Immune thrombocytopenia and pregnancy

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Summary: Immune thrombocytopenia (ITP) is not infrequently encountered during reproductive years with an estimated incidence of 0.1–1 per 1000 pregnancies. An international consensus group recently re-defined ITP and outlined standardized response criteria and up-to-date investigation and management. The pathogenesis encompasses autoantibody platelet destruction and immune-mediated decreased platelet production. Maternal antibodies may cross the placenta and have the potential to cause fetal and/or neonatal thrombocytopenia. The diagnosis and subsequent management of ITP in pregnancy requires a multidisciplinary approach involving the midwife, obstetrician, haematologist and anaesthetist. Women with ITP diagnosed prior to pregnancy should receive preconception counselling to outline potential treatments and provide information regarding expected maternal and neonatal outcome. Management prior to 36 weeks aims to avoid treatment in the absence of bleeding and ensure an acceptable platelet count for planned procedures. At 34–36 weeks, women are generally reviewed to consider whether a tailored course of treatment is required in preparation for delivery. Further research is required to determine a suitable platelet count for neuraxial anaesthesia. The mode of delivery should be guided by obstetric indication. It is pertinent to consider both the risk of maternal bleeding and thrombosis in maternal ITP. The risk of neonatal intracranial haemorrhage in association with ITP is less than 1%. Postpartum a cord blood platelet count should be checked. Additional management is dependent upon the neonatal platelet count. Data collection using the new standardized terminology should provide robust comparable epidemiological data regarding ITP in pregnancy.

Keywords: immune thrombocytopenia, pregnancy, high-risk pregnancy, haematology

DEFINITION

Comparison of definitions and clinical criteria in studies of immune thrombocytopenia (ITP) also known as immune/idiopathic thrombocytopenic purpura, highlight wide discrepancies, supporting the need for standardization.¹ In 2007 an international working group convened in Italy and published recommendations regarding the standardization of terminology, definitions and outcome criteria in ITP.² The panel recommended the acronym ITP should stand for Immune ThrombocytoPenia, emphasizing the immune mechanism and avoiding the term purpura as bleeding symptoms may be absent in a large proportion of cases. In healthy non-western populations platelet count values between 100 and $150 \times 10^9/L$ are frequent.^{3,4} In addition, a prospective cohort study of healthy subjects with platelet count between 100 and $150 \times 10^9/L$ showed only a 6.9% 10-year probability of developing a more severe thrombocytopenia.⁵ The consensus group recommended a platelet count of less than $100 \times 10^9/L$ to support a diagnosis of ITP. These reduced platelet threshold will avoid the inclusion of most women with gestational thrombocytopenia. These proposals regarding terminology and

outcome criteria will support more robust and comparable national and international data collection regarding ITP in pregnancy.

EPIDEMIOLOGY

The incidence of ITP in the UK is 3.9 per 100,000 person years with a female propensity 4.4 per 100,000 person years.⁶ The incidence rate reported in the UK is similar to US data 5.8–6.6 per 100,000 person years.⁷ Female incidence rates are constant from childhood until 60 years of age, after which time the incidence increases.⁶ Therefore ITP is a diagnosis not infrequently encountered during reproductive years. Mild thrombocytopenia occurs in up to 10% of pregnancies; ITP however accounts for only 3% of cases of thrombocytopenia in pregnancy⁸ with an estimated incidence of 0.1–1 case per 1000 pregnancies.^{9,10} Despite accounting for only 3% of cases of thrombocytopenia in pregnancy, ITP is the most common cause of an isolated thrombocytopenia in the first and early second trimester.^{8,11–14}

PATHOGENESIS

The historical and prevailing hypothesis regarding the pathogenesis of ITP is autoantibody platelet destruction. More recently, increasing evidence suggests concomitant immune-mediated decreased platelet production.¹⁵

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Evidence to support increased platelet destruction includes thrombocytopenia in normal subjects, following infusion of plasma from subjects with ITP,¹⁶ *in vitro* antibody-dependent platelet phagocytosis,¹⁷ decreased platelet survival in ITP patients,^{18–22} response to therapies that prevent *in vivo* platelet phagocytosis and evidence of cytotoxic T lymphocytes inducing platelet lysis in ITP.²³

Evidence to support decreased production include reduced platelet turnover in untreated ITP,^{24–29} evidence of megakaryocyte damage,^{30,31} autoantibody induced suppression of megakaryopoiesis *in vitro*^{32,33} and the response of platelet counts in ITP patients to thrombopoietin receptor agonists.

