islam	75	69.4
Christianity	32	29.6
Other	1	0.9
GA at booking		
<20 weeks	15	14.2
20-24 weeks	93	86.1

Table II.
Symptomatic malaria among clients at booking.
Relevant history

	Frequency	Percentage
Symptoms		
Headache/fever	2	1.9%
Dizziness/weakness	1	0.9%
Joint pains	1	0.9%
None	104	96.3%
Signs		
Pallor	2	1.9%
None	106	98.1%

client (0.9%) took quinine after completion of SP.

Figure 1 show PCV at booking and at delivery. Ninety-nine of the client (91.6%) had a PCV of greater 30% at booking, while 103 (95.3%) had a PCV of greater than 30% at delivery.

Figure 2 shows result of Malaria Parasitamia. At booking 39 (36.1%) of the participants had positive malaria parasitaemia in their blood, at delivery this figure was reduced to 28 (25.9%). For placental parasitaemia, 18 (16.6%) was positive at delivery.

Table III shows results of sensitivity (by simple proportion) of placental tissue biopsy and peripheral Blood smear methods for the diagnosis of malaria at delivery. At delivery the peripheral blood detected 25.9% of malaria parasitaenia while the placental tissue biopsy detected 16.6%. By this simple proportion, peripheral blood smears method was more sensitivity than placental tissue biopsy in the diagnosis of malaria infection at delivery.

Table IV shows relationship between sensitivity of placental tissue biopsy and peripheral blood smear at delivery. The sensitivity of placental tissue biopsy was 16.6% and that of Malaria Parasitamia at delivery was 25.9%. The P value was 0.0000 and this was statistically significant

Figure 2.
Result of Malaria Parasitamia.

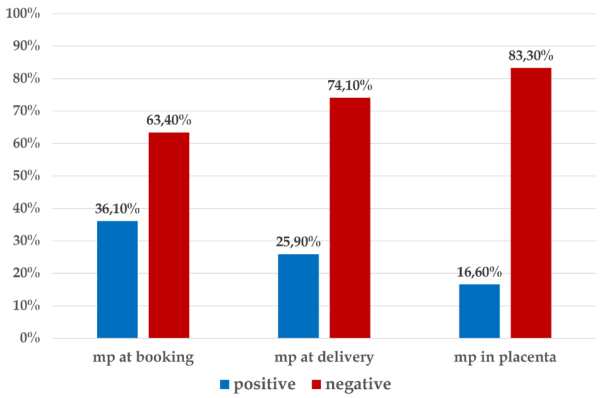

Table V shows the relationship between malaria parasitaemia in the peripheral blood before and after administration of SP. Before administration of SP (at booking), 39 of the participants had positive malaria parasitaemia in their blood, after administration of SP (at delivery), 28 of the participant had positive malaria parasitaemia in their blood. The P value was 0.138 and this was not statistically significant.

DISCUSSION

The prevalence of malaria at booking was 36.1%. This figure was lower than 58% reported by Nwagha et al.[9] and 59.9% reported by Ogbodo et al[10]. Nnaji and colleagues[11] has reported a

Table III.
Results of sensitivity (by simple proportion) of placental tissue biopsy and peripheral Blood smear methods for the diagnosis of malaria at delivery

	Positive	Negative	Total
Placental tissue biopsy	18 (16.6%)	90 (83.3%)	108
Peripheral Blood Smear	28 (25.9%)	80 (72.1%)	108
Total	46	170	

Table IV.
Relationship between sensitivity of placental tissue biopsy and peripheral Blood smear at delivery

		Placental parasitaemia		Total
		Positive	Negative	
Peripheral parasitaemia at delivery	positive	12	16	28
	negative	16	74	80
	Total	18	90	108

Pearson's chisquare ($\chi 2$) = 18.669, df=1, P-value=0.0000
This was statistically significant

Table V.
Relationship between malaria parasitaemia in the peripheral blood before and after administration of SP

		Malaria parasitaemia after SP		Total
		Positive	Negative	
Malaria parasitaemia before SP	positive	13	26	39
	negative	15	54	69
	Total	28	80	108

Pearson's chisquare ($\chi 2$) = 1.744, df=1, P-value=0.138
This was not statistically significant

prevalence rate as high as 79.3%. The prevalence rate less than 36.1% gotten in this study have been reported in various studies. Taye and colleagues[12] reported a prevalence rate of 34.2% while Nwonwu and colleagues[13] reported a prevalence rate of 29%. Prevalence rate as low as 2.9%, 4.8% and 8.4% have been reported by Laminkara[14], Isah et al[15] and Falade et al[16] respectively. It is worthy to note that there is a wide variation in prevalence rate of malaria at booking and this is not related to the sample size. Isah et al[15] have speculated that the group of pregnant women selected (symptomatic or asymptomatic) and the sampling method used might have contributed to this. Perhaps, the pattern of malaria (stable or unstable) in that region and the period of the year in which the study was conducted might also influence the prevalence.

The prevalence of malaria after completion of IPT with SP was 25.9%. There was a reduction in peripheral malaria parasitaemia from 36.1 to 25.9%. Bako et al[17] reported peripheral malaria parasitaemia of 28.8% after sp with reduction in peripheral parasitaemia from 60.3% to 28.8%. Challis et al[18] reported an incidence of 6.3% of peripheral parasitaemia after SP with a reduction from 30.6% to 6.3%.

The prevalence of placental parasitamia was 16.6%. This value was more than 13.8% and 10.4% reported by Van Ejik et al[19] and Falade et al[20] respectively. Other workers have reported higher incidence of placental parasitaemia on histology. Shulman et al[21], Okoko et al[22] and Judith et al[23] reported incidences of 64%, 51% and 60.4% respectively. A higher incidence of placental parasitaemia was reported by these authors because they recorded both active and past placenta infection as positive, while this study as well as those by Van Ejik et al[19] and Falade et al[20] only reported active placental infection. Also, they were not strict on whether their subjects took SP or not. By summing up active and past placental infections, the percentage of positivity will be higher for placental parasitaemia relative to peripheral blood parasitaemia and this is what was done and reported by those three authors[21,22,23]. In this study, the past placental infection constituted 18.5% (20/108), but it was not added to active placental infection (but rather counted as negative) since the study was looking at the prevalence of malaria parasitaemia in blood and placental after the completion of IPT with SP. Counting past infection as positive does not reflect drug use. If past placental infection were added to active infection, it will give a prevalence rate of 34% which is higher than that of peripheral blood. Since there is no means of diagnosing past infection in peripheral blood yet, it will fair to use the same yard stick of measurement.

The prevalence of malaria parasitaemia in the peripheral blood (25.9%) was higher than that of placental parasitaemia (16.6%) and this result was statistically significant attesting to the fact that the peripheral blood smear method was more sensitive that the placental tissue biopsy. The peripheral blood smear method has the advantage of being cheaper, easier or quicker (within an hour) to perform and requires less training compared to placental histology which is more expensive, takes days to perform and requires technicalities with high expertise which are not widely available.

The result of peripheral parasitaemia before and after the administration of SP showed a

reduction from 36.1% at booking to 25.9% at delivery; this result however, was not statistically significant, but the resultant effect of SP was a reduction in malaria parasitaemia.

CONCLUSION AND RECOMMENDATION

In conclusion, the prevalence of malaria parasitaemia in the peripheral blood and placental tissue reduced with IPT using SP though this effect was not statistically significant. SP use also improved pregnancy outcome. By simple proportion, peripheral blood smear method was more sensitive than placental tissue biopsy in the diagnosis of malaria infection at delivery.

While the use of SP for IPT may suffice for now, there is a need for further research in other to revalidate or invalidate the efficacy of SP or to consider combination therapy or a newer drug.

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I want to declare that no any special interest in this study or any clash of interest what so ever (either financially or otherwise).

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A Conservative Protocol for the Management of Postpartum Hemorrhage. Evaluation of its effectiveness in high risk patients

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ABSTRACT

Aim: In the present study a conservative management protocol to treat postpartum hemorrhage (PPH) in high risk patients with the diagnosis of placenta previa major is reported.

Materials and methods: Retrospective analisys of 55 patients with placenta previa major who underwent cesarean section, treated with the following protocol: preliminary prophylactic transfemoral/transhomeral catheterization, cesarean section, use of multiple square endouterine hemostatic sutures, application of an intrauterine Bakri balloon combined with B-Lynch suture and devascolarizating ligature/selective embolization of the uterine arteries followed by hysterectomy in case of failure.

