Special Article

Pyrexia: An update on importance in clinical practice

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ABSTRACT

Pyrexic patients are usually attended with some scepticism by anaesthesiologists. Main reasons are the absence of comprehensible guidelines pertaining to anaesthesia in such patients and the presence of innumerable aetiologies of pyrexia. This article has tried to fill the existing void in the medical literature regarding anaesthesia in a patient with pyrexia. The article aims to discuss common and relevant causes of pyrexia, their pathophysiology in anaesthetic perspective, and the subsequent anaesthetic management, though a detailed discourse on all the entities causing pyrexia is beyond the scope of this article. This article will also touch upon the thermoregulatory alterations during anaesthesia. The literature search was performed manually using text and reference books, peer-reviewed journals, online and offline and through internet search engines Google, PubMed and Medline databases, using search terms 'perioperative pyrexia or fever, anaesthesia and thermoregulation'. Articles from 1980 to 2013 in English language were selected.

Key words: Anaesthesia, infection, management, pathophysiology, pyrexia, thermoregulation

INTRODUCTION

Pyrexia is one of the commonest causes of disability, perplexing to medical professionals due to its varied aetiologies and pathophysiologies. It is a potent biologic response modifier with consequences that are profound, but difficult to predict.[1] As a result, anaesthesia in such patients becomes a challenge, especially when the existing medical literature lacks in consensus guidelines on anaesthesia in a patient with pyrexia.[2] Henceforth, this article will try to encompass the existing literature pertaining to pyrexia, with an endeavour to fill in the existing vacuum. The literature search was performed using books, peer-reviewed journals and internet search engines like Google, PubMed and Medline databases, using search terms 'perioperative pyrexia or fever, anaesthesia and thermoregulation'. Articles published from 1980 to 2013 and in English language were selected.

THERMOREGULATION

Body temperature is not homogenous: Peripheral thermal compartment, which physically consists of arms and legs, is usually 2–4°C cooler than the core compartment (i.e. trunk and head).[3] Therefore, core temperature monitoring is the best single indicator of the thermal status in humans.

Thermoregulation is a tightly regulated process, maintaining the temperature within a narrow range. Interthreshold range (core temperature not triggering autonomic thermoregulatory responses), over which autonomic reflexes are activated, is 36.5°C to 37.5°C. It is bound by the sweating threshold at its upper end and the vasoconstrictor threshold at the lower end. It is 0.2–0.4°C in humans.[3,4]

THERMOREGULATION DURING ANESTHESIA

Almost all general anaesthetics so far tested markedly impair normal thermoregulatory control. During anaesthesia, warm response thresholds are elevated slightly, if at all, whereas cold-response thresholds are markedly reduced. Consequently, the interthreshold range increases 10-fold to approximately 2–4°C.[4] Besides acting centrally, most anaesthetics cause direct (peripheral) vasodilatation. Hence, hypothermia is the common thermal perturbation occurring during anaesthesia.[2]

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In contrast to general anaesthesia (GA), central thermoregulatory control is only slightly impaired by neuraxial anaesthesia.[5] However, labour epidural analgesia has been reported to cause a gradual increase in maternal core body temperature.[2] The conventional assumption is that hyperthermia is caused by the technique. However, it has been shown that hyperthermia during epidural analgesia should not be considered a complication of anaesthetic technique *per se* because pain in control patients is treated with opioids, which themselves attenuate fever, while it is expressed normally during epidural analgesia.[6]

Causes

They can be divided into pre-operative, intra-operative and post-operative causes [Table 1].

