

# Permissive Hypotensive Resuscitation - an Evolving Concept in Trauma

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## Introduction

Currently there is considerable debate in the trauma literature, about the administration of intravenous isotonic fluids in hypotensive trauma patients with suspected uncontrolled hemorrhage, prior to control of the bleeding. The traditional approach of the emergency physician and the trauma surgeon is to correct any traumatic, hypovolemic hypotension as rapidly as possible. This stems from indoctrination during medical training that hypotension is uniformly deleterious to the patient. The American College of Surgeon's Advanced Trauma Life Support Course® also promotes the rapid infusion of large volumes of crystalloids to hypotensive trauma patients.<sup>1</sup> As a result, rapid infusion devices have become standard equipment in emergency rooms in trauma centers. This emphasis on immediate post-injury fluid resuscitation was based on early experimental data showing that rapid restoration of blood volume and pressure led to improvement of vital organ function and long term survival, by avoiding the late sequelae of hypovolemic shock. However a number of trauma surgeons have challenged this conventional dictum. They expressed concern that overzealous fluid resuscitation before control of bleeding, may be detrimental to the patient by increasing the rate and amount of blood loss. On the other hand, many opponents of this concept suggest that uncorrected severe hypotension may lead to early death by increasing the risk of post resuscitative organ failure and exacerbating secondary brain injury in patients with associated traumatic brain injuries. This monologue will explore this evolving concept in greater detail and offer some guidelines.

The concept of limited fluid resuscitation, or even non-resuscitation of trauma patients is not novel. In the mid sixteenth century, the famous French surgeon Ambrose described the conservative treatment of a soldier with an abdominal gunshot wound, who survived with no operation or fluid resuscitation. Canon, in the early part of the twentieth century alluded to the disadvantages of giving fluids to a bleeding hypotensive patient, as it may "pop the clot" and hasten exsanguination. This has even greater applicability to the combat field setting, and consequently military medical research focussed on determining the ideal resuscitation method and type of fluids to use in war time casualties.<sup>2</sup>

Since then considerable experimental evidence has accumulated to support that aggressive fluid resuscitation leads to increased bleeding by a variety of proposed mech-

anisms. Increased mean arterial and venous pressure leads to a greater pressure-head for blood loss, by dislodging a nascent hemostatic clot, hemodilution of platelets and clotting factors and alterations in the viscosity and rheologic properties of blood. In addition there is some evidence that at the cellular level, hemodilution reduces the oxygen-carrying capacity of whole blood and decreases oxygen delivery to the tissues. This is confounded by the proposed mechanism of "resuscitation injury" secondary to the ischemia-reperfusion phenomenon. Almost forty years ago, Shaftan et al<sup>3</sup> demonstrated in a dog model of unrelenting arterial bleeding, that aggressive fluid resuscitation actually increased the amount of blood loss. This finding was confirmed by subsequent animal model studies on uncontrolled intra-abdominal and intra-thoracic hemorrhage.

Stern and colleagues<sup>4</sup> showed in a porcine model with abdominal aortic injury with near fatal hemorrhage, that attempts to restore blood pressure with rapid infusion of crystalloids led to increased bleeding and mortality. Capone and associates<sup>5</sup> also confirmed this adverse result in a murine model, and showed that judicious fluid administration improved short-term survival. Solomonov et al<sup>6</sup> and Krauz et al<sup>7</sup> independently showed, that in an experimental sheep model of splenic injury, with uncontrolled hemorrhage, vigorous infusion of isotonic and hypertonic saline to achieve a normal blood pressure resulted in increased bleeding and mortality. These authors found a direct correlation between the volume of infusate and the degree of pressure elevation with the adverse outcome.

Very few clinical trials investigating the role of the timing and volume of fluid resuscitation in hypotensive trauma patients have been performed. This may stem from a perceived reluctance to withhold fluids from an actively bleeding patient as being unethical. However, Bickell et al<sup>8</sup> in a large prospective study of almost 600 trauma patients with penetrating torso injuries and hypotension, reported a significantly lower survival in patients who received fluid resuscitation before surgical control of the hemorrhage, than in those who received delayed fluids in the operating room (62% vs. 70%,  $p=0.04$ ). They also found that postoperatively, there was a trend towards reduced organ dysfunction in the delayed resuscitation cohort.

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This is in stark contrast to another prospective, randomized clinical trial, which included patients with both blunt and penetrating trauma and initial systolic blood pressure of 90 mmHg or less. In this study, Dutton et al.<sup>9</sup> evaluated the role of titration of fluid resuscitation to a below normal systolic blood pressure, until surgical control of bleeding was achieved. They randomized their patients (n=110) into two resuscitative protocol groups. The hypotensive resuscitation protocol group with a target systolic blood pressure of <70mmHg and the normotensive resuscitative protocol group with a target systolic blood pressure of >100 mmHg. These goals were accomplished with titration of crystalloid administration and use of pharmacologic agents i.e. vasopressors, narcotics and sedatives. They found that there was no statistically significant difference in hospital mortality in both these groups. The researchers concluded that titration of initial fluid therapy to a lower than normal systolic pressure, did not influence survival.

