Damage Control Resuscitation

11

Damian Keene

11.1 Introduction

The most common cause of death from all causes of trauma is haemorrhage. Within the UK it accounts 40% of all deaths from trauma and for 80% of deaths in the operating theatre [1]. It remains the leading preventable cause of trauma-related death and the most frequent reason for death within the first hour of injury [2]. A similar picture has been seen in the recent conflicts in Iraq and Afghanistan with the majority of deaths from ballistic and blast injury occurring within the first hour [3]. The most common preventable cause of death being from exsanguination due to uncontrollable haemorrhage [4].

In 2003 Brohi et al. demonstrated that traumatic injury leads to coagulopathy as part of the primary physiological response to trauma. Known as acute trauma coagulopathy (ATC) it results from the injury process itself and its severity is directly related to the severity of injury [5]. Our increased understanding of the physiology of trauma haemorrhage has been fundamental to the development of the current approach to its management. This is encompassed by the concept of damage control resuscitation (DCR). DCR describes a multi-faceted approach aimed at reducing mortality from trauma. The concept has evolved rapidly over the last decade based on military experience in Iraq and Afghanistan, leading to significant improvement in casualty survival from ballistic injury [6, 7]. It encompasses three main resuscitative strategies; permissive hypotension, haemostatic resuscitation and damage control surgery (DCS).

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11.2 History of DCR

In 1983 Stone et al. described the concept of truncated exploratory laparotomy. Surgery was stopped with the onset of clinically apparent coagulopathy [8]. This approach was further developed by Rotondo et al. in 1993 with the concept of 'damage control.' They described deliberately short and rapid surgical control of haemorrhage, damage control surgery DCS, followed by resuscitation aimed at correcting hypothermia, correcting coagulopathy and re-establishing normal cardiovascular parameters. A further definitive period of surgery then followed. This was opposed to waiting for the onset of clinical coagulopathy before termination of surgery. This approach demonstrated improved outcomes in the most severely injured [9]. Johnston et al. expanded the remit of damage control in 2001 suggesting both short pre-hospital times and early emergency department warming and volume resuscitation may be responsible for improved survival in their trauma network [10].

The onset of conflict in Iraq and Afghanistan further developed the concept of damage control; the severity and complexity of the casualties driving efforts to improve their management subsequently leading to significant reductions in mortality [6, 7]. Over this period, the multiple stages and interventions of trauma resuscitation have been unified under one concept, damage control resuscitation (DCR). The three key facets of DCR are [11, 12];

1. Haemostatic resuscitation (HR)
2. Permissive hypotension (PH)
3. Damage control surgery (DCS)

These are undertaken in parallel rather than sequentially as previously described (Fig. 11.1).

The UK military definition of DCR encompasses all care from point of injury through to post-surgical care on the Intensive Care Unit. The overall aim being 'to minimise blood loss, maximise tissue oxygenation and to optimise outcome' [11]. This has pushed the point of initiation of DCR even closer to the point of injury with

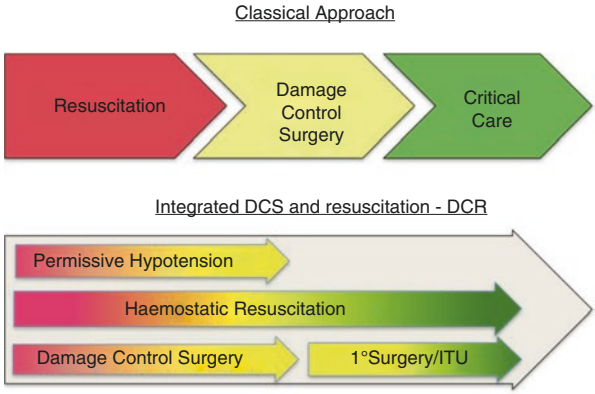

Fig. 11.1 Key aspects and timings of DCR

the advent of 'self or buddy aid.' This entails early use of tourniquets and haemostatic dressings at the point of wounding by the casualties themselves or fellow soldiers [13–15]. With the increased occurrence of MTFA incidents there is an increasing drive to educate and empower the public in the concept of self or buddy aid [16]. This is now being pushed forward to UK civilians as the 'citizenaid' programme [17].

