Postpartum pyrexia

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Abstract

Pyrexia in the postpartum period is a common finding. Differentiating between potentially fatal and benign causes is fundamental in reducing the mortality rate from sinister causes such as sepsis. Sepsis, most frequently originating from the genital tract, is the commonest cause of postpartum pyrexia and is a frequent cause of maternal death and morbidity world-wide. The UK has experienced a significant reduction in the death rate secondary to sepsis following a national campaign directed at improving the speed with which it is diagnosed and treated. Non-infective causes of postpartum pyrexia include venous thromboembolism and epidural catheter use for pain relief in labour. In the following article, we shall focus on the pathophysiology of pyrexia and the diagnosis and management of postpartum sepsis. Non-infective causes will also be discussed, in addition to their management.

Keywords group A streptococcus; influenza; postpartum; pyrexia; sepsis; thromboembolism

Introduction

There is not a single agreed upon definition of what temperature constitutes a pyrexia, with a range spanning 37.5–38.3°C used in the literature. Pyrexia can be defined therefore, as a body temperature above the normal range. Pyrexia in the postpartum period (the six weeks following delivery of the fetus) is a common finding. The differentiation between self-limiting causes that have a low potential for harm and potentially fatal causes is of utmost importance. In the following review article, we shall discuss the causes of postpartum pyrexia, the investigations as well as the management that should be considered in women with a fever post-partum.

Pathophysiology of pyrexia

Pyrexia is an adaptive response to an immune challenge. Fever is generally thought to be a useful response to infection and has been shown to potentiate leucocyte mobilization and phagocytosis, increase T cell numbers and reduce endotoxin effects. In addition, it reduces replication rates of many bacteria and viruses. Type 1 interferons such as interferon alpha are produced by fibroblasts and monocytes in response to viral infections, and induce transcriptional changes that inhibit viral replication. Interferon alpha has been shown to be more active at temperatures in the human febrile range. In general, human temperature does not rise above 42°C and whilst causing unpleasant symptoms, fever is rarely harmful. In fact, in children, national guidance in the USA and the UK recommends that anti-pyretics should not be used to reduce a fever, but only for symptom relief.

The hypothalamus controls body temperature homeostasis. Prostaglandin E2 acts on neurons at the thermoregulatory centre of the brain, within the pre-optic area of the anterior hypothalamus, causing a change in the set body temperature point. This causes a rise in the body temperature by means of increased heat generation and retention. When there is increased heat generation, shivering occurs. In addition, peripheral vasoconstriction improves heat retention. Pyrogens are substances that induce fever. These may be endogenous or exogenous. An example of an exogenous pyrogen is lipopolysaccharide (LPS), from the cell wall of gram negative bacteria. LPS activates the arachidonic acid pathway as shown in Figure 1.

Endogenous pyrogens are cytokines such as interleukin (IL) 1 and IL 6. LPS binds with the CD14 receptor on a nearby macrophage and causes the release of IL 1 and IL 6. IL 1 is a pro-inflammatory endogenous pyrogen which upregulates expression of adhesion factors on endothelial cells to induce migration of immunocompetent cells such as macrophages to sites of infection. IL 6 is also pro-inflammatory and is released by macrophages in response to microbial infection. It stimulates acute phase protein synthesis and neutrophil production.

Causes of postpartum pyrexia

Infective causes

Sepsis: The commonest cause of puerperal pyrexia is sepsis. Sepsis is a systemic inflammatory response in the proven or suspected presence of microbial infection. Severe sepsis is defined as evidence of hypo-perfusion or dysfunction of at least one organ in the presence of infection. Septic shock is diagnosed if there is systemic hypotension or a need for vasopressors despite adequate fluid rehydration.

Sepsis is a leading cause of maternal morbidity and mortality according to the *Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK* (MBRRACE-UK) report in 2016. Despite the UK direct death rate from sepsis falling from 0.67 to 0.29 per 100,000 maternities between 2009 and 2014, it remains the second commonest cause of total (combined direct and indirect) deaths in the UK and in London and was the leading cause of direct maternal deaths in 2016. Sepsis is a common complication in the postpartum period, and its diagnosis and treatment should be expedited. The most recent NICE guideline on sepsis (2016) identified women who are pregnant or have been pregnant within the past 6 weeks as being at highest risk. Timely diagnosis and treatment of sepsis in pregnancy and the postpartum period cannot be over-emphasized; the role of the 'sepsis six' care bundle in facilitating this will be discussed in this section.

It is of evolutionary advantage for the pregnant woman's immune system to be moderated, so that the feto-placental unit is not rejected. Whether there is a state of immunosuppression in normal pregnancy, or whether there are more complex changes at work is the subject of current research. Against a simplistic

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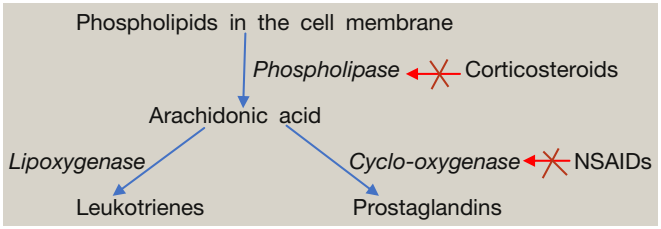

Figure 1 Arachidonic acid pathway.

theory of a state of immunosuppression, research has shown that during pregnancy, the decidua contains high levels of immune cells such as natural killer cells and macrophages. Reduction in the proportion of natural killer cells, for example, is associated with a high rate of pregnancy loss.