The clinical heterogeneity of ITP including the varied response to treatment may reflect the concomitant mechanisms contributing to thrombocytopenia in ITP. The maternal IgG anti-platelet antibodies are able to cross the placenta and therefore have the potential to cause fetal/neonatal thrombocytopenia.

DIAGNOSIS OF ITP IN PREGNANCY

In pregnancy the platelet count falls by approximately 10% compared with prepregnancy levels^{34,35} and 10% of pregnant women have a platelet count below the normal laboratory range.³⁶ This reflects physiological dilution, activation and accelerated clearance.³⁷

The majority of cases of thrombocytopenia in pregnancy are discovered incidentally following a booking full blood count.

ITP is a diagnosis of exclusion. Unless the diagnosis of ITP predates pregnancy, alternative causes of a thrombocytopenia in pregnancy need to be considered (Table 1). The differential diagnosis encompasses the common and self-limiting conditions requiring no intervention, i.e. gestational thrombocytopenia and the less common potentially life-threatening conditions, i.e. thrombotic thrombocytopenic purpura (TTP) or haemolysis, elevated liver function low platelets (HELLP) syndrome which may be associated with significant maternal or neonatal morbidity and mortality if the diagnosis is not considered and promptly managed.

A detailed history should elucidate any personal or family history of bleeding, concomitant medical disorders including thrombosis, risk factors for viral transmission, drug and vaccine history, diet, alcohol intake, systemic symptoms suggestive of an autoimmune disorder, fevers, night sweats, weight loss, abdominal pain, neurological symptoms and previous obstetric history including preeclampsia, thrombocytopenia in pregnancy and neonatal thrombocytopenia. Examination is essential to look for mucocutaneous bleeding, skeletal abnormalities, hepatosplenomegaly, tenderness in the right upper quadrant and lymphadenopathy, features of preeclampsia and neurological signs.

LABORATORY INVESTIGATIONS

Baseline investigations of thrombocytopenia in pregnancy include a full blood count, reticulocyte count and blood film, coagulation screen, liver function and virology screen. It is important to exclude a spurious thrombocytopenia.

A full blood count and film enables detection of spurious thrombocytopenia. Spurious thrombocytopenia is observed in 0.1% of individuals due to ethylene diamine tetra-acetate (EDTA) platelet agglutination.³⁹ When platelet agglutination is present a citrate sample should be obtained to check the

Table 1 Differential diagnosis of maternal thrombocytopenia in pregnancy

Isolated thrombocytopenia
Spurious – EDTA-induced platelet aggregation
Gestational thrombocytopenia
Primary immune thrombocytopenia
Drug induced
Prescription/non-prescription
Alcohol abuse
Consumption of quinine (tonic water)
Exposure to environmental toxins
Congenital thrombocytopenia
Thrombocytopenia absent radius syndrome
Radioulnar synostosis
Congenital amegakaryocytic thrombocytopenia
Wiskott–Aldrich syndrome
MYH9-related disease, Bernard–Soulier syndrome
Type IIB von Willebrand's disease
Thrombocytopenia associated with a systemic disorder
Preeclampsia and HELLP syndrome
Acute fatty liver
Haemolytic uraemic syndrome (HUS)
Thrombotic thrombocytopenic purpura (TTP)
Systemic lupus erythematosus (SLE)
Thyroid disease
Antiphospholipid syndrome
Disseminated intravascular coagulation
Viral infection
Human immunodeficiency virus (HIV)
Ebstein Barr virus (EBV)
Cytomegalovirus (CMV)
Hepatitis B and hepatitis C
Folate deficiency
Hypersplenism
Liver disease
Coincidental marrow disease
Myelodysplastic syndromes
Leukaemias
Other malignancies and fibrosis
Aplastic anaemia
EDTA, ethylene diamine tetra-acetate
The table is adapted from Terry Gernsheimer and Keith R McCrae. ³⁸ Immune thrombocytopenic purpura in pregnancy. <i>Curr Opin Hematol</i> 2007; 14 :574–80