PATHOPHYSIOLOGY AND ANAESTHETIC RELEVANCE

The most common pre-operative cause of fever is infections, with upper respiratory tract infections (URTI) being the most common, especially in children. About 95% of URTI in children are of viral aetiology. However, allergic and vasomotor rhinitis can also be a presenting aetiology.[7] Though URTI makes the airways prone to constriction, the relationship between epithelial damage, viral infection, airway reactivity, and anaesthesia remains unclear. URTI also alters pulmonary functions, but the impact of these alterations on anaesthesia and surgery remains uncertain.[8]

Febrile episodes following blood transfusion may be due to sepsis from bacterially contaminated units or due to non-infectious complications of transfusion. These episodes may be acute, or they may be delayed, occurring between 24 h and 1 week, when fever may or may not be present.[9]

Occasionally, dehydration can also lead to post-operative fever. Fever was seen in 21–45% patients of paediatric dental GA, which was described to be due to longer duration of pre-operative fasting and inability to eat post-operatively.[10]

Reactionary fever due to tissue trauma and wound infection is an important facet of post-operative fever, with infection manifesting until days later.[11] Various perioperative factors can contribute to wound infection. Perioperative hypothermia to 2°C below normal triples the incidence of wound infection, besides increasing operative blood loss and the need for transfusion during surgery.[11] Blood transfusion and smoking increases susceptibility to surgical wound infection by impairing immune function.[11,12]

Fever may occasionally be due to meningitis with incidence being 1 in 500,000 after epidural and 1 in 5000 after spinal anaesthesia. Symptoms occur hours to days or sometimes up to a month after anaesthesia. Meningitis could be due to failure of aseptic technique or due to bacteria in patient's blood gaining access to the subarachnoid space at the time of lumbar puncture because of microscopic bleeding caused by insertion of the needle.[13]

Contamination of lipid-based agents like propofol, with even very small number of organisms, may result in clinical disease.[14]

Allergic reactions to drugs or the drug itself can be the another reason for perioperative pyrexia.[3,15] Other less reported causes include vertebral osteomyelitis following epidural catheterisation;[16] and non-infective causes like thrombosis; autoimmune disorders; malignancies, connective tissue disorders or metabolic or thermoregulatory disorders.[15,17]

Table 1: Common causes of perioperative pyrexia[2,3,7-16]

Pre-operative	Intra-operative	Post-operative
Common cold (nasopharyngitis)	Allergic reaction	Reactionary fever
Croup (laryngotracheo-bronchitis)	Mismatched blood transfusion	Sepsis
Influenza	Thyroid storm	Blood transfusion
Epiglottitis	Malignant hyperthermia	Dehydration
Hepatitis	Anaesthetic agents	Meningitis after neuraxial anaesthesia
Herpes-simplex	Urological and other surgical manipulations	Contamination by intravenous agent especially propofol
Pneumonia		Deep venous thrombosis
Urinary tract infection	Neurolept malignant syndrome	Drug fever (phenytoin, beta lactam antibiotics, sulfonamides)
Abscess/osteomyelitis		Pancreatitis
Viral hemolytic syndromes		Alcohol withdrawal
Some immunisations, e.g., diphtheria, tetanus		Other emergent causes (myonecrosis, pulmonary embolism, bowel leak, adrenal insufficiency, malignant hyperthermia)

Effects of fever

Fever is defined as an increase in core body temperature above 38°C, which is secondary to an increase in hypothalamic set point. The human body temperature rarely exceeds 42°C.[17,18]

There are suggestions that increased body temperature aids in the activation of host immune response.[18] Some of the enzymes involved in immune defence have their temperature optima not at 37°C but at a higher temperature. We may have evolved to mount over best immune defence at an increased temperature.[2]

Clinical studies suggest that the effect of fever depend in part on the underlying illness. In non-life threatening illnesses, fever due to bacterial infection is shown to be associated with improved survival, but not in more severe diseases. Furthermore, survival decreases when core temperature exceeds 39.4°C, suggesting there is an upper limit to the optimum febrile reaction.[1,2]

The use of febrile-range whole body hyperthermia (FR-WBH) to booster immunological functions has been reported to be an important therapy in oncology and even in non-cancer surgery. The positive effects of FR-WBH are mainly due to a direct physical anti-tumour action at the cellular level, enhanced mobilisation and migration of immune cells.[19]