11.3 Physiology of Trauma

11.3.1 The Lethal Triad

The lethal triad of hypothermia, coagulopathy and acidosis was first described in 1982 and is associated with increased mortality in trauma [18]. Shock due to blood loss leads to tissue hypoperfusion resulting in anaerobic metabolism and the generation of a metabolic acidosis. Prolonged acidosis, pH <7.1, is associated with multiple negative effects on coagulation including reduced fibrinogen levels, thrombin generation and platelet count [19].

Poor tissue perfusion leads to hypothermia, this is compounded by removal of casualties clothes to find injury and the administration of cold fluids. Hypothermia results in reduced platelet function and coagulation enzyme activity. Its presence is an independent predictor of mortality [20, 21].

Coagulopathy is not only a product of hypothermia and acidosis, clotting factors are consumed and lost due to clot formation. The administration of crystalloid fluids can worsen it further due to haemodilution [22]. The coagulopathy leads to further blood-loss and hypothermia leading to a vicious cycle of worsening physiology that if allowed to continue will result in death [18].

11.3.2 Acute Trauma Coagulopathy

In the last decade it has been shown that coagulopathy will develop independently of the lethal triad as part of the primary physiological response to traumatic injury [5]. In 2003 Brohi et al. demonstrated that coagulopathy was present in up to one-third of trauma patients (Injury Severity Score >15) presenting to emergency department even before the administration of fluids, its severity was directly related to the degree of tissue damage and duration of shock. This has led to the concept of Acute Traumatic Coagulopathy (ATC) [5]. Patients with ATC have significantly higher mortality and are at greater risk of multi-organ failure [5, 23].

The exact pathophysiology of ATC is yet to be fully understood, it is likely there are a number of interplaying processes. Both pro-coagulant and anti-coagulant processes appear to be enhanced but with the balance tipping toward anticoagulation by increased fibrinolysis. This is the rationale for tranexamic acid (TXA) administration which has been shown to reduce mortality from trauma haemorrhage [24].

Activated protein C (APC) levels are raised in patients with ATC with tissue hypoperfusion implicated as the initiating factor [23, 25]. APC is an anticoagulant protein that exerts its effects by inhibition of plasminogen activator inhibitor (PAI) resulting in fibrinolysis. It also combines with Protein S on endothelial cells resulting in inactivation of FVa and FVIIIa thereby reducing thrombin formation [23]. APC levels have been shown to be elevated and both FVa and VIIa levels reduced in casualties with ATC [26]. A recent study has shown that whilst FVa and FVIIIa are reduced they are not reduced enough to explain the degree of coagulopathy suggesting that APC induced fibrinolysis is the predominant effect [23].

Hypoperfusion results in hypoxia as well as epinephrine and vasopressin release which activates tissue plasminogen activator (t-PA), also inhibiting PAI thereby promoting fibrinolysis [27].

Platelets are a key contributor to both clot initiation and final clot strength [28]. Whilst platelet counts are typically normal, significant dysfunction has been demonstrated on admission even after minor injury [29–31]. It has been postulated that this occurs due to massive ADP release from tissue trauma resulting in exhaustion of the ADP receptor mediated response pathways [29]. The role of platelet dysfunction is supported by recent findings that platelet administration is associated with improved mortality and decreased transfusion requirements in major trauma [32].

11.4 Components of Damage Control Resuscitation

The aim of DCR is to optimise the physiological status of the patient at all stages, in particular with regards to coagulopathy, with the aim of stopping or preferably reversing the physiological deterioration of the casualty.

11.4.1 Permissive Hypotension (PH)

The aim of PH is to maintain perfusion of vital organs without causing clot disruption, due to raising blood pressure, and to minimize the administration of crystalloid fluids. Crystalloid fluids contain electrolytes similar to that of the plasma but no clotting factors, platelets or red blood cells.

Whilst bleeding is uncontrolled, 250 ml fluid boluses are given to achieve a target systolic blood pressure of 80–90 mmHg, approximately 80% of the normal value in a young adult [33]. A radial pulse can be used as a surrogate until a blood pressure is available however, whilst absence of a radial pulse signifies significant shock its presence does not guarantee a blood pressure of 80 mmHg [34, 35]. If there is no head injury, fluid can be titrated to maintain consciousness as this is a direct marker of end organ perfusion.