platelet count. In the UK it is standard practice in pregnancy to screen for hepatitis B and HIV. If a diagnosis of ITP is considered additional testing for hepatitis C is recommended.⁴⁰ History and examination findings in conjunction with provisional results direct further testing, i.e. renal function, direct antiglobulin test, folate, thyroid function, autoimmune profile and antiphospholipid antibodies.

ITP and gestational thrombocytopenia may be associated with variation in the size of platelets. However if the majority of platelets are large in association with a history of a bleeding disorder, a congenital giant platelet disorder needs to be considered. In the presence of large platelets, automated impedance counters underestimate the platelet count and flow cytometry if available may provide a more accurate platelet count.

The film may demonstrate abnormalities suggestive of alternative diagnoses: red cell fragmentation in HUS/TTP/preeclampsia/HELLP syndrome; spherocytes in Evans syndrome; micro/macrocytosis in dietary deficiencies, chronic bleeding, excess alcohol intake; white cell inclusions in congenital platelet disorders and abnormal white cell morphology, immature cells and tear drops suggestive of concomitant bone marrow pathology.

Bone marrow biopsy is only indicated in a minority of cases eg in the presence of symptoms (fevers, night sweats, weight loss) and signs (splenomegaly, lymphadenopathy, leukoerythroblastic film) suggestive of concomitant bone marrow pathology, following a lack of response to adequate treatment of a presumptive diagnosis of ITP or prior to splenectomy. Platelet associated immunoglobulin may be elevated in both immune and non-ITP; therefore, routine measurement is not recommended.^{40,41}

GESTATIONAL THROMBOCYTOPENIA

Gestational thrombocytopenia is the commonest cause of thrombocytopenia in a healthy pregnant woman.³⁴ When considering the diagnosis, review of maternal platelet counts and neonatal platelet counts available from previous pregnancies and platelet counts outside of pregnancy alongside the current trend is informative. Features of gestational thrombocytopenia include a tendency to recur in each pregnancy, typically in the second–third trimester, the platelet count remains $>70 \times 10^9/L$, neonatal platelet counts are normal and postpartum the platelet count returns to normal within a few weeks.

A platelet count $<70 \times 10^9/L$ or thrombocytopenia documented prior to pregnancy or persisting postpartum should prompt consideration of alternative diagnoses. However a platelet count $<70 \times 10^9/L$ is not an absolute cut-off to exclude a diagnosis of gestational thrombocytopenia and it is not infrequent to review women in pregnancy whose platelet count falls as low as $50 \times 10^9/L$ and normalizes postpartum being more suggestive of gestational rather than ITP. We speculate that changing population demographics which re-define normal platelet count reflect this observation and contribute to the difficulty in defining gestational thrombocytopenia. There is no associated increased incidence of maternal bleeding or neonatal thrombocytopenia in gestational thrombocytopenia.

MANAGEMENT OF ITP IN PREGNANCY

Preconception counselling

Women with a diagnosis of ITP prior to pregnancy should be offered preconception counselling. This meeting should explore details of the diagnosis of ITP, bleeding history, prior medical treatment, splenectomy, response to treatment and obstetric history including previous neonate platelet count. The need for additional blood tests and follow-up during pregnancy and the potential need to consider treatment of ITP in one-third of pregnant women⁴² should be explained. The small risk of maternal and fetal complications should be discussed; however it should be emphasized that pregnancy in women with ITP can proceed safely with a low risk of haemorrhage for both infants and mothers. Women should not be discouraged from pregnancy and should be reassured regarding good outcome with modern management.