Results: In four cases we used selective embolization of the uterine arteries (7.2 %). In three cases, we performed hysterectomy (5.4 %). Fourteen patients (25.4%) underwent blood transfusion. Four patients (7.3%) were admitted to the general intensive care unit for one day.

Conclusions: We evaluate the effectiveness of the use of this protocol which could represent the leading treatment option of PPH in these high risk patients.

Key words:
Postpartum hemorrhage, conservative protocol, uterine sandwich technique.

RIASSUNTO

Obiettivo dello studio: In questo studio abbiamo descritto un protocollo conservativo per il trattamento dell' emorragia post-partum in pazienti ad alto rischio emorragico, con diagnosi di placenta previa major.

Materiali e metodi: Si tratta di uno studio retrospettivo su 55 pazienti con diagnosi di placenta previa major, sottoposte a taglio cesareo e trattate con tale protocollo: preliminare cateterizzazione profilattica transfemorale/transomerale, taglio cesareo, utilizzo di suture quadre endouterine a scopo emostatico, applicazione intrauterina di Bakri balloon combinata con sutura di B-Lynch e legatura devascolarizzante/ embolizzazione selettiva delle arterie uterine seguita da isterectomia in caso di fallimento di tale strategia.

Risultati: In quattro casi è stata utilizzata l'embolizzazione selettiva delle arterie uterine (7,2%) . In tre casi è stata effettuata l'isterectomia (5,4 %). Quattordici pazienti (25,4 %) sono state sottoposte a trasfusioni di sangue. Quattro pazienti (7,3 %) sono state ricoverate in unità di terapia intensiva generale per un giorno.

Conclusioni: Valutando la reale efficacia dell'utilizzo di tale protocollo, possiamo affermare che questo potrebbe rappresentare una opzione terapeutica per il trattamento dell'emorragia postpartum nelle pazienti ad alto rischio.

Parole chiave:
Postpartum hemorrhage, conservative protocol, uterine sandwich technique.

INTRODUCTION

Postpartum hemorrhage (PPH) is the leading cause of maternal death worldwide. In addition to death, serious morbidity may follow[1].

PPH is commonly defined as an estimated blood loss of more than 500 ml after vaginal delivery or more than 1000 ml after cesarean section; however assessment of blood loss is often inaccurate[2]. The severity of the bleeding can be rapidly evaluated using the ACOG scheme, which provides 4 degrees of progressive severity (Table I).

Table I.
ACOG scheme to evaluate the severity of the bleeding.

CLASS I	**Compensated**	**Blood loss between 500-1000 ml**
CLASS II	**Slight**	**Blood loss between 1000-1500 ml**
CLASS III	**Moderate**	**Blood loss between 1500-2000 ml**
CLASS IV	**Severe**	**Blood loss between 2000-3000 ml**

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All pregnancies are at risk of PPH[4], but the main causes are represented by placenta previa/accreta, retention of placental cotyledons or flaps, lacerations of the soft tissues of the birth canal, uterine atony, uterine rupture and coagulopathies.

Several maternal factors, play an important role as risk factors such as maternal age, multiparity, multiple pregnancy, obesity, previous episodes of PPH, protracted and/or precipitous labor, abnormal placentation, operative delivery and previous cesarean sections.

The risk of maternal death, in fact, doubles if the woman has more than 35 years; moreover the cesarean section is associated with maternal death three times more than natural childbirth.

Placenta previa is the main condition related to the risk of severe hemorrhage. According to the last RCOG guideline, placenta previa (placenta inserted wholly or in part into the lower segment of the uterus) can be classified in major previa if the placenta lies over the internal cervical os, and minor or partial praevia if the leading edge of the placenta is in the lower uterine segment but not covering the cervical os[5].

One of the most dreadful complications of placenta previa is its association with accretism. This pathological condition is characterized by the invasion of placental trophoblast into the endometrium beyond the Nitabuch's layer due to a defect in the decidua basalis. If the trophoblast invades the myometrium or the serosa, placenta increta or percreta respectively are defined[5, 6]. The frequent association between placenta previa and accretism is related to a greater maternal morbidity and mortality[6].

According to the Italian Guidelines (Italian National Institute of Heath – National System of Guidelines: SNLG-ISS) on cesarean section (January 2012), placenta previa represents an indication for cesarean delivery and must be performed in a tertiary level hospital to manage possible fetal-maternal emergencies, in order to reduce perinatal/maternal mortality and morbidity[7].

The treatment of massive PPH can be summarized in two points: replacement of circulating blood volume to maintain perfusion and tissue oxygenation; stop the bleeding by treating the causes or using surgical procedures.

Treatment options of PPH during cesarean section provide, first of all, conservative management: uterotonic drugs, external compression with specific uterine sutures (B-Lynch, Hayman, Cho), intrauterine packing and selective devascularization by ligation or embolization of the uterine arteries or of the internal iliac arteries in relation to the amount of bleeding and to the success of procedures to reduce bleeding. Failure of these options necessitates hysterectomy[2].

Uterine compression sutures and balloon tamponade can be combined to apply pressure synergistically to both surfaces of the myometrium and this procedure has been described as effective in cases of persistent uterine atony and massive hemorrhage[8].

The aim of the study is to report our experience with a conservative management protocol to treat PPH in cases of high risk patients with the diagnosis of placenta previa major. The presents conservative approach is characterized by a philosophy of liberal use of resources and treatment options/devices with the contemporary involvement of all professionals in a multidisciplinary approach.

MATERIALS AND METHODS

Retrospective analisys of 55 patients with placenta previa major who underwent cesarean section at the Maternity Hospital of Perugia between January 2009 and June 2012 were carried out. The patients were included in a diagnostic-therapeutic protocol for the prevention and management of PPH that consisted in a conservative procedure managed by a multidisciplinary team including gynecologists, anesthesiologists, interventional radiologists, blood bank, central laboratory, midwives and, in few cases, urologists and general surgeons.

The main aspects of this organizational model were: extensive information and discussion with the patient and the couple of issues related to risk factors; presence of interventional radiologists in the surgery room; temporary clamping of uterine vessels before placental delivery; systematic association of B-Lynch suture and Bakri balloon application.

The diagnosis of placenta previa major was based on clinical findings, sonography and on Magnetic Resonance Imaging (MRI), planned at 32-34 weeks of gestation.

The patients were adequately hydrated during the 4 hours before intervention (1000 ml of saline solution 4 hours before the surgery and 1000 ml 1 hour before) and were wearing support stockings. Central venous catheter (CVC) positioning was applied before surgery. Cells separator, 4 blood bags (2 ready for use and 2 in standby) and portable digital angiography were available in the operating theatre. Radiolucent operating

table, medical thermal blankets and lead aprons were used for the procedure. Positioning of the graduate sterile bag was aimed to the evaluation of the blood loss during cesarean section.

The protocol for management of PPH used in our institution is shown in Figure 1 and can be briefly summarized as follows: preliminary prophylactic transfemoral/transhomeral catheterization using 5 french catheter. (This step was not applied in case of urgency and/or emergency);

Delivery of the fetus, administration of oxytocics (carbetocine) within one minute, temporary clamping of uterine arteries by ring forceps, followed by placental delivery. Multiple square endouterine hemostatic sutures[2] (Affronti's sutures). Their application (on the anterior or posterior uterine wall) was related to the prevalent site of bleeding. Preparation of B-Lynch compressive sutures. Application of hydrostatic balloon (Bakri balloon) and partial filling with 30-60 ml of saline solution. Hysterorrhaphy. Repositioning of uterus followed by hydrostatic balloon inflation with a maximum of 400 ml (depending on the size of the uterus) and B-Lynch ligature, finally further inflation of 100 ml of saline solution in the Bakri balloon.

When required, especially in case of previous cesarean section, surgical sealants were used.

In case all the previous maneuvers failed, devascolarizating ligature/selective embolization of the uterine arteries was performed.

When even the previuos described procedures failed, hysterectomy were done.

Maternal hematologic parameters monitorin was carried out 24 hrs before cesarean section and 2 hrs after the procedure, then every 2-4 hrs for the following 24 hrs, in relation to clinical conditions/ blood loss and, finally, at 48 hrs.

Blood transfusion was performed only in case the hemoglobin values dropped above 7 g/dl and/or hematocrit value was less than 21%.

Bakri balloon was removed 24 hrs from delivery, 30 minutes after rectal administration of misoprostol 400 mcg.