The negative aspects of fever include increased basal metabolic rate and increased cardiac demand. It is estimated that for every 1°C increase in temperature, the metabolic rate increases by up to 13%.[2] Fever during pregnancy is associated with increased perinatal morbidity. Maternal immune function decreases even in normal pregnancy. Hyperthermia in labouring patients result in higher maternal oxygen consumption and decrease in foetal oxygen delivery.[18]

Fever in neurosurgical patients or patients with acute cerebral damage decreases all measures of outcome, even in those without infection.[2,20]

PRE-OPERATIVE ASSESSMENT

The main concern while dealing with pyrexic patients is whether febrile hyperthermia (fever) is a harmful by-product of infection or is a beneficial host-defence response.[2] Trying to bring the temperature down has its own perils. The patient might post-operatively or intra-operatively, mount a response to increase his or her temperature back to the elevated set point similar to a non-febrile patient who becomes hypothermic. This response has high metabolic cost and is undesirable. Furthermore, there are inherent risks in administering antipyretic therapy and antipyretics may be ineffective.[2]

The decision to proceed with surgery in the face of acute viral infection, especially in children, is controversial and is associated with both medical and economic considerations. Chest radiograph findings typically lag behind the presentation of clinical symptoms in lower respiratory infection.[7] In general, children presenting with symptoms of uncomplicated upper respiratory infection and who are afebrile with clear secretions and appear otherwise healthy, or there are non-infectious conditions, should be able to undergo surgery. Those with severe symptoms – mucopurulent secretions, productive cough, fever more than 38°C, nasal congestion, lethargy and signs of pulmonary involvement – should have their elective surgery postponed for ≥4 weeks.[8]

Neurological injury (e.g. following carotid endarterectomy, during neurosurgery and cardiac surgery) is greater in the presence of an increased temperature. In paediatric patients, there is a risk of febrile seizures. In pregnant patients, one is concerned about the effects of maternal hyperthermia on foetus. In addition, tachycardia may be harmful in patients with ischemic heart disease, valvular heart disease and obstructive cardiomyopathy.[2] Hence, in such patients efforts to normalise the temperature should be done, unless the surgery is deemed to be urgent and imperative.

ANAESTHETIC MANAGEMENT

Once the decision to proceed with the surgery has been made, the further management entails the reduction in perioperative complications. Most drugs used during GA and in particular opioids, have immunosuppressive effects – decrease cell-mediated immunity and promote metastasis. In contrast, propofol is immunologically inert and even has antitumour properties. Regional anaesthesia alone or as an adjunct to GA has an opioid-sparing effect.[19]

Well-debated issue is whether regional anaesthesia is safe in patients who are at risk of bacteraemia. The catheter acts as a nidus for infection in the

epidural space or surrounding structure in the pathway of its tract. If regional anaesthesia is given to a patient with bacteraemia, a prudent approach may be to administer prophylactic antibiotics before anaesthesia.[15] Incidence of meningitis following neuraxial anaesthesia can be mitigated by improved standard of hygiene involving sterility control, use of disposable syringes and single-use vials,[13] in addition to adequate antibiotic cover.

Viral invasion of the respiratory mucosa may render the airway sensitive to secretions or potentially irritant anaesthetic gases. Airway complications occur in increased frequency with the type of airway device (endotracheal tube > laryngeal mask airway > face mask) or the type of anaesthetic (thiopentone > halothane > sevoflurane > propofol). Adequate perioperative hydration of a child should be ensured (by intravenous hydration).[7,8,10]

Outbreaks due to contamination of lipid-based agents (like propofol) may be suspected when an unusual organism is isolated from one or more patients, the infection occurs in clean and uncomplicated surgical procedures, unusual endotoxin reactions occur perioperatively, or the index of suspicion is high. Aseptic handling procedures should be followed with restriction to use of a single vial in a single patient.[14]

Viral haemorrhagic fever associated systemic involvement of the liver, brain and coagulation, should be investigated for the severity of disease and anaesthesia managed accordingly.