Antenatal management

How often should these women be seen in pregnancy?

Close liaison should be maintained between obstetrician, midwife, haematologist and paediatrician. While the frequency of monitoring does not have a strong evidence base, the general recommendation is to monitor women monthly until 28 weeks,

fortnightly until 36 weeks and weekly thereafter.⁴³ However this will vary dependent upon platelet count and whether the woman is symptomatic.

What is the treatment aim?

The aim is to treat when required to maintain an adequate platelet count to avoid maternal haemorrhagic complications in the antenatal, intrapartum and postnatal period.

When is treatment required?

Recommendations for the management of ITP in pregnancy are based upon clinical experience and expert consensus.⁴⁰ Local practice and guidance should be drawn from international consensus recommendations, national guidance and local expertise.

During prenatal counselling or the early stages of pregnancy our practice is to discuss if and when treatment may be required and what the treatment options are. This will be outlined in a letter which the woman carries in her hand-held maternity notes.

In the absence of symptoms or planned intervention in the first and second trimester prompting treatment, the international consensus report recommends treatment be initiated when the platelet count falls below $20\text{--}30 \times 10^9/L$.⁴⁰

Women are reviewed throughout the pregnancy and at 34–36 weeks women should be reviewed to discuss again whether or not treatment needs to be commenced to minimize the risk of haemorrhage around the time of delivery based upon consideration of individual clinical features, obstetric factors, trend in platelet count and personal wishes. If the woman is asymptomatic and platelets are stable and greater than $50 \times 10^9/L$ no treatment is generally required; if platelets are less than $50 \times 10^9/L$ our practice is to consider treatment. In the event that a woman with a platelet count $>50 \times 10^9$ and $<70 \times 10^9/L$ wishes to be in a position to consider neuraxial anaesthesia/analgesia or there is a planned caesarean delivery due to an obstetric indication our practice is to consider treatment.

A platelet count $>50 \times 10^9/L$ is deemed safe for a normal vaginal delivery.^{40,41,44,45} Some experts extend this to a platelet count of $30\text{--}50 \times 10^9/L$.⁴⁶ A platelet count of $>50 \times 10^9/L$ is also deemed safe for a caesarean section^{40,41,44} but in practical terms needs to be considered in conjunction with a platelet threshold suitable for neuraxial anaesthesia.

A specific platelet count predictive of neuraxial anaesthetic complications has not been determined. A systematic review of neuraxial techniques for anaesthesia included 14 papers reporting 326 neuraxial techniques in 325 patients diagnosed with ITP, all but one were obstetric patients, of which nine had a platelet count $<50 \times 10^9/L$ and 19 had a platelet count of $50\text{--}75 \times 10^9/L$. There were no haemorrhagic complications associated with neuraxial techniques.⁴⁷ The author acknowledged that there is a paucity of data. The platelet threshold deemed safe to administer spinal or epidural anaesthesia remains controversial due to the theoretical risk of epidural haematoma formation and neurological damage.

Archived BCSH ITP guidance⁴¹ recommended a platelet threshold of $>80 \times 10^9/L$ in women with a normal coagulation profile. The more recent consensus report suggests that obstetric anaesthetists generally recommend a platelet count $>75 \times 10^9/L$. This assumes the absence of bruising, bleeding history or anticoagulation and the presence of a normal international

normalized ratio, activated partial thromboplastin time and fibrinogen. A small consensus of obstetric anaesthetists agree no change to routine practice is required until the platelet count drops below $50 \times 10^9/L$.⁴⁰

Some centres perform thromboelastography (TEG) in women with ITP when considering neuraxial anaesthesia. Further work is required to evaluate the use of TEG in ITP.

Women should be reviewed by an anaesthetist and counselled regarding the risks and benefits of regional anaesthesia versus general anaesthesia. This may also depend upon the availability of an experienced operator. Our local practice is for women with thrombocytopenia to be referred for an individual antenatal anaesthetic consultation.