RESULTS

The average age of the patients and gestational age at delivery was 35.6 years and 36.0 weeks respectively. The range of parity was 0 - 3 and the number of previous cesarean sections was 1 in 13 cases and 2 in 5 cases. Placenta was suspected to be accrete in 13 cases (23.6%).

In four cases we used selective embolization of the uterine arteries (7.2 %).

In three cases, it was necessary to perform hysterectomy (5.4%). In two of the three cases, due to a massive blood loss, hysterectomy was performed immediately after extraction of fetus and placental delivery.

In one case even if embolization of uterine arteries were performed, the bleeding did not stop, and therefore hysterectomy and following embolization of internal iliac arteries was done due to massive bleeding from implants of pelvic endometriosis.

Fourteen patients (25.4%) underwent intraoperative or postoperative blood transfusion. Four patients (7.3%) were admitted to the general intensive care unit for one day, due to postoperative hemodynamic instability (Table II).

Table II.
Main procedures applied in cases of massive bleeding.

Procedures	%
Embolization	7.2
Hysterectomy	5.5
Blood transfusion	25.4
General intensive care unit	7.3

The mean surgery time was 46 minutes. All patients received oxytocics (carbetocin) and prostaglandins (misoprostol). Hematologic parameters were checked postoperatively and at 2 days (Table III). The mean estimated blood loss was 1640 cc (range: 900-4200 cc).

The mean hospital stay was 6 days. Eighteen patients (32.7%) experienced complication as fever (mean body temperature 38°C) within 48 hrs from cesarean section. Intravenous antibiotic therapy was administered to all patients.

DISCUSSION

The present study updates our previous experience[2] published in 2010 in evaluating the effectiveness of a conservative management protocol in placenta previa.

The diagnosis of placenta previa was carried out by ultrasound and confirmed by MRI. Esakoff et al demonstrated that ultrasound examination is a good diagnostic tool to evaluate accretism in women with placenta previa. The importance to make a correct diagnosis is related to the significantly increased risk of patients with accretism[6]. Otherwise Derman et al[9] identified the most sensitive MRI signs of accretism and proposed criteria for the classification of invasive placentation with abnormal placental vascularity.

A massive obstetric hemorrhage, resulting

Table III.
Hematologic values (preoperative, postoperative and at two days) of PPH cases.

	Preoperative	Postoperative (6 hrs)	At 2 days	Δ Mean Preoperative-postoperative *(range %)*	Δ Mean Preoperative-2 days *(range %)*
HCT, %	**33.50**	**27.89**	**28.24**	**-5.61** *(-15.4 to -0.6)*	**-5.26** *(-11.9 to -0.3)*
HGB, g/dl	**11.14**	**9.46**	**9.43**	**-1.68** *(-12.7 to 0)*	**-1.71** *(13 to -0.3)*
RBC, 10^6 g/dl	**3.88**	**3.32**	**3.42**	**-0.56** *(-4.26 to 0)*	**-0.46** *(-4.19 to 0.05)*
PLT, 10^3 g/dl	**208.73**	**182.27**	**212.88**	**-26.46** *(-179 to 4)*	**-4.15** *(-225 to 5)*

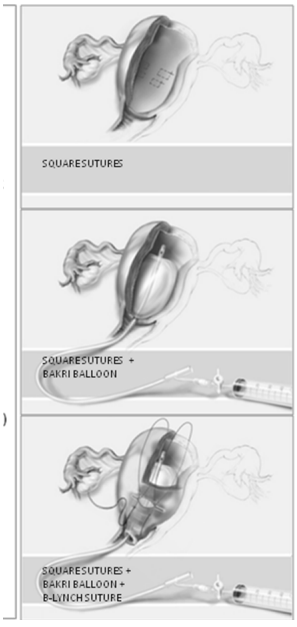
from the failure of normal obstetrical, surgical and/or systemic hemostasis, has been estimated, from a recent review, to be responsible for 25% of maternal deaths worldwide each year [10] and uterine atony is an indication for emergency peripartum hysterectomy in 20.6% to 43% of the cases[11]. This is the reason why primary prevention of PPH begins with an assessment of identifiable risk factors.

Abnormal placentation includes a group of important conditions at risk not only of severe hemorrhage with maternal complications comprising maternal death, but also of neonatal sequel and/or death[6,12].

The aim of the management of PPH is to apply conservative intervention and use the hysterectomy as the last possible treatment option.

In our protocol (Figure 1), the first step of the conservative management is the use of uterotonics. We supported the use of carbetocin associated with misoprostol. Carbetocin is a long-acting oxytocin agonist; with respect to oxytocin, it shows higher elimination half-life (40 min vs 5 min) and higher duration of action (5 hrs vs 1.5 hrs). Moreover, in comparison to oxytocin, it is associated with reduced need for additional oxytocics and uterine massage. That is why it appears to be the drug of choise for the prevention/treatment of PPH[13,14].

Misoprostol, an E1 prostaglandin analog, has been explored as an alternative due to its ability to induce uterine contractions, low cost, stability at room temperature and ease of administration.



CONSERVATIVE MANAGEMENYT PROTOCOL

1-Preliminary prophylactic transfemoral/transhomeral catheterization using 5 french catheter. This is the only step that was not applied in case of urgency and/or emergency;
2-Delivery of the fetus, administration of oxytocics (carbetocine) within one minute, temporary clamping of uterine arteries by ring forceps, followed by placental delivery;
3-Multiple square endouterine hemostatic sutures (Affronti's sutures)[2]. Their application (on the anterior or posterior uterine wall) was related to the prevalent site of bleeding;
4-Preparation of B-Lynch compressive sutures;
5-Application of hydrostatic balloon (Bakri balloon) and partial filling with 30-60 ml of saline solution;
6-Hysterorrhaphy
7-Repositioning of uterus with
a-Hydrostatic balloon inflation with a maximum of 400 ml (depending on the size of the uterus)
b-B-Lynch ligature, followed by further inflation of 100 ml of saline solution in the Bakri balloon.
When necessary, especially in case of previous cesarean section, application of surgical sealants
8-If these maneuvers failed, the next step was the devascolarizating ligature/selective embolization of the uterine arteries.
9-If all the above described procedures failed, hysterectomy

Figure 1
Scheme of the protocol

There is now good evidence that justifies its use for PPH[15].

The "uterine sandwich" technique is a combination of external (B-Lynch suture) and internal (Bakri balloon) uterine compression for simultaneously applying pressure to both surfaces of the uterine wall. There is evidence that the application of this method is an effective tool to treat uterine atony and PPH, avoiding in most cases hysterectomy[2,8,16,17]. The present protocol, provides the combination of the "uterine sandwich" technique with Affronti endouterine sutures, to achieve hemostasis at the site of placental insertion in the lower uterine segment[2]. The application of the above described approach is in sequential steps and it is characterized by the wide use of technical and professional resources.

In the present series, we had a very low incidence of embolization of the uterine arteries (7.2%), internal iliac arteries (1 case), hysterectomy (5.4 %), intraoperative or postoperative blood transfusion (25.4%) and admission to the general intensive care unit (7.3%). It is also to note that the potential main complication of embolization, i.e. uterine necrosis[18], was not observed in our cases.

All pregnancies were at risk of PPH. The management was finalized mainly to preserve the patient's life and it was influenced by other considerations such as desire to preserve fertility. It highlights the pressing need for research and for clinical audit focusing on etiological factors, preventative measures and quality of care, to guide current clinical practice[19]. A conservative management should represent the leading aim for treatment of PPH in high risk patients with placenta previa major and/or with other risk factors. The results of the present conservative protocol was encouraging and suggested that all tertiary level obstetric units should have the facilities, professionals and equipments in place to manage properly such emergency[1].

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Postpartum pubic symphysis diastasis: a case report and review of literature

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ABSTRACT

BACKGROUND: Symphysis pubis diastasis is defined as an abnormally wide gap of more than 10 mm between the two pubic bones. The present report describes a case of woman who experienced a symphysis pubic diastasis.

CASE: Following delivery, a 38-year-old gravida 3 para 0 at 41,5 weeks gestation complained of severe pain in the symphysis pubic region. We formulated the suspect diagnosis of pubic symphysis diastasis, that was confirmed by an anterior – posterior pelvic x–ray, which showed a pubic separation of 16 mm. We decided to perform a conservative approach and patient was discharged from hospital 1 week after delivery. One month later she was seen at the outpatient clinic. Assessment by the orthopaedic team found her to be in good health. The obtained results were considered successful.

