

INTRODUCTION

The concept of intentionally decreasing arterial blood pressure to hypotensive levels during surgery was first proposed by *Cushing* in **1917** for intracranial surgery and was introduced into clinical practice by *Gardner* in **1946**. **Deliberate hypotension gained popularity in Great Britain** after *Griffiths and Gillies* advocated the "hypotensive spinal technique" in **1948**. In **1950** *Enderby* introduced ganglionic blockade using pentamethonium to decrease arterial blood pressure. Subsequent techniques included decreasing cardiac output with volatile anesthetics such as halothane (*Enderby, 1960*) and administering vasodilators such as sodium nitroprusside, adrenergic receptor blocking drugs, which were initially used with trimethaphan (*Hellewell and Pott's, 1966*), or a combination of α and β adrenergic receptor blocking drugs (*Scott et al., 1978*). More recently, nitroglycerin (*Fahmy, 1978*), **purine derivatives** (*Fukunaga et al., 1982*), and isoflurane (*Lamb and Gelb, 1983*) have also been used.

As early as 1950, Enderby emphasized that bleeding could be controlled not only by decreasing mean arterial blood pressure (MAP) but also by properly positioning the patient. Since that time, the decision to induce hypotension has often been controversial, primarily because of an inability to define the lowest safe MAP with confidence

(Leigh, 1975). The terms controlled hypotension; induced hypotension, deliberate hypotension, and hypotensive anesthesia have all been used.

Most studies define deliberate hypotension as a reduction in systolic blood pressure to 80 to 90mmHg. According to another definition, deliberate hypotension is a decrease in MAP no more than 20-30% lower than baseline which is 50 to 65mmHg in normotensive patients **(Van Aken et al., 1986).**

The main purpose of deliberately inducing hypotension is to decrease blood loss, thereby improving operating conditions or decreasing the need for blood transfusions. Therefore, benefit to the patient should be the single criterion determining the need for deliberate hypotension. The potential for transmitting disease by blood transfusion has made deliberate hypotension an even more important consideration today than ever before. The possible benefit to the surgeon of improved visibility of the operative field during delicate procedures (e.g., plastic surgery) is a strong incentive, but it is more difficult to quantitate **(Miller, 2000).**

AIM OF THE WORK

Prospective study to evaluate the reduction of blood loss during hypotensive epidural anesthesia as compared with hypotensive general anesthesia with sodium nitroprusside in primary total hip replacement.

THE ABILITY OF DELIBERATE HYPOTENSION TO REDUCE BLOOD LOSS

Enderby's, (1960) first report demonstrated that of **35 patients, 18 had excellent and 8 had moderate** reduction in blood loss during deliberate hypotension, and **9 patients had no reduction. This inconsistency was** attributed to differing vascular responsiveness to the hypotensive drugs and, in some cases, inadequate positioning. Enderby emphasized that the absolute MAP may not be as important to bleeding as positioning of the surgical field. He mentioned that bleeding at the surgical site would be minimized if the wound were kept uppermost (rather than dependent): arterial vessels would have less pressure, veins would drain more easily, and bleeding at the surgical site would be less.

Deliberate hypotension certainly can decrease blood loss in many surgical procedures. In **1953, Boyan** used hexamethonium (C₆) to lower systolic blood pressure to 65 to 70mmHg in 112 patients undergoing radical cancer surgery (*Boyan, 1953*).

Usually MAP of 50 to 65mmHg is considered safe for deliberate hypotension. *Eckenhoff and Rich, (1982)* supplied objective data that deliberate hypotension can indeed decrease blood loss. Blood loss was compared for patients undergoing rhinoplasty, portacaval shunt, or

craniotomy for aneurysm or suspected tumor. For each of these procedures, blood loss decreased by 50 percent or more with hypotension (**Sood et al., 1987**).

The best documentation that decreasing arterial blood pressure decreases blood loss applies to patients undergoing major orthopedic procedures. Often blood loss is significant during these procedures, and the effect of deliberate hypotension can be documented more readily (**Sharrock and Salvati, 1996**).

Deliberate hypotension has also been used successfully for a variety of other surgical procedures, including head and neck surgery, (**Quist et al., 1982**) procedures on the cranium (**Diaz and Lockhart, 1979**) and middle ear (**Kerr, 1977**), and radical cancer operations.

Shortly after the introduction of deliberate hypotension, drug therapy focused on keeping arterial blood pressure at the surgical site at 50 to 65mmHg, a level believed to decrease blood loss significantly. Because intraoperative measurement of cardiac output was not done routinely, the specific mechanism by which reduction of arterial blood pressure decreased blood loss could not be defined precisely. **Sharrock, (1993)** suggested that depression of cardiac output correlated better with a dry field than did MAP.