Treatment options

First-line therapy

Corticosteroids and *immunoglobulin* are the first-line treatments for maternal ITP.⁴⁰ The choice of agent requires assessment of the individual case and consideration of potential side-effects, how long the platelet increment needs to be maintained and how quickly the platelet increment is required. There are no randomized trials of intravenous immunoglobulin versus corticosteroids in women with ITP in pregnancy.

Corticosteroids. Corticosteroid therapy during pregnancy for ITP was first described in 1957.⁴⁸ In 1966 a review of corticosteroid treatment in 21 cases of ITP in pregnancy⁴⁹ reported complete haematological and or symptomatic remission in 30%, significant improvement in 25% and no response in 45%. This review showed no significant improvement in perinatal mortality or the incidence and severity of neonatal thrombocytopenia, compared with previously published series of patients not treated with steroids. A randomized study confirmed corticosteroid treatment in the antenatal period demonstrated no beneficial effect on the fetal platelet count.⁵⁰

An attenuated dose of 10–20 mg once daily oral prednisolone is commonly used when treatment is required in pregnancy, unless the thrombocytopenia is severe and associated with significant major bleeding. The dose may be tapered to maintain an effective haemostatic platelet count. Corticosteroids have the advantage of being an oral therapy, which is inexpensive and enables avoidance of a blood product. However the initial response may be slow 3–7 days and a maximal response may not be attained until 2–3 weeks. Maternal side-effects include hyperglycaemia, immunosuppression, osteoporosis with long-term use and hypertension. Less than 10% of oral prednisolone reaches the fetus as prednisolone is converted in the placenta by the enzyme 11- β hydroxysteroid dehydrogenase to 11-keto forms which are relatively inactive. In humans there may be a very small increased risk of cleft palate or oral clefts from exposure in the first trimester. Data suggest embryonic exposure to corticosteroids might increase the rate of oral cleft from one per 1000 birth to three per 1000 births.⁵¹ Baseline immunoglobulin profile to exclude a common variable immunodeficiency prior to a trial of steroids is recommended.⁴⁰ Small amounts of prednisolone are secreted in breast milk and long-term maternal use of high-dose corticosteroids could theoretically affect the neonate's adrenal function. However with doses less than 30 mg per day this is unlikely.^{52,53}

Immunoglobulin. The first case report of high-dose intravenous immunoglobulin was published in 1984.⁵⁴ There are no

comparative trials of immunoglobulin versus corticosteroids in pregnant women with ITP although response rates are similar to those in non-pregnant patients and data suggest a shorter time to response in non-pregnant patients.⁴¹ A recent case report describes using antenatal immunoglobulin in a woman with ITP and previous splenectomy in view of a previously affected neonate. Neonatal thrombocytopenia did not occur. The authors concluded it is unknown whether this treatment influenced the fetal platelet count and that the case indicates antenatal immunoglobulin may be effective in women with risk factors for severe neonatal thrombocytopenia.⁵⁵ It is not possible to reliably predict whether or not neonatal thrombocytopenia will occur. However it is more likely if the mother has had a splenectomy or severe ITP or a previous sibling had neonatal thrombocytopenia. Antenatal treatment when the risk of neonatal thrombocytopenia is considered to be increased is controversial. Invasive testing with an associated risk of haemorrhage is not advisable and the platelet count nadir occurs postpartum.

The treatment dose is 2 g/kg divided over 2–5 days. The response to immunoglobulin is more rapid when compared with corticosteroids; however administration requires intravenous access, takes 2–5 days and is expensive. The response is often transient (1–4 weeks) and further courses may be required. Intravenous immunoglobulin is the alternative to corticosteroids. Immunoglobulin is a pooled plasma product and there is a potential risk of pathogen transmission. Side-effects include infusion reactions, aseptic meningitis and headache.

Second line options in pregnancy

Prior to embarking upon second line options, the balance of treatment-related side-effects versus the risk of bleeding needs to be again considered. In certain circumstances it may be appropriate to accept an increased risk of haemorrhage versus aggressive management. Cases where treatment is deemed necessary should be considered upon an individual basis.