Permissive hypotension should be thought of as a state of ‘controlled’ shock where a significant proportion of the bodies’ tissues will deliberately be inadequately perfused, resulting in ongoing acidosis. It is vital that as soon as bleeding is controlled, a normal blood pressure is targeted to reverse the acidosis [36]. Not all

bleeding will require surgical control; application of a tourniquets or a pelvic binder may initially be adequate.

PH is contraindicated in patients with head injuries. Hypotension in this group is associated with increased mortality, recent studies have suggested that the threshold for intervention in this cohort should be increased to a systolic blood pressure of 110 mmHg [37, 38].

Evidence for improved mortality from PH is still lacking. Improved mortality in penetrating trauma has been demonstrated, however this was in a system of no fluid versus fluid, rather than fluid titrated to a target blood pressure [39]. Evidence from animal studies shows that in blast injury hypotension can be maintained for up to 60 min but past this point the oxygen debt of the tissues may be impossible to overcome even with aggressive DCR [40–42].

11.4.2 Haemostatic Resuscitation (HR)

The aim of HR is to restore normal patient physiology by reversing the effects of the lethal triad and ATC. Rapid control of blood loss is vital if this is to be achieved [43, 44]. Whilst bleeding is ongoing even aggressive HR will at best only halt the coagulopathy and not reverse it [44]. This highlights the importance of parallel HR and control of bleeding.

Improved mortality from the use of high ratio Packed Red Blood Cell (PRBC) and Fresh Frozen Plasma (FFP) resuscitation, at a ratio of 1:1, was first demonstrated in 2007 based on casualties treated at a US combat support hospital [45]. Multiple subsequent retrospective studies in civilian hospitals have supported this initial finding [46]. The exact ratio that confers improved survival has been questioned with one retrospective study showing no benefit of 1:1 ratio (PRBC:FFP) administration over a ratio of 2:1. Subsequently the PROPPR prospective randomised control trial compared 1:1:1 or 1:2:1 (FFP:PRC:Plts) in resuscitation of trauma haemorrhage. There was no difference in the 24 h or 30 day mortality with each ratio but haemostasis was achieved in more patients in the 1:1:1 group [47]. A recent prospective cohort study demonstrated that not only did a high ratio of FFP to PRBC improve survival, a high ratio of platelets to PRBC (of 1:1 or greater) was associated with improved survival and reduced transfusion rates [32].

Heamostatic resuscitation itself can be considered as consisting of two phases: resuscitation before and after control of bleeding.

11.4.2.1 Massive Transfusion Protocols

The logistical challenges in undertaking massive transfusions are significant even in single casualties, with the complexities rising significantly with increased casualty load [48]. The rapid restoration of blood volume in severely shocked trauma patients can require significant volumes of blood products, with one UK study of military casualties having a median administration of 27 units of PRBC and FFP [43]. In order to achieve adequate volume and composition of blood products massive transfusion protocols are used (Fig. 11.2) [48].