Likewise, post-operative temperature rises should be duly evaluated and adequately managed. A helpful mnemonic for post-operative fever evaluation can be 4 W's – wind (pulmonary causes), water (urinary tract infection), wound (surgical site infection) and what we did (drug fever, blood reaction).

Thus, one can view fever as a biologic response modifier, the consequences of which may be beneficial or deleterious, depending on the disease patho-physiology. The available literature though limited, still has discrepancies regarding maintenance of temperature at its elevated range or to normalise it. Further studies are still needed to conclusively affirm or refute these suggestions. In emergent or semi-emergent surgeries, it is always better to have vitals normalised so as to do away with harmful effects of high metabolic rate and increased oxygen demand, especially in patients undergoing neurological or cardiac surgery and in paediatric patients. However, for urgent surgeries, a risk-benefit analysis should be done before proceeding.

CONCLUSION

Managing a patient with febrile entity entails the understanding of detailed pathophysiology of the disease, along with associated impacts of anaesthesia and surgery. High temperature may be beneficial, but temperatures > 38.3°C (101°F) should be treated before taking up for surgery. It is always better to have a patient with physiological parameters as close as possible to the normal range. Still some believe in maintaining febrile patient at his or her elevated temperature (with exceptions). Till further evidences accrue, a definite inference cannot be established.

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Announcement

Conference Calender - 2015

Name of the conference: 63rd Annual National Conference of the Indian Society of Anaesthesiologists, ISACON 2015
Date: 25th to 29th December 2015
Venue: B. M. Birla Auditorium & Convention Centre, Jaipur, India
Organising Secretary: Dr. Suresh Bhargava
Contact: +91 98290 63830
E-mail: suresh3559@yahoo.com
Website: www.isacon2015jaipur.com

Name of the conference: TRISZAC 2015, 31st Annual Conference of Indian Society of Anaesthesiologists, South Zone and 39th Annual Conference of Kerala State Chapter
Date: 6th to 9th August 2015
Venue: Hotel KTDC Samudra & Uday Samudra Beach Hotel, Kovalam, Trivandrum
Organising Secretary: Dr. Gopakumar D
Contact: +91 98476 39616
E-mail: triszac2015@yahoo.in
Website: www.triszac2015.com

Name of the conference: KISACON2015, 31st Annual Conference of Indian Society of Anaesthesiologists, Karnataka State Chapter
Date: 9th to 11th October 2015
Venue: S N Medical College, Bagalkot
Organising Secretary: Dr. Ramesh Koppal
Contact: +91 98455 04515
E-mail: rameshkoppaldr@gmail.com
Website: www.kisacon2015.com

Name of the conference: 6th National Airway Conference 2015 (NAC 2015)
Date: 18th to 20th September 2015
Venue: Workshop: Srinagar, Conference: Gulmarg (J&K)
Organising Secretary: Dr. Zulfiqar Ali
Contact: +91 94190 86761
E-mail: nacsrinagar2015@gmail.com
Website: http://aidiaa.org/NAC2015/NAC_home.html

Name of the conference: 48th Gujarat State Conference of Indian Society of Anaesthesiologists 6th National Airway Conference 2015 (GISACON 2015)
Date: 9th to 11th October 2015
Venue: Shanku's Water World Resort (Ahmedabad-Mehsana Highway)
Organising Chairman: Dr. R G Agrawal
Organising Secretary: Dr. H G Bhavsar
Contact: +91 98242 33694
E-mail: info@gisacon2015.com
Website: www.gisacon2015.com

Name of the conference: 7th Annual Conference of ICA
Date: 13th to 15th November 2015
Venue: Hotel Savera, Chennai
Organising Chairman: Dr. K Balakrishnan
Contact: +91 98410 29259