Combination therapy with high-dose methylprednisolone combined with intravenous immunoglobulin in refractory patients in the weeks prior to delivery may be appropriate.^{39,45}

Safety data regarding azathioprine in systemic lupus erythematosus (SLE) and renal transplantation in pregnancy would support a trial of azathioprine in refractory symptomatic women.^{56–58} Although the delayed time to response (6–8 weeks) may limit its use, the maximum recommended dose is 2 mg/kg.⁵¹ The fetus is thought to be protected from potential teratogenic effects as it lacks the enzyme inosinotriphosphorylase, which is required to convert azathioprine to the active metabolite 6-mercaptopurine.⁵⁹ Low doses of azathioprine are found in maternal breast milk. However the absence of adverse effects on the child has led some units to continue low-dose azathioprine in lactating mothers with SLE to avoid the risk of a postpartum flare. In the event low-dose azathioprine was deemed necessary for ITP in the postpartum phase, local practice would be to discuss previous experience of local cohort of women who have breast fed whilst taking azathioprine for SLE with no adverse effect. In the event the woman decides to continue to breast feed we would support this.

In modern practice splenectomy in pregnancy is rare. When a splenectomy is deemed necessary it is best carried out in the second trimester and may be performed laparoscopically. In

women who have had a splenectomy for ITP with a normal platelet count, the neonate is still at risk of thrombocytopenia due to transplacental passage of circulating antibodies.

The efficacy of intravenous anti-D in non-splenectomized Rh D-positive patients with ITP has been demonstrated.⁶⁰ However no anti-D preparation is currently licensed in the UK for the treatment of ITP regardless of pregnancy status. Anti-D is widely used in pregnancy via the intramuscular route at considerably lower doses in the prevention of haemolytic disease of the newborn. The higher dose used in ITP intravenously may result in an increased risk of neonatal haemolysis. However, the limited number of cases reported to date suggests intravenous anti-D is effective and safe for the mother and fetus in the second and third trimester.^{61,62} When anti-D has been used in non-splenectomized RhD positive pregnant women with ITP, it is recommended that the neonate is monitored for neonatal jaundice and anaemia postpartum including a direct antiglobulin test.

Cytoreductive agents (excluding azathioprine), i.e. vinca alkaloids, cyclophosphamide; androgen analogues, i.e. danazol; rituximab or thrombopoietin receptor agonists should not be used in pregnant women with ITP due to potential teratogenicity.³⁹ Rituximab has not been proven to be teratogenic in primates; however, it should not be used because of the extremely limited data in pregnant women with ITP. The drug company recommends discontinuing the drug 12 months prior to planning pregnancy. There is currently no data regarding thrombopoietin receptor agonists; prospective observational registries of cases where women have inadvertently become pregnant while taking these drugs will be informative.

MANAGEMENT OF DELIVERY

Mode of delivery

Historically, concerns regarding the risks of severe neonatal thrombocytopenia and haemorrhage dominated decisions regarding the mode of delivery in maternal ITP. There is no evidence to suggest caesarean section reduces the risk of neonatal haemorrhage in mothers with ITP versus an uncomplicated vaginal delivery in susceptible neonates.⁶³ The incidence of postpartum haemorrhage in ITP is greater following caesarean section compared with vaginal delivery. The volume of blood loss with caesarean section is inversely related to the platelet count although this pattern is not evident in vaginal deliveries.⁶⁴

Large studies of ITP in pregnancy report the incidence of severe neonatal thrombocytopenia $<50 \times 10^9/L$ to be 8.9–14.7%, with intracranial haemorrhage in less than in 0–1.5% of infants.^{1,65–67}

The risk of neonatal intracranial haemorrhage in association with maternal ITP is less than the procedure-related risk of cordocentesis prior to delivery. Measurement of the fetal platelet count is not recommended³⁹ and the mode of delivery should be guided by obstetric need. However fetal scalp electrodes, fetal blood samples, ventouse and rotational forceps which may be associated with an increased risk of haemorrhage should, where possible, be avoided.⁴⁰ However in a situation where the head is deeply engaged the obstetrician will need to consider and balance the risk of straight forward forceps delivery versus the potential force exerted upon the fetal head

during a second stage caesarean section. Active management of the third stage of labour should be considered.