However, during pregnancy, there are elevated levels of hormones such as glucocorticoids and oestradiol which affect transcriptional immune and inflammatory response signalling, and elevated levels of progesterone, which have been shown to suppress immune system activity. Shifts in the T cell immune system towards a Th-2 anti-inflammatory state have been demonstrated, with a slow return to Th-1 dominated immunity during the postpartum period. These changes are thought to explain why diseases with an inflammatory component such as multiple sclerosis tend to remit in pregnancy and why bacterial infections, which are mitigated by inflammatory responses are more poorly tolerated in pregnancy. This may also explain why pregnant or postpartum women with influenza infections are more likely than their non-pregnant counterparts to be admitted to the intensive care unit with severe sepsis. Additional risk factors for sepsis can be found in Table 1.

The signs and symptoms of sepsis in the postpartum woman may not be as obvious as in the non-pregnant/postpartum woman, which can make the diagnosis challenging. A high index of suspicion is therefore required to ensure the diagnosis is not delayed or missed. Table 2 provides the signs commonly associated with the diagnosis of sepsis. Even a single abnormal finding should be taken seriously given the potentially fatal consequences of a delay in the treatment of sepsis.

Immediate assessment and management of puerperal sepsis: Once a diagnosis of sepsis is suspected, a sepsis care bundle should be instituted. Prospective analyses have indicated that immediate institution of these care pathways reduces mortality from sepsis. The UK Sepsis Trust produced one such care bundle in 2013, the 'Sepsis Six Care Bundle', and recommend that this be completed within an hour of diagnosis of sepsis, as shown in Table 3.

Timely institution of the above bundle cannot be overemphasized. Studies have shown that from recognition of the signs and symptoms of sepsis, each hour's delay in starting intravenous antibiotics increases mortality by up to 8%. The 2014 Saving Lives, Improving Mothers' Care report by MBRRACE-UK focussed on maternal deaths secondary to sepsis. The report highlighted that a delay in diagnosis and initiation of treatment feature prominently in the care of the women who died from sepsis; often with a delay in the initial evaluation and treatment, including escalation to Consultant Obstetrician.

Lactate levels may be transiently raised post-partum, but if there is a suspicion of sepsis, an elevated lactate level should not be dismissed. A level of 2 mmol/L or more suggests severe sepsis and a level of 4 mmol/L or more indicates septic shock. Women diagnosed with septic shock should be nursed in a high dependency unit, with their vital signs plotted on a Modified Early Warning Signs (MEWS) chart. Multidisciplinary team care, with involvement of a Consultant Anaesthetist, should be instituted early and the threshold for transfer to an intensive care unit should be discussed.

With regards to intravenous fluid rehydration, the blood pressure response to this should be monitored. If there is no sustained response to initial fluid rehydration, the need for vasopressor support should be considered. The choice of antibiotic will depend on local protocol and the suspected source of sepsis. A broad spectrum intravenous antibiotic that covers the suspected source should be commenced once a full septic screen has been completed. A septic screen includes a mid-stream urine sample (or catheter specimen if the woman is already catheterized or if she is oliguric and severely septic) for microscopy, culture and sensitivity, peripheral blood cultures and a high vaginal swab. Other samples will be dictated by the suspected focus of infection, for example wound swabs, throat swabs and/or sputum.

Causes of puerperal sepsis: ***Genital tract sepsis*** – Genital tract sepsis is a common cause of postpartum pyrexia and includes women with endometritis and pelvic abscesses. Women at increased risk of genital tract sepsis include those with prolonged labour with multiple vaginal examinations, prolonged rupture of membranes and women who have undergone instrumental vaginal delivery or who have vaginal/perineal trauma. Retained products of conception are also a significant risk factor.

Women with endometritis often complain of fevers, lower abdominal pain, heavy lochia and/or offensive vaginal discharge. Management includes abdominal and speculum examination, including a high vaginal swab for microscopy and culture, followed by the immediate commencement of antibiotics. If retained products of conception (RPOC) are suspected, an ultrasound scan of the pelvis should be performed to confirm the diagnosis, followed by an evacuation of the uterus to remove the infective focus.

Infected RPOC may present with a secondary postpartum haemorrhage. Surgical evacuation of the RPOC is required as part of the treatment, with the timing of this dependent on how heavy the bleeding is and how septic the woman is. Liaison with a Consultant Anaesthetist is strongly recommended in managing the acutely septic woman with infected RPOC so that her condition can be optimized prior to surgery where possible.

Group A Streptococcus – The majority of deaths from genital tract sepsis reported in the UK in the last five years were a result of Group A Streptococcus (GAS), a beta haemolytic streptococcus. GAS commonly causes upper respiratory tract infection, particularly pharyngitis, in children and adults and is also responsible for Impetigo and Scarlett fever. It is thought that GAS genital tract sepsis is the result of translocation of bacteria from the respiratory tract to the genital tract, caused, for example, by a woman wiping her nose and then touching the perineum when wiping after using the toilet.

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