CONCLUSION: It is important for physicians and other health care providers involved in the care of pregnant women to be aware of symphysis pubis diastasis as a potential complication.

Keywords: pubic symphysis diastasis, pubic symphysis, pregnancy complication, diastasis, post partum

RIASSUNTO

BACKGROUND: la diastasi sinfisi pubica è definita come un anomalo ampio divario di più di 10 mm tra le due ossa pubiche. Il presente relazione descrive uno caso di donna che ha sperimentato una diastasi sinfisi pubica.

CASO: A seguito del parto, una donna di 38 anni gravida 3 para 0 a 41,5 settimane di gestazione lamentava forti dolori nella regione sinfisi pubica. Abbiamo formulato la diagnosi di sospetto di diastasi sinfisi pubica, che è stato confermata da un x-ray antero-posteriore del bacino, che ha mostrato una separazione pubica di 16 mm. Abbiamo deciso di effettuare un approccio conservativo e la paziente è stata dimessa dall'ospedale 1 settimana dopo il parto. Un mese dopo è stata vista in ambulatorio. La valutazione da parte del team ortopedico è stata di essere in buona salute. I risultati ottenuti sono stati considerati ottimi.

CONCLUSIONE: È importante per i medici e gli altri operatori sanitari coinvolti nella cura delle donne incinte di essere a conoscenza della diastasi sinfisi pubica come potenziale complicazione.

Parole chiave: diastasi sinfisi pubica, sinfisi pubica, complicazione della gravidanza, diastasi, post parto

INTRODUCTION

Symphysis pubis diastasis is an uncommon intrapartum complication. The reported incidence of peripartum pubic diastasis varies widely in the literature, from 1 in 300 to 1 in 30.000 deliveries[1-5].

The pubic symphysis is a secondary cartilage–like joint, classified as amphiarthrosis, covered by a layer of hyaline cartilage separated by a softer fibrocartilagineous disc, acting as a buffer, and reinforced by 4 ligaments[6,7]. It is a joint that allows only very limited movement except under hormonal stimulation during the third trimester of pregnancy or during birth when it becomes progressively looser[6,7]. This increase in elasticity of the pubic ligaments results from exposure to elevated levels of progesterone and relaxin[6,8,9].

In a non-pregnant woman, the normal pubic symphysis gap ranges from 4 to 5 mm[1] and the limited possible movements mentioned before are in the range of 0.5-1 mm[7]. Starting from the seventh month of pregnancy a widening of the sacro-iliac joint and the pubic symphysis occurs (4-8 mm)[7]. After delivery, the laxity of the ligaments decreases and pelvic stability returns[6].

Indeed, separation of less than 1 cm is considered normal[6]. However, in some cases with accompanying risk factors pathologic symphysis pubis diastasis may occur. This condition is defined as an abnormally wide gap of more than 10 mm between two pubic bones[8].

We present a case of woman who experienced a symphysis pubic diastasis after a straightforward, uncomplicated, non-operative, term vaginal delivery, with the aim to perform a review of literature on this topic and inform all clinicians about this condition.

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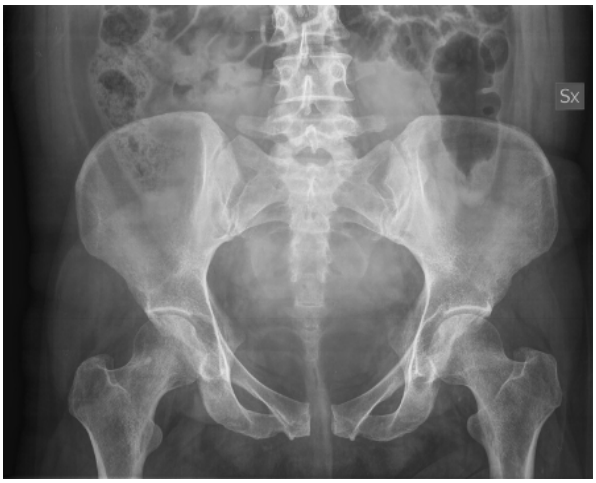
CASE REPORT

A 38-year-old gravida 3 para 0 at 41,5 weeks gestation was admitted to Niguarda Ca' Granda Hospital Obstetric Department in Milan after spontaneous rupture of the membrane. She was known be group B Streptococcus negative. She had an uneventful antenatal history, and all her routine antenatal blood investigations and ultrasound scans were normal. The pelvic examination on admission revealed a 70% effaced cervix, dilated 1 cm, vertex at stage -3 and a drip of clear fluid. Cardiotocography was normal. After 24 hours of waiting, the local conditions of the patient were unchanged compared to admission. So labor was induced with a Dinoprostone 10 mg vaginal slow-release system. After another 24 hours, the examination revealed an unchanged local condition. The patient had an inadequate contraction pattern with a high level of discomfort. So the patient received an epidural for pain relief and labor induction with oxytocin was begun. After nine hours and 30 minutes she delivered a 3460 g male baby without complications.

On the first post partum day, she complained of severe pain in the symphysis pubic and sacral region and was unable to walk. On examination, there was a gap and local tenderness and edema in the region of the symphysis pubis. Palpation caused the patient a great deal of pain. We formulated the suspect diagnosis of pubic symphysis diastasis. As a result, we suggested the use of analgesics, bed rest and a radiography of the pelvis. An anterior – posterior and lateral pelvic x–ray was done, which showed a pubic separation of 16 mm (Figure 1).

Figure 1
Anterior – posterior pelvic x–ray shows a pubic separation of 16 mm (white arrow) whereas the sacro-iliac and hip joints appears to be intact.



The sacro-iliac and hip joints appeared intact. At this point, and after our diagnostic doubts were confirmed, a referral was made to the orthopedic surgeon, who recommend bed rest, with the possibility of movement from bed to chair, avoiding prolonged standing station. Furthermore he asked to plan a clinical and radiological test after 30 days. A consultation with the anaesthesiologist was obtained, for the severe pain experienced by the patient. An intravenous administration of fluids, opioids and drugs for gastroprotection was started. The patient was discharged from hospital 1 week after delivery. She was advised to maintain active ambulation and start physiotherapy. One month later she was seen at the outpatient clinic. She was able to walk independently and no longer experienced any pain. Physical and pelvic examinations were unremarkable. Assessment by the orthopaedic team found her to be in good health. Clinically the patient did not complain of any pain whatsoever, even during pubic manual pressure. The obtained results were considered successful. She was counseled regarding the possibility of a recurrence in her next pregnancy.

DISCUSSION

Despite the pubic symphysis has been extensively studied, several aspects of the anatomy and physiology of this structure remain unknown and unclear. The reported incidence of the postpartum diastasis varies widely and it is refer only to the symptomatic forms. This variation is due to lack of studies that have analyzed systematically the behavior of the symphysis pubis during pregnancy and labor. Furthermore, the detection rate depends on physician's concern about this condition. The detection rate would be low if patients and physicians neglect a diastasis considering pubic pain as a transient uneventful symptom around labor[10].

A symptomatic diastasis of the pubic symphysis after birth is a rare, but painful complication that causes serious distress to the patient[7].

Pathophysiology of this condition is not clearly defined in literature. During pregnancy pelvic joint relaxation caused by relaxin and progesterone is a physiological adaptation that enables normal vaginal delivery[6,8,9,11]. The symptomatic gap of >10mm is considered abnormal[8]. The gap was 16 mm in the present case.

The clinical factors thought to contribute most to the development of symptomatic symphyseal separation are fetal macrosomia and cephalopelvic disproportion[6]. Other contributing factors

include multiparity, precipitous labor or rapid progression of second stage labor, rapid descent of presenting part, intense uterine contractions, prior pelvic trauma to the pelvic ring, the use of oxytocin, epidural anesthesia, malpresentation, difficult forceps delivery and forceful abduction of the thighs during delivery[5,6,9,11,12]. Abnormalities caused by connective tissue disorders, congenital dysplasia, osteomalacia, chondromalacia, rickets, tuberculosis, arthritis, or hormonally related softening of the ligaments during pregnancy may also play a role[6,8,9,11]. However, these factors were speculative, which were not verified statistically[10].

The most consistent finding is pain in the symphyseal region that radiates to the lower back and thighs and is exacerbated by leg movement[6]. Pain is often immediate and preceded by a "popping" or "snapping" sensation [2,12]. The pain increases when manual pressure is applied to the pelvis in a latero–lateral and antero–posterior direction[7]. Other symptoms include tenderness, instability, allodynia, hyperaesthesia or hyperalgesia at and around the joint site[6,8]. In addition, many women will have difficulty walking, in fact the gait is described as waddling, or potentially be unable to stand or walk due to pain[2,5,11,12]. In some case it is possible to hear a clicking sound when the patient walks[7]. Palpation of the symphysis pubis may reveal a gap with edema or hematoma on the soft tissue overlying the symphysis pubis[11].