Management of an unexpected delivery, emergency intervention or haemorrhage

When a woman with ITP presents with a suboptimal platelet count in labour or when an emergency intervention is required treatment options depend upon the individual clinical scenario. The combination of high-dose intravenous methylprednisolone 0.5–1 g daily for 2–3 days and 2 g/kg total dose intravenous immunoglobulin over 2–3 days dependent upon timing may be considered with or without platelet support and oral/intravenous tranexamic acid. In the presence of a major haemorrhage intravenous tranexamic acid 1 g followed by further doses or an infusion according to the evolution of the haemorrhage should be given. The benefit of tranexamic acid for the prevention of obstetric haemorrhage is not proven and is currently being studied in a large UK trial. In the authors' experience normal delivery may occur without excessive haemorrhage; however, it is advisable to have platelets available in case required.

Postpartum maternal management

In the event of a postpartum haemorrhage, in addition to routine blood component support and tranexamic acid, intravenous immunoglobulin and/or intravenous methyl prednisolone may be required. Postpartum non-steroidal medication, anti-inflammatory analgesia and intramuscular injections should be avoided. Postpartum follow-up with a haematologist is necessary to consider postpartum treatment requirements and tapering of steroids encompassing any postpartum complications.

Standard postpartum thromboprophylaxis risk assessment should be performed and then considered in conjunction with any evidence of bleeding and the postpartum platelet count. In the presence of what would be considered normal postpartum bleeding and lochia, the absence of bleeding elsewhere and a platelet count $>50 \times 10^9/L$, our practice is to give thromboprophylaxis if indicated according to postpartum thromboprophylaxis risk assessment. In the presence of bleeding elsewhere or a platelet count $<50 \times 10^9/L$ the individual case should be discussed with a haematologist.

POSTPARTUM MANAGEMENT

Postpartum neonatal management

Cord blood obtained by clean venepuncture of a cord vessel should be analysed to determine the cord blood platelet count.³⁹ If the cord sample suggests neonatal thrombocytopenia, a neonatal venous sample should be performed to confirm this. If the platelet count is less than $50 \times 10^9/L$ at delivery, a transcranial ultrasound should be performed and oral vitamin K (2 mg at birth, 2 mg at one week and 2 mg at one month) should be given instead of intramuscular vitamin K. If thrombocytopenia is present, the neonate should be observed for signs of haemorrhage and alternate day platelet counts checked. The platelet count usually reaches a nadir 3–5 days postpartum. Treatment of the neonate is rarely required. If haemorrhage is evident or the neonatal platelet count is less than $20 \times 10^9/L$, treatment should be commenced. Intravenous immunoglobulin is the treatment of choice commencing with a

1 g/kg infusion repeated if necessary. In the presence of life-threatening haemorrhage platelet support should be given in addition to intravenous immunoglobulin. Following intravenous immunoglobulin the thrombocytopenia may recur at approximately 4–6 weeks. Further treatment may be required dependent upon the platelet count and clinical picture until the maternal antibody is cleared. Neonatal thrombocytopenia is uncommon in association with maternal ITP. When neonatal thrombocytopenia is present, further tests to exclude neonatal alloimmune thrombocytopenia should be completed.

CONCLUSION

The management of ITP and pregnancy has evolved over the last 50 years alongside the haematologists' and obstetricians' understanding of the disease. The recent work by international consensus group has re-defined ITP and outcome criteria² and provided guidance regarding investigation and management including a valuable focus upon ITP in pregnancy.⁴⁰ Standardization of terminology and responses should enable more robust prospective epidemiological studies. Possible research opportunities include developing a national and international database of ITP in pregnancy to further our understanding of ITP in pregnancy.

DECLARATIONS

The authors have no conflicts of interest to declare.

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