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Review

Clarification of the circulatory patho-physiology of anaesthesia – Implications for high-risk surgical patients

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HIGHLIGHTS

- The article clarifies the adverse effects of anaesthesia on circulatory physiology.
- It outlines how increased venous capacity lowers CO and MAP and impairs tissue DO_2 regulation.
- Pre-emptive use of venoconstrictor and/or appropriate fluid infusion improves DO_2.
- Understanding the glycocalyx improves rational administration of fluid.
- Restorative action during anaesthesia prevents development of oxygen debt.

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ABSTRACT

The paper examines the effects of anaesthesia on circulatory physiology and their implications regarding improvement in perioperative anaesthetic management. Changes to current anaesthetic practice, recommended recently, such as the use of flow monitoring in high risk patients, are already beginning to have an impact in reducing complications but not mortality [1]. Better understanding of the patho-physiology should help improve management even further. Analysis of selected individual clinical trials has been used to illustrate particular areas of patho-physiology and how changes in practice have improved outcome. There is physiological support for the importance of achieving an appropriate rate of oxygen delivery (DO_2), particularly following induction of anaesthesia. It is suggested that ensuring adequate DO_2 during anaesthesia will avoid development of oxygen debt and hence obviate the need to induce a high, compensatory, DO_2 in the post-operative period. In contrast to the usual assumptions underlying strategies requiring a global increase in blood flow [1] by a stroke volume near maximization strategy, blood flow control actually resides entirely at the tissues not at the heart. This is important as the starting point for understanding failed circulatory control as indicated by 'volume dependency'. Local adjustments in blood flow at each individual organ – auto-regulation – normally ensure the appropriate local rate of oxygen supply, i.e. local DO_2. Inadequate blood volume leads to impairment of the regulation of blood flow, particularly in the individual tissues with least capable auto-regulatory capability. As demonstrated by many studies, inadequate blood flow first occurs in the gut, brain and kidney. The inadequate blood volume which occurs with induction of anaesthesia is not due to blood volume loss, but probably results from redistribution due to veno-dilation. The increase in venous capacity renders the existing blood volume inadequate to maintain venous return and pre-load. Blood volume shifted to the veins will, necessarily, also reduce the arterial volume. As a result stroke volume and cardiac output fall below normal with little or no change in peripheral resistance. The resulting pre-load dependency is often successfully treated with colloid infusion and, in some studies, 'inotropic' agents, particularly in the immediate post-operative phase. Treatment during the earliest stage of anaesthesia can avoid the build up of oxygen debt and may be supplemented by drugs which maintain or restore venous tone, such as phenylephrine; an alternative to volume expansion. Interpretation of circulatory patho-physiology during anaesthesia confirms the need to sustain appropriate oxygen delivery. It also supports reduction or even elimination of supplementary crystalloid maintenance infusion, supposedly to replace the

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"mythical" third space loss. As a rational evidence base for future research it should allow for further improvements in anaesthetic management.

1. Introduction

There has been a great deal of controversy recently concerning perioperative haemodynamic and fluid management, particularly of high risk surgical patients. Although blood flow monitoring is reducing complications in high risk surgical patients [1] controversies surround the amount and type of fluid and the drugs designed to increase cardiac output (CO) and oxygen delivery (DO_2). Some studies show beneficial effects while others do not. What is the explanation for this disparity?

1. Optimising haemo-dynamics immediately, or very soon after the insult – e.g. from an acute reduction in MAP/CO during induction of anaesthesia or as a result of blood loss – will usually work well, in contrast to measures introduced later (e.g. starting therapy after 24 h).
2. Measures principally aimed at sustaining blood pressure (MAP) may fail to maintain tissue need for oxygen, unless DO_2 (and hence CO) are taken into account.
3. Recent studies make a strong case that current routine crystalloid maintenance regimens result in a gross excess of tissue fluid and sodium ion load and may well be a confounder for so called goal directed therapy; the protocol aimed at treating pre-load dependency.