To determine whether a decrease in arterial blood pressure or cardiac output was the primary cause of decreasing blood loss, **Sivarajan et al., (1980)** studied 20 healthy subjects undergoing bilateral sagittal osteotomy of the mandible. Cardiac output decreased 37 percent with trimethaphan but increased 27 percent with sodium nitroprusside. Blood loss was similar for both groups, even though cardiac output was two times greater with sodium nitroprusside. **Sivarajan et al., (1980)** concluded that blood pressure, not cardiac output, determined blood loss.

In summary, most patients will have less blood loss if MAP is decreased to 50 to 65 mm Hg. Patient positioning and attention to ventilation, both of which influence venous return, play important roles in minimizing blood loss. Clinical experience suggests that blood loss can be decreased with less severe degrees of hypotension and that attention to the surgical field may be a better monitor than the absolute value for MAP. Most clinical studies do not support the belief that deliberate hypotension decreases operating room time (**Miller, 2000**).

DELIBERATE HYPOTENSION

Controlled hypotension is the elective lowering of arterial blood pressure. The safe level of hypotension depends on the patient. Healthy young individuals tolerate MAP as low as 50-60mmHg without complications. On the other hand, chronically hypertensive patients have altered autoregulation of cerebral blood flow and may tolerate a MAP no more than **20–30% lower than baseline. Patients with a history of transient ischemic attacks may not tolerate any decline in cerebral perfusion (Meibner et al., 1997).**

Techniques to induce deliberate hypotension

I. Physiologic Techniques

Body positioning, the hemodynamic effects of mechanical ventilation, and changes in heart rate and circulatory volume can be used with drugs to lower blood pressure to the desired level. The appropriate use of physiologic maneuvers helps decrease the dose of potentially toxic drugs needed to produce hypotension **(Morgan, 2002).**

II. Pharmacologic Techniques

The ideal agent for inducing hypotension would have ease of administration, a predictable and dose-dependent effect, rapid onset and recovery from effects, quick elimination without the production of toxic metabolites,

and minimal effects on blood flow to vital organs (**Morgan, 2002**).

In addition, the ideal agent would not increase brain size or affect cerebral autoregulation during neurosurgery. Although such an agent does not yet exist, many anesthetic and vasoactive drugs have been used successfully to produce deliberate hypo-tension, including (1) spinal and epidural anesthesia, (2) volatile anesthetics (halothane, enflurane, isoflurane, sevoflurane, desflurane) (3) direct-acting vasodilating drugs (sodium nitroprusside, nitroglycerin, hydralazine, purine derivatives), (4) auto-nomic ganglion-blocking drugs (trimethaphan), (5) α -adrenergic receptor blocking drugs (phentolamine, urapidil), (6) β -adrenergic receptor blocking drugs (propranolol, esmolol) (7) combined (α -and β -adrenergic receptor blocking drugs (labetalol), (8)calcium channel entry blocking drugs (nicardipine), and (9) prostaglandin E₁ (PGE₁).

a. Spinal and Epidural Anesthesia

In **1948 Griffiths and Gillies** used subarachnoid block to produce intentional hypotension. In **1952 Greene** advocated the use of general anesthesia in which hypotension was induced using a high spinal technique to relieve the distressing symptoms of hypotension. Epidural anesthesia was introduced in the early 1950s and is now considered an effective method of inducing hypotension. Pharma-cologic sympathectomy with local anesthetics is a

very effective way of inducing hypotension. Epidural or spinal anesthesia produces arteriolar and venous dilation and hypotension. These effects are enhanced by a pooling of blood in the venous system that decreases venous return and cardiac output. If the block is extended to the midthoracic region, sympathetic innervation of the heart (T1-T4) is also affected, thereby preventing compensatory tachycardia (**Donald, 1983**).

The unpredictable degree of hypotension and the necessity for large infusions of fluids are the principal drawbacks of this technique. It was recently demonstrated, however, that if hemodynamic stability is maintained by intravenous infusion of low-dose epinephrine (50ng/kg/min), this technique can be used safely (**Sharrock et al., 1991**). An epidural anesthetic technique is most commonly used to minimize blood loss during lower abdominal or pelvic surgery.

b. Volatile Anesthetic Drugs

Clearly one can decrease MAP by increasing the inspired concentration of inhaled anesthetic. Cardiovascular effects, hypotension after halothane results primarily from myocardial depression that produces a dose-dependent decrease in arterial blood pressure, cardiac output, and stroke volume, plus a dose-dependent increase in right atrial pressure (Fig. 1). Although halothane also dilates vessels in the skin, brain, and viscera, systemic vascular resistance (SVR) does not

decrease significantly because skeletal muscle tone increases; in addition, renal vascular resistance increases (Fig. 1) (Simpson, 1983).