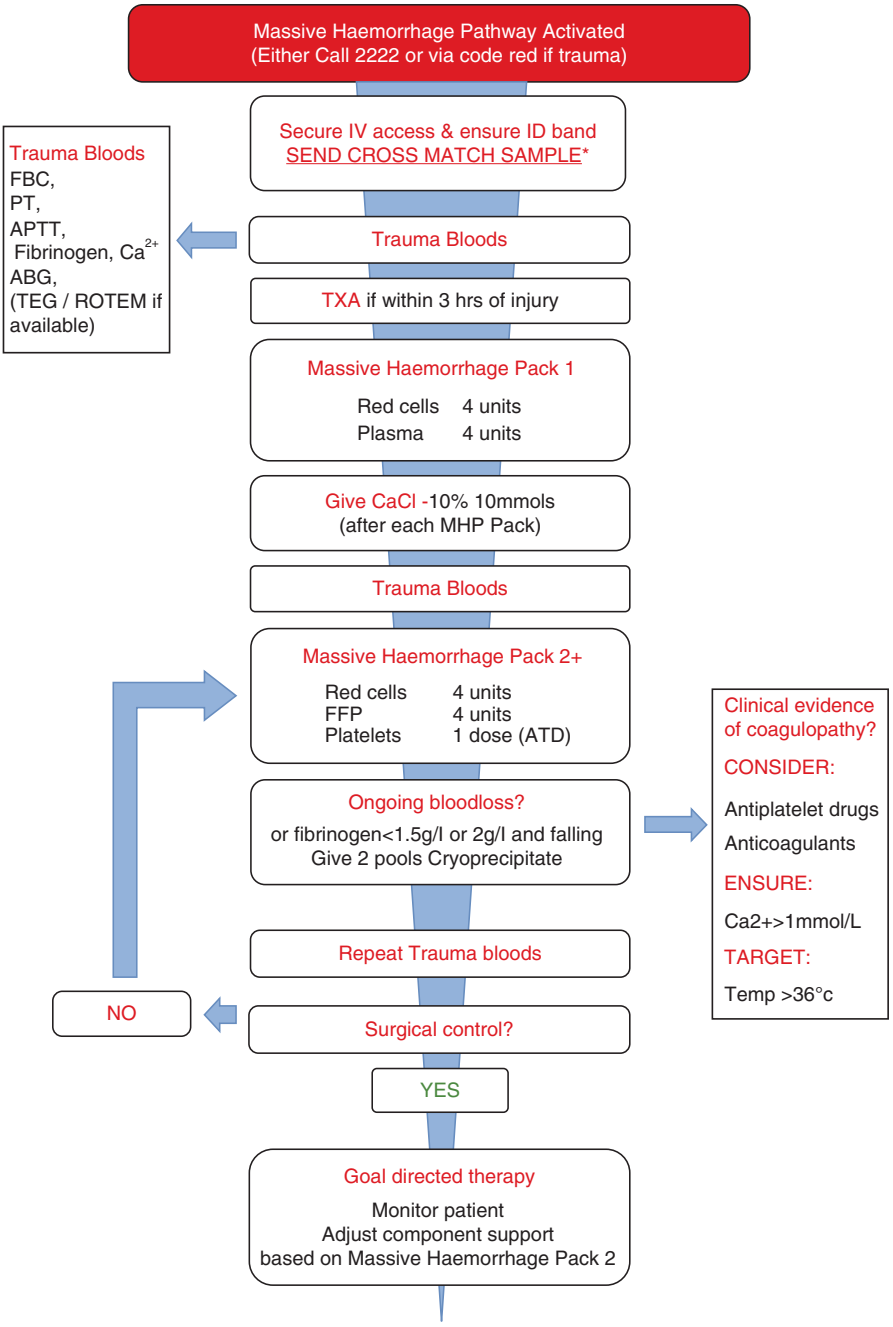

Fig. 11.2 Example of a massive transfusion protocol—based on Queen Elizabeth Hospitals Birmingham (UK) massive haemorrhage protocol Standard operating procedure Nov 2016

Once the recognition or expectation of a massive transfusion is present, one call to a dedicated phone line can be made to trigger the protocol. Blood boxes containing pre-defined blood products are released until the protocol is terminated by the treating clinicians. This allows rapid administration of fixed ratios of Fresh Frozen Plasma (FFP), Packed Red Blood Cells (PRBC) and platelets. Whilst bleeding is uncontrolled fixed ratio transfusion is recommended.

Use of laboratory coagulation studies in this phase is likely to be unhelpful as these tests require time to send, analyse and return, taking up to 60 min to provide results [49]. In this time the patient's blood volume may have been replaced several times, making the results historic [50].

11.4.2.2 Targeted Resuscitation

Once bleeding is controlled a more tailored approach is employed to both the volume and the type of blood products administered. Efforts are made to reduce the sympathetic drive of the casualty using opiates. Any resulting drop in blood pressure is then corrected with PRBC and FFP (1:1) with the aim of restoring the patients normal blood volume. The degree of metabolic acidosis is used as a marker of adequate resuscitation, the target being normalization of the base excess and improving lactate [51]. This is tested at least every 30 min, more frequently if the casualty is unstable. The aim of this process is to restore their physiological reserve allowing them to tolerate further blood loss that may occur during surgical debridement that they would not have tolerated initially.

Standard vital signs are poor markers of adequate resuscitation [52]. Anecdotally once initial surgical control is gained, the patient may be normo or hypertensive due to a high sympathetic tone. They will still be significantly acidotic and volume deplete. If surgical control were to be lost prior to adequate volume resuscitation and correction of their acidosis, rapid deterioration or death may result. At this point a pause in surgery allowing time to 'catch up' maybe necessary with surgery continuing once physiological stability is improved. This approach requires close communication between the anaesthetic and surgical teams [53].