A pubic diastasis must be suspected if the patient complains of acute and persistent pain in the pelvic area. Symptoms may be noted during labor and up to 48 hours postpartum. Discovery of a peripartum pubic symphysis separation can be delayed for a significant interval after birth if the patient used epidural anesthesia[2,6,12].

The diagnosis is based primarily on clinical findings. Often the first diagnostic test used to identify the pubic diastasis is an anteroposterior x–ray of the pelvis [2,6,7,8,11]. The ultrasonography is another useful diagnostic tool in the diagnosis, it is simple to perform and provide an optimal assessment of the symphysis separation extension [2,6,8,13]. The ultrasonography is performed in the following way: place the probe in transverse orientation on the pubic symphysis (identified by palpation) with an approximately 30° caudal scanning plane, with the purpose of measuring the width of the symphyseal joint at its upper margin. Literature also reports the use of the magnetic resonance imaging and computer tomography of the pelvis to diagnose this condition[2,8,14]. The measurement of interpubic gap confirms the diagnosis, but does not appear to predict outcome[10,13,15]. Unfortunately, any imaging techniques fail to show a correlation between the size of the symphysis separation and severity of the patient's symptoms[2].

Most cases of symphysis pubis diastasis following vaginal birth can be successfully managed conservatively with strict bed rest, analgesia (e.g. Non-steroidal anti-inflammatory drug and Opioids), activity restriction and later on physiotherapy and pelvic exercise[3,6,7,8,9,10,11,12,13,15,16,17,18,19,20,21,22]. This conservative treatment is helpful in most patient and functional recovery is excellent in 6 – 8 weeks[2,11,12]. However, an wide separation > 4 cm is usually associated with an skin – rupture of sacroiliac joint and instability of the pelvic ring, which necessitate a surgical intervention[10,23,24,25].

In our case we consulted an anaesthesiologist and an orthopedic surgeon, so we decided the best therapy for our patients together. We decided to perform a conservative approach and patient was discharged with the recommendation to start physiotherapy. We think that a successful treatment requires a multidisciplinary approach involving obstetrics, an anaesthesiologist, an orthopedic surgeon and a physical therapist.

There is little information in the literature about the management of subsequent pregnancies in women with prior pubic symphysis separation. Based on a literature review, there is a significant risk of repeat symphysis diastasis with subsequent vaginal delivery[3,6]. Indeed, there appears to be an approximately 50% recurrence risk in subsequent pregnancies[2,3,18].

In summary, minimal separation of the pubic symphysis during pregnancy and delivery is normal, but if the separation becomes wide enough, it can be pathological. It is important, for physicians and other health care providers involved in the care of pregnant women, to be aware of symphysis diastasis as a potential complication.

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CASE REPORT: UNEVENTFUL AT TERM TWIN PREGNANCY STARTING THREE MONTHS AFTER COMPLETE HYDATIDIFORM MOLE DIAGNOSIS

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ABSTRACT

OBJECTIVE: To report an uneventful twin pregnancy begun only three months after evacuation of complete hydatidiform mole.
DESIGN: Case report.
SETTING: Department of obstetrics and gynecology of P.O. M. Melloni, Milan.
PATIENT: A 38 year-old woman, gravida, treated for complete hydatidiform mole with successive uterine cavity evacuation 85 days before her last menstrual period.
INTERVENTIONS: After being diagnosed with hydatidiform mole the patient was treated with uterine cavity evacuation. One undetectable hCG level was then obtained. With the occurrence of a new pregnancy, the patient underwent transvaginal ultrasound (US) that revealed a twin dichorial diamniotic pregnancy; she then underwent normal antenatal tests and care. Histological examination of the placentas was performed after delivery.
MAIN OUTCOME MEASURES AND RESULTS: The pregnancy progressed normally until the 38th week of gestation, when spontaneous rupture of membranes and uterine contractions occurred. Two healthy foeti were delivered vaginally.
CONCLUSIONS: Patients who conceive before the completion of the full 6-12 months hCG follow-up, albeit having one undetectable hCG value, should be encouraged to continue their pregnancy.

Key-words: hydatidiform mole, hCG, gestational trophoblastic disease surveillance, pregnancy outcome

RIASSUNTO

OBIETTIVI: riportare il caso di una gravidanza gemellare priva di complicanze insorta a soli 3 mesi dalla diagnosi di mola idatiforme completa
TIPO DI STUDIO: case-report
SEDE: Dipartimento di ostetricia e ginecologia; P.O. Melloni, Milano
PAZIENTE: una donna di anni 38, gravida, con revisione della cavità uterina in seguito a diagnosi di mola idatiforme completa in anamnesi solo 85 giorni prima della data dell'ultima mestruazione.
INTERVENTI: dopo la diagnosi di mola idatiforme la paziente è stata sottoposta a revisione della cavità uterina. E' stato ottenuto un solo dosaggio nullo di hCG prima della diagnosi di gravidanza. Durante la successiva gestazione la paziente è stata sottoposta ad ecografia transvaginale che rivelava una gravidanza gemellare bicoriale biamniotica; è stata poi sottoposta ai controlli standard dell'iter gravidico. Dopo il parto è stato eseguito l'esame istologico delle placente.
RISULTATI: la gravidanza è evoluta fisiologicamente fino alla 38° settimana gestazionale, quando è avvenuta la rottura spontanea delle membrane di parto e l'insorgenza del travaglio di parto. Due feti sani sono poi stati partoriti per via vaginale.
CONCLUSIONI: le pazienti che concepiscono prima di completare i 6-12 mesi di follow-up post diagnosi di mola idatiforme, anche se in possesso di un solo dosaggio nullo di hCG, dovrebbero essere esortate a proseguire la gravidanza.

Parole chiave: mola idatiforme, hCG, sorveglianza della malattia gestazionale trofoblastica, outcome gravidico

Gestational trophoblastic disease (GTD) includes a spectrum of interrelated but histologically distinct tumors including partial and complete hydatidiform mole. Both complete and partial moles may develop persistent gestational trophoblastic neoplasia (GTN) with local uterine invasion and dissemination[1,2,3]. The incidence of GTD is approximately 1 to 2 per 1.000 deliveries in the United States and Europe[4,5,6].

The disease occurs mostly in women under the age of 35; it is therefore necessary to consider the risks of successive pregnancies, especially the possibility of GTD recurrence[5,7].

There are no pathologic or clinical features at diagnosis that accurately predict which patients will ultimately develop GTN[8]. All GTDs produce human chorionic gonadotropin (hCG), which can be measured in both serum and urine. The serum hCG level is a sensitive indicator for disease progression, including response to treatment and detection of relapse. Pregnancies that occur during the monitoring period, and the resulting hCG production, can hinder detection of progression to GTN[9].

Normal practice is that, once undetectable hCG levels are obtained, follow-up measurements are

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made at 1-2 months intervals an additional 6-12 months[10]. After completing an exhaustive follow-up, the expectation of a normal future pregnancy is comparable to that of the general population, except for a somewhat higher risk of repeated mole occurrence[11].

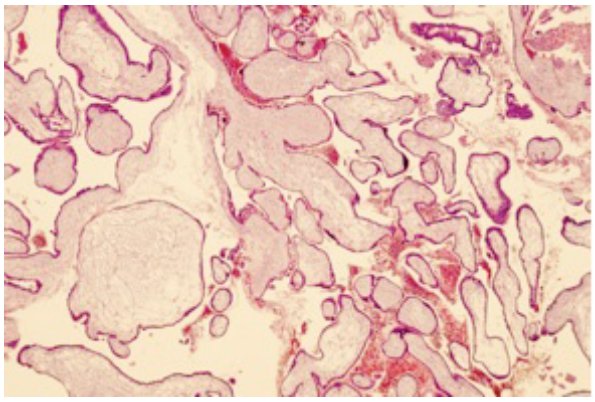
Some patients diagnosed with hydatidiform mole, however, get pregnant before completing the aforementioned follow-up, disregarding the physician's advice to hold-up conception [9-12]. Nevertheless, 42% to 63% of GTD patients fear the possibility of persistence of molar disease and the results of later pregnancies[13].