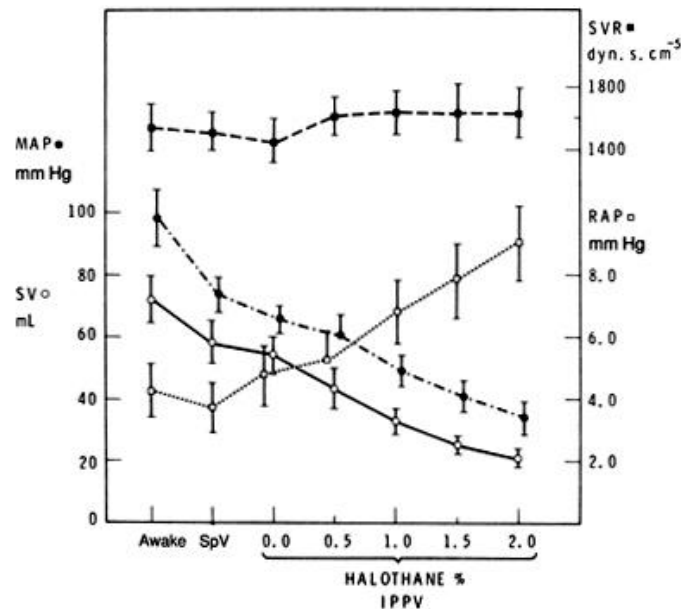


Fig. (1): Effect of increasing concentrations of halothane anesthesia on mean arterial blood pressure (MAP), stroke volume (SV), and systemic vascular resistance (SVR) during the awake state, spontaneous ventilation (SpV), and controlled ventilation (intermittent positive-pressure ventilation, IPPV). Elevation in right atrial pressure (RAP) is evidence of myocardial depression (From Prys-Roberts et al., 1974).

In studies on patients and animals, isoflurane decreased blood pressure by decreasing SVR, whereas cardiac output was maintained constantly at clinically relevant concentrations of the anesthetic (Van Aken et al., 1986).

The intravascular volume status of the patient before induction of hypotension affects the degree of reduction in cardiac output during isoflurane anesthesia.

Volatile anesthetics should not be used as the sole agent to induce hypotension in patients who have intracranial disease because the high concentrations that may be required can worsen brain edema. Such a technique may also increase ICP before opening of the dura and may affect autoregulation. The combination of increased ICP and decreased MAP can reduce cerebral perfusion pressure to less than 40mmHg, a circumstance that can produce brain ischemia. Recent studies in animals and patients showed that combining isoflurane with either an α -adrenergic receptor blocking drug or a combined α and β adrenergic receptor blocking drug attenuated the negative effects of using isoflurane as the sole hypotensive agent (*Meibner et al., 1997*).

In summary, isoflurane should only be used as an adjuvant drug (and in low concentrations) during induced hypotension. This method has the advantages of decreased cerebral metabolism and preserved pulmonary gas exchange (*Van Aken et al., 1986*). The profile of hemodynamic changes induced by sevoflurane and desflurane is very similar to that of isoflurane.

However, due to the pharmacokinetic properties of these volatile agents, including a low blood/gas solubility,

these hemodynamic effects can be better controlled with them as compared with isoflurane. Therefore, sevoflurane and desflurane appear to be superior to isoflurane when used as an agent to facilitate deliberate hypotension. Surprisingly, these drugs have not been investigated yet with respect to their suitability in deliberate hypotension (*Van Aken et al., 1986*).

c. Intravenous Drugs

Many intravenous drugs have been used to decrease arterial blood pressure acutely. Certainly, drugs that permit moment-to-moment control of blood pressure are the most popular. Most of these drugs are titrated to obtain the desired surgical field or predetermined MAP, or both. The differences in pharmacologic properties among agents suggest that combinations of these drugs may provide a better pharmacologic profile than could be provided by any agent used alone.

1 – Sodium Nitroprusside

Sodium nitroprusside is a vasodilating drug most commonly used to induce hypotension during surgery. Its onset of action is rapid, of short duration, and readily controllable. Sodium nitroprusside acts primarily on arteriolar tone; only 65 to 70 percent of arterial sodium nitroprusside is recovered in venous plasma (*Artru et al., 1982*). **Studies on the cardiovascular effects of sodium**

nitroprusside have yielded contradictory results. Some studies report an increase in heart rate and cardiac output with no change in stroke volume (*Bendo et al., 1993*). Yet others report either no change in cardiac output (*Enlund et al., 1996*) or a decrease (*Toivonen et al., 1992*). However, sodium nitroprusside clearly has no adverse effect on myocardial contractility (*Meibner et al., 1997*).