In this paper, results are presented from a highly specific selection of clinical trials and experimental results, to illustrate perioperative mechanisms which interfere with circulatory delivery of oxygen, and illustrate ways these can be countered. Optimum management ensures sustained adequacy of oxygen delivery. Suggested therapeutic manoeuvres simplify management, relating it to the need for an adequate, but not excessive rate of oxygen supply to the tissues (DO_2) and emphasise the need to obtain pre-induction SV, CO, MAP and DO_2 reference values in elective patients and maintain them intraoperatively. This strategy may result in an improvement in outcome [2].

2. Evidence from specific trials and experimentation

2.1. An intra-operative study – Noblett et al. (2006) [3]

The study of Noblett et al. [3] demonstrates that correction of pre-load dependency (volume responsiveness) during the earliest stages of anaesthesia, can improve outcome compared with similar colloid volume given later. The patients underwent elective colorectal resection; standard volatile-based general anaesthesia was used for all patients. The control group received peri-operative fluid at the discretion of the anaesthetist in contrast to the 'intervention' (or protocol) group who received colloid boluses throughout the operative period, prompted by Doppler assessment suggesting pre-load responsiveness. The colloid for the intervention group was predominantly given in the earliest stages of the operation, whereas a similar total colloid volume, given to the control group, was predominantly administered during the later stages. Cardiac index (CI) was consistently higher in the intervention group compared to the control patients (Fig. 1).

Outcomes were much improved in the intervention group including; a shorter hospital stay (7 versus 9 days), reduced morbidity (2% versus 15% major complications in the control group) and significantly lower interleukin (IL) 6 values. The intervention group patients were also able to take food earlier than the control patients (2 versus 4 days). Early and effective compensation for pre-load dependency therefore appears to have been responsible for the improvements.

The reason behind the insufficient circulatory volume in anaesthesia is not immediately obvious since, the fluid responsive state is frequently found as early as the immediate post induction period prior to any fluid loss. There is evidence that fluid responsiveness is due to an increase in venous capacity as a result of reduced sympathetic activity. The relaxation of venous wall smooth muscle tone [4], means that the original, unchanged, blood volume is low relative to the new higher venous capacity. Hence, administration of early colloid fills the new extra capacity.

2.2. Evidence for venous relaxation and its effect on cardiac output

Evidence for venous relaxation comes from a series of experiments with dogs, where nine had complete sympathetic blockade from spinal anaesthesia [5]. The immediate result was a fall in mean arterial blood pressure to about 45 mm Hg. Normal pressure was restored by an infusion of noradrenalin (nor-epinephrine – 0.0052 mg kg^{-1} min^{-1}). The return to normal was a result of restoration of venous wall tone since, *in vitro* experimentation using rings of venous tissue has shown that nor-adrenaline causes venous wall constriction [6].

Consistent with the idea that induction of anaesthesia does not change the blood volume, but increases the capacity of the venous

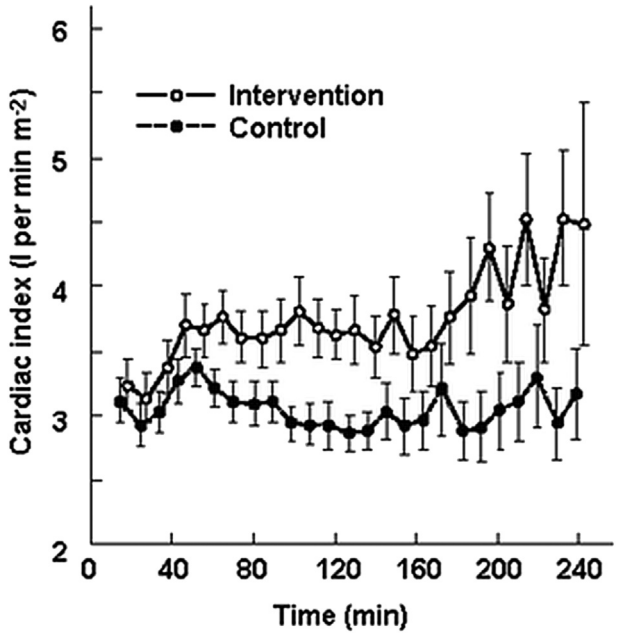

Fig. 1. Cardiac index measured at 10-min intervals during surgery, timed from immediately post-induction of anaesthesia. Values are mean (±s.d.). Noblett et al. [3] (With permission from John Wiley and Sons, publishers of the British Journal of Surgery).