This article reports the successful outcome of a pregnancy in a patient previously treated for complete molar pregnancy who conceived before completing the hCG follow-up. To our knowledge, this is the first case that reports an uneventful twin pregnancy starting only three months after evacuation of complete hydatidiform mole.

CASE REPORT

A 38 year-old Italian woman, gravida 4, para 2, 1 hydatidiform complete mole came to our practice. She had been treated with uterine cavity evacuation for a molar pregnancy 85 days before last period. Histological exam was performed on the evacuation material and confirmed hydatidiform complete mole diagnosis. (Figure 1)

Figure 1
Histological finding of complete hydatidiform mole.



Forty days after evacuation, hCG levels were undetectable and a transvaginal ultrasound (US) scan revealed a normal uterine cavity. After this first undetectable hCG level, despite the physician's recommendations, the patient decided to disregard the planned follow-up. She undertook a pregnancy test as soon as the first pregnancy signs and symptoms appeared. Transvaginal US scan revealed a twin dichorial diamniotic pregnancy at 8 weeks + 4 days of gestation. The pregnancy had a monthly clinical and ultrasonographical follow-up and progressed normally until the 38th week of gestation, when spontaneous rupture of membranes and uterine contractions occurred. Twelve hours after rupture of membranes, two healthy foeti were delivered vaginally (male 2750g, female 2650g). Histological examination of the placenta showed a normal tissue, with some microinfarcted areas with calcium salt deposits.

DISCUSSION

GTD is relatively easy to diagnose by transvaginal (US) scan, human chorionic gonadotropin (hCG) level measurement and confirmed by histological analysis on uterine cavity evacuation material. It is known that GTD responds well to suction curettage and chemotherapy, and such modern therapy for molar pregnancy and GTN results in high cure rates and preservation of fertility[14].

Patients and their partners facing a future pregnancy after treatment for GTD express fear related to the risk of persistence of the disease affecting the outcome of subsequent pregnancies[15]. Follow-up is usually performed by testing hCG levels (having high sensibility and specificity), to ensure complete remission and the absence of any persistent postmolar tumor cells. GTN develops approximately in 15% to 20% of complete moles[16,17]. In contrast to this, GTN develops in only 2% to 4% of partial moles following evacuation[18,19]. Malignant transformation into metastatic choriocarcinoma occurs, but is fortunately exceedingly rare (0.1%)[20,21].

Ideally, serum hCG levels should be obtained within 48h of evacuation and every 1-2 weeks until undetectable; they should then be evaluated at monthly intervals for an additional 6-12 months. Use of contraception is usually recommended whilst hCG levels are monitored. After remission is documented for 6-12 months, women who desire a pregnancy may discontinue contraception[22].

The rationale for a 6-months interval of monitoring hCG levels after their normalization is to identify patients who develop malignant postmolar GTN. Indeed, although rare instances of long periods of latency have been reported, most episodes of malignant sequalae after hydatidiform moles occur within 6 months of evacuation[23,24].

Nevertheless poor compliance with the 6 months of monitoring has been reported,

especially among specific ethnic groups and indigent women. Furthermore when patients must travel long distances for the follow-up, the likelihood it not being completed increases significantly[25].

Actually, it is possible that the interval of hCG monitoring of patients with molar pregnancy may be shortened without compromising patient health and safety[23]. Once a patient with molar pregnancy achieves undetectable hCG values, the risk of gestational trophoblastic tumor relapse is extraordinary low. As recently reviewed by Sebire NJ et al.[26], the extended hCG level measurement beyond 6 months after the return of serum hCG level to normality provides minimal additional benefit, whilst having significant financial, healthcare and emotional cost; the authors suggest that this policy is no longer justified. It is possible that, given such a low risk of recurrence, a shorter post-evacuation screening could be acceptable for uncomplicated molar cases given that negative hCG levels are attained[27]. Prolonged hCG monitoring can be an economic, social and emotional burden for patients with molar pregnancy. A shorter follow-up period does not appear to negatively impact patient health or safety and certainly would improve percentages of follow-up completion. Resources would be best directed to encourage follow-up until the normalization of hCG levels[28].

Other recent literature reports that a single blood sample demonstrating an undetectable hCG level following molar evacuation is sufficient to exclude the possibility of progression to GTN. Patients could be then discharged safely from routine surveillance[27,23,19,17]. In accordance with these authors, in our case a single undetectable hCG value was associated with the remission of GTD, excluding any progression to GTN.

In addition, literature reports that conceptions occurring after molar pregnancy and started after only one undetectable hCG level, the gestational course is usually normal and leads to uneventful delivery of healthy babies. As reported in previous studies on hydatidiform mole[29,13,11,14], the rates of full term live birth, premature delivery, stillbirth delivery, spontaneous abortion, ectopic pregnancy and congenital anomalies in former GTD patients are similar to the overall average rates, and antepartum and postpartum complications and neonatal weight are similar to those of normal pregnancies[30].

Z. Selcuk Tuncer et al.[31] describe the outcome of pregnancies in 44 patients with previous molar pregnancy who conceived before completion of hCG follow-up, but after achievement of at least one undetectable hCG level: 22.7% had spontaneous abortion, 4.5% preterm delivery, 2.3% ectopic pregnancy, 70.5% term live birth. None of the live births had any detectable fetal anomaly. Equally, data from Garner E. et al.[32] concerning 1278 conceptions in patients with complete mole, show that the subsequent pregnancy experience is similar to that of the general population.

After having one molar pregnancy, the risk of molar disease in a future conception is higher than that of it naturally occurring, but still at a low rate of about 1%[33]. In the present case, the two foeti were healthy.

Once undetectable hCG levels are achieved, the risk of persistent tumor is low and reproductive outcome is favorable. Neither patients nor physicians need to fear a new pregnancy after molar disease; however, this is easier said than done.

To our knowledge, there are no data on incidence of twin pregnancies after recent hydatidiform mole diagnosis. However, we can assume that a period of ovarian hyper-stimulation by elevated hCG levels, as we observed in the course of the disease, can lead to increased incidence of twin pregnancies in the period immediately following its resolution.

Pregnancies occurring before the completion of hCG follow-up must be allowed to continue under careful surveillance. If the patient develops vaginal bleeding or any suspicious sign or symptom, she should be evaluated promptly and carefully. During the first trimester of a new pregnancy, an US transvaginal scan should be obtained to confirm normal gestational development. At the completion of any future pregnancy, the placenta or products of conception should undergo pathologic review, and hCG levels should be measured 6 weeks later to exclude occult persistent trophoblastic tumor.

In any case, our report gives evidence that patients who conceive before the completion of hCG level follow-up, having just one undetectable hCG level, should be encouraged to allow the physiological progression of pregnancy, even if it is a twin one.