The different results concerning cardiac output and stroke volume probably relate to differences in circulatory volume and cardiac filling pressures before hypotension. Patients with subarachnoid hemorrhage have low circulatory volume (*Milde and Milde, 1991*), a condition that can decrease preload and cardiac output. *Bernard et al., (1991)* found that stroke volume and cardiac output increased during sodium nitroprusside-induced hypotension in deliberately overhydrated patients undergoing orthopedic surgery.

Because the intact sodium nitroprusside contains five cyanide groups, toxicity is a concern *Bernard et al., (1991)* (Fig. 2). The breakdown of sodium nitroprusside in the blood produces free cyanide, the concentration of which depends on the quantity of sodium nitroprusside infused. Cyanide diffuses rapidly into the tissue, where it binds with high affinity to cytochrome oxidase. Such binding causes interference with electron transport and produces tissue hypoxia.

Some of the cyanide ions diffuse out of the erythrocytes and are metabolized in the liver and kidney to thiocyanate, which is excreted in the urine. *Styles et al., (1973)* challenged the concept that cyanide is released in vivo, arguing that any cyanide found in the blood of patients given sodium nitroprusside is caused by photodegradation of the drug in vitro, either before infusion or during assay of the samples. These investigators also stated that "it may well be safe to infuse quantities larger than those currently recommended" (Fig. 2).

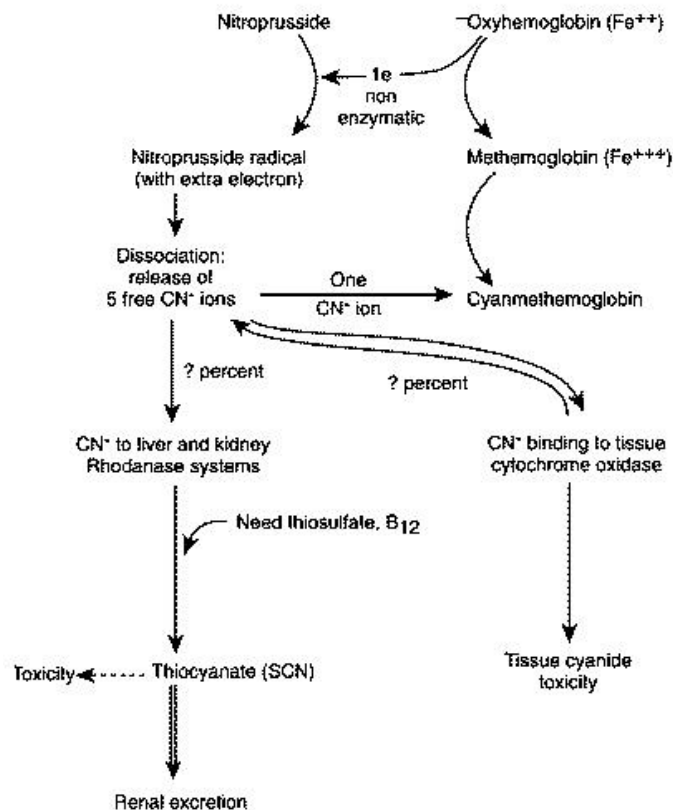


Fig. (2): Schematic representation of the breakdown of sodium nitroprusside in vivo. The high affinity of cytochrome oxidase for cyanide leads to tissue hypoxia (*Modified from Tinker and Michenfelder, 1976*).

Experiments examining the question of photodegradation concluded that cyanide measured in the blood of patients given sodium nitroprusside did not appear to be an artifact of assay methods (*Adams et al., 1974*). **Furthermore, degraded nitroprusside remains** biologically active and may be more toxic than intact nitroprusside, as free cyanide is a product of degradation.

Shortly after the widespread use of sodium nitroprusside, reports of toxicity began to appear (*Meibner et al., 1997*). In some of the initial reports, large concentrations of sodium nitroprusside had been infused. However, in some individual cases, younger patients appeared to show resistance to the effects of nitroprusside.

The sympathetic nervous system and the renin-angiotensin system are activated. Also, the release of vasopressin increases (*Bernard et al., 1991*). This increase in vasopressin was greater than the increase in plasma catecholamines or plasma-renin activity during sodium nitroprusside-induced hypo-tension.

The question of resistance or tachyphylaxis to sodium nitroprusside is complex. Normal patients had significant increases in plasma levels of norepi-nephrine