Another large prospective, randomized study to evaluate the effects of pre-hospital fluid resuscitation in blunt trauma, was conducted in the United Kingdom.<sup>10</sup> Over 1300 patients were enrolled, 54% of whom were randomized to the "no fluid resuscitation" in the field protocol, and the remainder received normal fluids as directed by the routine paramedic's protocol. The mortality rates were 9.1% and 8.8%, and the major complication rates were 8.5% and 7.5% respectively. In the subset of patients with severe injuries, with an injury severity score (ISS) >15, although the adjusted odds ratio for death was 1.96 in the "restricted fluid" group and 0.51 in the "routine fluid" group, it was not found to be statistically significant (p=0.45). A multivariate analysis also did not identify pre-hospital fluid administration to be a contributory risk factor for mortality. The authors concluded that routine fluid resuscitation in the field, did not adversely impact mortality in blunt trauma patients.

Given these findings, some surgeons have voiced concern that avoiding adequate fluid resuscitation in near-fatal hemorrhage may actually hasten mortality, prior to possible surgical control of the bleeding. They stated that aggressive fluid administration to these patients could maintain sufficient remaining blood volume to prolong survival, until definitive hemorrhage control. In addition to this, prolonged hypotension and tissue hypoperfusion/ hypoxia may lead to increased organ dysfunction and late mortality. However, none of the studies performed to date provide long-term followup. Therefore no conclusions can be drawn. Experimental work has confirmed that uncorrected severe hypovolemic shock does lead to increased mortality in the small animal model.<sup>11</sup>

Matsuoka et al<sup>12</sup> demonstrated in the murine model

of uncontrolled hemorrhage, that even small volumes of hypertonic saline infusion, improved blood pressure and survival, compared with no fluid resuscitation.

Another potential problem with a policy of limited fluid resuscitation prior to haemorrhage control, is the possible increase in the number of unnecessary celiotomies. Many initially hypotensive trauma patients stabilize with fluid administration and therefore do not require operative intervention. It is conceivable that without adequate fluid resuscitation, many of these patients would have undergone non-therapeutic operations. This can be compounded by the fact that delaying an operation in the anticipation of spontaneous correction of the hypotension without fluid resuscitation can be detrimental.

The concept of an "ideal" mean arterial pressure (MAP) is an elusive one. The optimal MAP is one which would provide a sufficient flow of blood to delicately balance hemostasis, maintain the rheologic properties of blood and simultaneously provide adequate tissue perfusion. MAPs of 40 - 80 mmHg have been used as end points of resuscitation in most clinical trials. However no studies conducted so far have explicated the ideal MAP in trauma fluid resuscitation, or correlated it to survival or degree of organ dysfunction. Physiologic data extrapolated from studies on renal perfusion and cerebral blood flow autoregulation indicate, that the minimal MAP for the functioning of at least these vital organs, is about 50 - 70 mmHg.

The incidence of traumatic brain injuries (TBI) is increasing worldwide. A major concern with hypotensive resuscitation, is the possible effect of exacerbating secondary brain damage in patients with concomitant severe head injuries. Pioneering clinical research by Rosner et al<sup>13</sup> strongly suggested that maintaining the cerebral perfusion pressure (CPP) more than 70 mmHg reduces morbidity and mortality in TBI patients. Recent work by Alspaugh et al<sup>14</sup> demonstrated that delaying fluid resuscitation in animals with combined grade IV splenic and traumatic brain injuries, led to a higher mortality rate. They also found that the size of the brain lesions on post mortem examinations were larger in the cohort with delayed fluid resuscitation.

## Summary

Trauma fluid resuscitation continues to be a hotly debated issue. There is overwhelming experimental evidence to suggest that administration of resuscitation fluids is not entirely innocuous. Aggressive intravenous crystalloid administration in the presence of uncontrolled hemorrhage promotes continued bleeding and increases mortality. However this is countered by concerns that avoidance of fluids in the resuscitative phase may lead to tissue hypoperfusion, organ failure and death prior to control of bleeding.

avoidance of fluids in the resuscitative phase may lead to tissue hypoperfusion, organ failure and death prior to control of bleeding. It may also have a deleterious effect on neurologic outcome in patients with TBI as well as increase the number of unnecessary operations. Currently there is no clear cut universal consensus pertaining to the optimal resuscitation strategy in trauma patients. However most prudent trauma surgeons propose, that a policy of judicious fluid administration to maintain the MAP in the 60 - 80 mmHg range is advisable and appropriate.<sup>15,16</sup> Fluid resuscitation in trauma should be considered a double edged sword (too much too early or too little too late!). It should not be considered definitive therapy; as in a number of trauma patients it is only a temporizing measure, until surgical control of bleeding can be achieved.

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