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Metronidazolo, Clotrimazolo

RIASSUNTO DELLE CARATTERISTICHE DEL PRODOTTO

1. DENOMINAZIONE DEL MEDICINALE: MECLON® "20% + 4% crema vaginale" MECLON® "200 mg/10 ml + 1 g/130 ml soluzione vaginale". **2. COMPOSIZIONE QUALITATIVA E QUANTITATIVA:** Crema vaginale. 100 g contengono: **Principi attivi:** Metronidazolo 20 g; Clotrimazolo 4 g. **Eccipienti:** contiene sodio metil p-idrossibenzoato e sodio propil p-idrossibenzoato. Per l'elenco completo degli eccipienti, vedere paragrafo 6.1. Soluzione vaginale. Flacone da 10 ml. 10 ml contengono: **Principio attivo:** Clotrimazolo 200 mg. Flacone da 130 ml. 130 ml contengono: **Principio attivo:** Metronidazolo 1 g. **Eccipienti:** contiene sodio metil p-idrossibenzoato e sodio propil p-idrossibenzoato. Per l'elenco completo degli eccipienti, vedere paragrafo 6.1. **3. FORMA FARMACEUTICA:** Crema vaginale. Soluzione vaginale. **4. INFORMAZIONI CLINICHE: 4.1 Indicazioni terapeutiche:** Crema vaginale. Cervico-vaginiti e vulvo-vaginiti causate da *Trichomonas vaginalis* anche se associato a *Candida albicans*, *Gardnerella vaginalis* ed altra flora batterica sensibile. MECLON® crema vaginale può essere impiegato anche nel partner a scopo profilattico. Soluzione vaginale. Coadiuvante nella terapia di cervico-vaginiti, vulvo-vaginiti causate da *Trichomonas vaginalis* anche se associato a *Candida albicans*, *Gardnerella vaginalis* ed altra flora batterica sensibile. MECLON® soluzione vaginale può essere impiegato anche dopo altra terapia topica od orale, allo scopo di ridurre il rischio di recidive. **4.2 Posologia e modo di somministrazione:** Crema vaginale. Somministrare profondamente in vagina il contenuto di un applicatore una volta al giorno per almeno sei giorni consecutivi, preferibilmente alla sera prima di coricarsi, oppure secondo prescrizione medica. Nelle trichomoniasi, maggior sicurezza di risultato terapeutico si verifica con il contemporaneo uso di Metronidazolo per via orale sia nella donna non gestante che nel partner maschile. Per un'ottimale somministrazione si consiglia una posizione supina, con le gambe leggermente piegate ad angolo. Per ottenere una migliore sterilizzazione è preferibile spalmare un po' di MECLON® crema vaginale anche esternamente, a livello perivulvare e perianale. Se il medico prescrive il trattamento del partner a scopo profilattico, la crema deve essere applicata sul glande e sul prepuzio per almeno sei giorni. Istruzioni per l'uso: Dopo aver riempito di crema un applicatore, somministrare la crema in vagina mediante pressione sul pistone, fino a completo svuotamento. Soluzione vaginale. Somministrare la soluzione vaginale pronta una volta al giorno, preferibilmente al mattino, oppure secondo prescrizione medica. Nella fase di attacco l'uso della soluzione vaginale deve essere associato ad adeguata terapia topica e/o orale. L'irrigazione va eseguita preferibilmente in posizione supina. Un lento svuotamento del flacone favorirà una più prolungata permanenza in vagina dei principi attivi e quindi una più efficace azione antimicrobica e detergente. Istruzioni per l'uso: Dopo aver versato il contenuto del flaconcino nel flacone, inserire la cannula vaginale sul collo del flacone stesso. Introdurre la cannula in vagina e somministrare l'intero contenuto. **4.3 Controindicazioni:** Ipersensibilità verso i principi attivi od uno qualsiasi degli eccipienti. **4.4 Avvertenze speciali e opportune precauzioni d'impiego:** Evitare il contatto con gli occhi. Il consigliato impiego contemporaneo di Metronidazolo per via orale è soggetto alle controindicazioni, effetti collaterali ed avvertenze descritte per il prodotto summenzionato. Evitare il trattamento durante il periodo mestruale. **Tenere il medicinale fuori dalla portata e dalla vista dei bambini. 4.5 Interazioni con altri medicinali e altre forme di interazione:** Nessuna. **4.6 Gravidanza e allattamento:** In gravidanza il prodotto deve essere impiegato solo in caso di effettiva necessità e sotto il diretto controllo del medico. **4.7 Effetti sulla capacità di guidare veicoli e sull'uso di macchinari:** MECLON® non altera la capacità di guidare veicoli o di usare macchinari. **4.8 Effetti indesiderati:** Dato lo scarso assorbimento per applicazione locale dei principi attivi Metronidazolo e Clotrimazolo, le reazioni avverse riscontrate con le formulazioni topiche sono limitate a: Disturbi del sistema immunitario: Non nota (la frequenza non può essere definita sulla base dei dati disponibili): reazioni di ipersensibilità. Patologie della cute e del tessuto sottocutaneo: Molto rari (frequenza <1/10.000): fenomeni irritativi locali quale prurito, dermatite allergica da contatto, eruzioni cutanee. L'eventuale manifestarsi di effetti indesiderati comporta l'interruzione del trattamento. **4.9 Sovradosaggio:** Non sono stati descritti sintomi di sovradosaggio. **5. PROPRIETÀ FARMACOLOGICHE: 5.1 Proprietà farmacodinamiche:** Categoria farmacoterapeutica: Antinfettivi ed antisettici ginecologici/Associazioni di derivati imidazolici - Codice ATC: G01AF20. Meccanismo d'azione/effetti farmacodinamici: Il MECLON® è una associazione tra Metronidazolo (M) e Clotrimazolo (C). Il (M) è un derivato nitroimidazolico ad ampio spettro di azione antiprotozoaria e antimicrobica. Ha effetto trichomonicida diretto ed è attivo su cocchi Gram-positivi anaerobi, bacilli sporigeni, anaerobi Gram-negativi. Presenta attività spiccata sulla *Gardnerella vaginalis*. Non è attivo sulla flora acidofila vaginale. Il (C) è un imidazolico con spettro antifungino molto ampio (Candida, etc.). È attivo anche su *Trichomonas vaginalis*, cocchi Gram-positivi, Toxoplasmi, etc. È stato documentato che l'associazione Clotrimazolo-Metronidazolo dà luogo ad effetti di tipo additivo, pertanto essa è in grado di conseguire tre vantaggi terapeutici principali: 1) Ampliamento dello spettro d'azione antimicrobica, per sommazione degli effetti dei due principi attivi; 2) Potenziamento dell'attività antimicotica, antiprotozoaria ed antibatterica; 3) Abolizione o ritardo della comparsa dei fenomeni di resistenza. Studi microbiologici in vitro hanno dimostrato che l'attività trichomonicida e antimicotica risulta potenziata quando il (M) e il (C) sono associati nelle stesse proporzioni che sono presenti nel MECLON®. Anche l'attività antibatterica esaminata su diversi ceppi di microorganismi è risultata elevata ed è emerso un potenziamento di essa quando i due principi attivi del MECLON® vengono associati. **5.2 Proprietà farmacocinetiche:** Dalle indagini farmacocinetiche sui conigli, cani e ratti risulta che dopo ripetute applicazioni topiche di MECLON® non si rilevano concentrazioni apprezzabili di Clotrimazolo e Metronidazolo nel sangue. Per applicazione vaginale nella donna il (M) e il (C) vengono assorbiti in una percentuale che varia tra il 10% e il 20% circa. **5.3 Dati preclinici di sicurezza:** La tossicità acuta del MECLON® nel topo e nel ratto (os) è risultata molto bassa, con una mortalità di appena il 20% dopo 7 giorni, a dosi molto elevate (600 mg/Kg di (C) e 3000 mg/Kg di (M), sia da soli che associati). Nelle prove di tossicità subacuta (30 giorni) il MECLON®, somministrato per via locale (genitale) nel cane e nel coniglio, non ha determinato alcun tipo di lesione nè locale nè sistemica anche per dosi molte volte superiori a quelle comunemente impiegate in terapia umana (3-10 Dtd nel cane e 100-200 Dtd nel coniglio; 1 Dtd = dose terapeutica/die per l'uomo = ca. 3,33 mg/Kg di (C) e ca. 16,66 mg/Kg di (M)). Il MECLON® somministrato durante il periodo di gravidanza per via topica vaginale nel coniglio e nel ratto non ha fatto evidenziare alcun segno di sofferenza fetale per dosi die di 100 Dtd, nè influssi negativi sullo stato gestazionale. **6. INFORMAZIONI FARMACEUTICHE: 6.1 Elenco degli eccipienti:** Crema vaginale. Eccipienti: Stearato di glicole e polietilenglicole; Paraffina liquida; Sodio metile p-idrossibenzoato; Sodio propile p-idrossibenzoato; Acqua depurata. Soluzione vaginale. Flacone da 10 ml. Eccipienti: Alcool ricinoleilico; Etanolo; Acqua depurata. Flacone da 130 ml. Eccipienti: Sodio metile p-idrossibenzoato; Sodio propile p-idrossibenzoato; Acqua depurata. **6.2 Incompatibilità:** Non sono note incompatibilità con altri farmaci. **6.3 Periodo di validità:** Crema vaginale: 3 anni. Soluzione vaginale: 3 anni. **6.4 Precauzioni particolari per la conservazione:** Questo medicinale non richiede alcuna particolare condizione per la conservazione. **6.5 Natura e contenuto del contenitore:** MECLON® crema vaginale. Tubo in alluminio verniciato internamente con resine epossidiche e fenoliche. Gli applicatori monouso sono di polietilene. Tubo da 30 g + 6 applicatori monouso. MECLON® soluzione vaginale. Flaconi di polietilene a bassa densità; flaconcini di polietilene; cannule vaginali di polietilene. 5 flaconi da 10 ml + 5 flaconi da 130 ml + 5 cannule vaginali monouso. **6.6 Precauzioni particolari per lo smaltimento e la manipolazione:** Nessuna istruzione particolare. **7. TITOLARE DELL'AUTORIZZAZIONE ALL'IMMISSIONE IN COMMERCIO:** ALFA WASSERMANN S.p.A. - Sede legale: Via E. Fermi, n. 1 - Alanno (PE). Sede amministrativa: Via Ragazzi del '99, n. 5 - Bologna. **8. NUMERI DELL'AUTORIZZAZIONE ALL'IMMISSIONE IN COMMERCIO:** MECLON® crema vaginale: A.I.C. n. 023703046. MECLON® soluzione vaginale: A.I.C. n. 023703059. **9. DATA DELLA PRIMA AUTORIZZAZIONE/RINNOVO DELL'AUTORIZZAZIONE:** 11.05.1991 (GU 07.10.1991) / 01.06.2010. **10. DATA DI REVISIONE DEL TESTO:** Determinazione AIFA del 27 Ottobre 2010.

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Metronidazolo, Clotrimazolo

RIASSUNTO DELLE CARATTERISTICHE DEL PRODOTTO

1. DENOMINAZIONE DEL MEDICINALE: MECLON® "100 mg + 500 mg ovuli". **2. COMPOSIZIONE QUALITATIVA E QUANTITATIVA:** Un ovulo da 2,4 g contiene: Principi attivi: Metronidazolo 500 mg; Clotrimazolo 100 mg. Per l'elenco completo degli eccipienti, vedere paragrafo 6.1. **3. FORMA FARMACEUTICA:** Ovuli. **4. INFORMAZIONI CLINICHE: 4.1 Indicazioni terapeutiche:** Cerviciti, cervico-vaginiti, vaginiti e vulvo-vaginiti da *Trichomonas vaginalis* anche se associato a *Candida* o con componente batterica. **4.2 Posologia e modo di somministrazione:** Lo schema terapeutico ottimale risulta il seguente: 1 ovulo di MECLON® in vagina, 1 volta al dì. **4.3 Controindicazioni:** Ipersensibilità verso i principi attivi od uno qualsiasi degli eccipienti. **4.4 Avvertenze speciali e opportune precauzioni d'impiego:** Evitare il contatto con gli occhi. Il consigliato impiego contemporaneo di Metronidazolo per via orale è soggetto alle controindicazioni, effetti collaterali ed avvertenze descritte per il prodotto summenzionato. MECLON® ovuli va impiegato nella prima infanzia sotto il diretto controllo del medico e solo nei casi di effettiva necessità. **Tenere il medicinale fuori dalla portata e dalla vista dei bambini. 4.5 Interazioni con altri medicinali e altre forme di interazione:** Nessuna. **4.6 Gravidanza e allattamento:** In gravidanza il prodotto deve essere impiegato solo in caso di effettiva necessità e sotto il diretto controllo del medico. **4.7 Effetti sulla capacità di guidare veicoli e sull'uso di macchinari:** MECLON® non altera la capacità di guidare veicoli o di usare macchinari. **4.8 Effetti indesiderati:** Dato lo scarso assorbimento per applicazione locale dei principi attivi Metronidazolo e Clotrimazolo, le reazioni avverse riscontrate con le formulazioni topiche sono limitate a: Disturbi del sistema immunitario: Non nota (la frequenza non può essere definita sulla base dei dati disponibili): reazioni di ipersensibilità. Patologie della cute e del tessuto sottocutaneo: Molto rari (frequenza <1/10.000): fenomeni irritativi locali quale prurito, dermatite allergica da contatto, eruzioni cutanee. L'eventuale manifestarsi di effetti indesiderati comporta l'interruzione del trattamento. **4.9 Sovradosaggio:** Non sono stati descritti sintomi di sovradosaggio. **5. PROPRIETÀ FARMACOLOGICHE: 5.1 Proprietà farmacodinamiche:** Categoria farmacoterapeutica: Antinfettivi ed antisettici ginecologici/Associazioni di derivati imidazolici - Codice ATC: G01AF20. Meccanismo d'azione/effetti farmacodinamici: Il MECLON® è una associazione tra metronidazolo (M) e clotrimazolo (C). Il (M) è un derivato nitroimidazolico ad ampio spettro di azione antiprotozoaria e antimicrobica. Ha effetto trichomonicida diretto ed è attivo su cocchi Gram-positivi anaerobi, bacilli sporigeni, anaerobi Gram-negativi. Presenta attività spiccata sulla *Gardnerella vaginalis*. Non è attivo sulla flora acidofila vaginale. Il (C) è un imidazolico con spettro antifungino molto ampio (*Candida*, etc.). È attivo anche su *Trichomonas vaginalis*, cocchi Gram-positivi, Toxoplasmi, etc. È stato documentato che l'associazione Clotrimazolo-Metronidazolo dà luogo ad effetti di tipo additivo, pertanto essa è in grado di conseguire tre vantaggi terapeutici principali: 1) Ampliamento dello spettro d'azione antimicrobica, per sommazione degli effetti dei due principi attivi; 2) Potenziamento dell'attività antimicotica, antiprotozoaria ed antibatterica; 3) Abolizione o ritardo della comparsa dei fenomeni di resistenza. Studi microbiologici in vitro hanno dimostrato che l'attività trichomonicida e antimicotica risulta potenziata quando il (M) e il (C) sono associati nelle stesse proporzioni che sono presenti nel MECLON®. Anche l'attività antibatterica esaminata su diversi ceppi di microorganismi è risultata elevata ed è emerso un potenziamento di essa quando i due principi attivi del MECLON® vengono associati. **5.2 Proprietà farmacocinetiche:** Dalle indagini farmacocinetiche sui conigli, cani e ratti risulta che dopo ripetute applicazioni topiche di MECLON® non si rilevano concentrazioni apprezzabili di Clotrimazolo e Metronidazolo nel sangue. Per applicazione vaginale nella donna il (M) e il (C) vengono assorbiti in una percentuale che varia tra il 10% e il 20% circa. **5.3 Dati preclinici di sicurezza:** La tossicità acuta del MECLON® nel topo e nel ratto (os) è risultata molto bassa, con una mortalità di appena il 20% dopo 7 giorni, a dosi molto elevate (600 mg/Kg di (C) e 3000 mg/Kg di (M), sia da soli che associati). Nelle prove di tossicità subacuta (30 giorni) il MECLON®, somministrato per via locale (genitale) nel cane e nel coniglio, non ha determinato alcun tipo di lesione nè locale nè sistemica anche per dosi molte volte superiori a quelle comunemente impiegate in terapia umana (3-10 Dtd nel cane e 100-200 Dtd nel coniglio; 1 Dtd = dose terapeutica/die per l'uomo = ca. 3,33 mg/Kg di (C) e ca. 16,66 mg/Kg di (M)). Il MECLON® somministrato durante il periodo di gravidanza per via topica vaginale nel coniglio e nel ratto non ha fatto evidenziare alcun segno di sofferenza fetale per dosi die di 100 Dtd, nè influssi negativi sullo stato gestazionale. **6. INFORMAZIONI FARMACEUTICHE: 6.1 Elenco degli eccipienti:** Eccipienti: Miscela idrofila di mono, di, tri-gliceridi di acidi grassi saturi. **6.2 Incompatibilità:** Non sono note incompatibilità con altri farmaci. **6.3 Periodo di validità:** 3 anni. **6.4 Precauzioni particolari per la conservazione:** Questo medicinale non richiede alcuna particolare condizione per la conservazione. **6.5 Natura e contenuto del contenitore:** 10 ovuli in valve in PVC, racchiusi in scatola di cartone. **6.6 Precauzioni particolari per lo smaltimento e la manipolazione:** Nessuna istruzione particolare. **7. TITOLARE DELL'AUTORIZZAZIONE ALL'IMMISSIONE IN COMMERCIO:** ALFA WASSERMANN S.p.A. - Sede legale: Via E. Fermi, n. 1 - Alanno (PE). Sede amministrativa: Via Ragazzi del '99, n. 5 - Bologna. **8. NUMERO DELL'AUTORIZZAZIONE ALL'IMMISSIONE IN COMMERCIO:** A.I.C. n. 023703010. **9. DATA DELLA PRIMA AUTORIZZAZIONE/ RINNOVO DELL'AUTORIZZAZIONE:** 27.11.1978 (GU 16.01.1979)/01.06.2010. **10. DATA DI REVISIONE DEL TESTO:** Determinazione AIFA del 27 Ottobre 2010.

100 mg + 500 mg ovuli, 10 ovuli. Prezzo: € 11,50.
Medicinale non soggetto a prescrizione medica (SOP). CLASSE C.

ALFA WASSERMANN


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