Correction of coagulopathy at this stage can be guided by coagulation studies which are available in most hospital laboratories. The standard tests of coagulation are platelet count, fibrinogen levels, prothrombin time (PT) and activated partial thromboplastin time (aPTT) (Fig. 11.3) [51, 54]. Their use as a guide to product

	Target	Treatment
INR and aPTT	< 1.5 of normal	If high give FFP 30ml/kg
Fibrinogen	1.5 – 2 g/L	Replace with cryoprecipitate
Platelet count	75 x10^9/L (100 if ongoing bleeding OR head injury)	Replace with 1 ATD

Fig. 11.3 Normal laboratory test treatment targets [55]

replacement is not without limitations. None look at whole blood clotting or take platelet function into account. PT and aPTT are measures mainly of clot initiation, patients can still be coagulopathic even with normal aPTT and PT values [55]. As previously stated test turnaround time can be prolonged leading to delays in treatment of any underlying coagulopathy [49].

Point-of-care coagulation monitoring using viscoelastic tests can provide meaningful results with in 10 min [56]. Their use is proving successful in targeting product replacement and has demonstrated a reduction in blood product administration but no reduction in mortality [57].

When using tests to guide resuscitation it is important to understand the difference between treatment targets versus triggers. A target is the minimal acceptable level that a value is allowed to reach, for example fibrinogen should be >1.5 g/dl [55]. If 1.5 g/dl is used as a treatment trigger the level would fall below acceptable minimal standards before correction as test turnaround is never instantaneous and there will likely be a delay before blood products are available. Falling levels need to be anticipated and acted upon before they reach minimal targets. Treatment triggers mean that early delivery can be considered based on the clinical situation and direction to maintain levels above the suggested minimal targets. The faster the test to intervention time the smaller the margin between target and trigger required.

11.4.3 Tranexamic Acid

Part of the coagulopathy in trauma is caused by fibrinolysis. To prevent this Tranexamic acid (TXA) should be given as early as possible, preferably in the prehospital phase. It must be given as soon as possible with in 3 h of injury, after this period it is associated with an increase in mortality [25]. Retrospective UK Military data showed that the survival effect was more pronounced in those receiving a massive transfusion [58]. Whilst Crash-2 showed a net increase in survival it did not identify which patients had ATC, the perceived target of action. Current studies are underway to assess if a particular cohort of patients can be identified that will gain maximal benefit from this therapy (PATCH 2) [59].

11.4.4 Hypothermia

As previously stated hypothermia is associated with increased mortality [20]. Once heat is lost rewarming can take significant periods of time to achieve. The best strategy here is prevention, limiting casualty exposure, warming intravenous fluids and methods to reduce evaporative losses [60]. If warming is required under casualty heating systems may provide the best option if surgical access is required to most of the casualty. Forced air warming devices can be used if the casualty is being operated on in limited body areas. It is vital to remember that blood can pool

under the casualty on the operating table this will lead to further cooling or difficulty warming.

11.4.5 Managing Electrolytes: Hypocalcaemia and Hyperkalaemia

Acute hypocalcaemia is a common complication of massive transfusion, calcium is bound by the citrate in transfused FFP reducing the ionized plasma levels [51]. Hypocalcaemia increases coagulopathy by reducing the function of the clotting cascade and platelets. Myocardial contractility and systemic vascular resistance are also reduced. Low ionized calcium levels are associated with increased mortality and need for massive transfusion [61].

During uncontrolled bleeding and the use of MTP calcium should be replaced at set intervals, more if the ionised calcium is still reduced. 10 ml of 10% Calcium Chloride or equivalent should be administered with every 4 FFP and 4 PRBC. Once bleeding is controlled regular arterial blood gases should guide calcium replacement.

Potassium concentrations in PRBCs can be over 60 mmol/L depending on the age of stored blood [62]. Whilst efforts to reduce potassium levels through washing and irradiation appear to have reduced the occurrence of hyperkalaemia in standard transfusions, it can still occur with the administration of large volumes of PRBC [62, 63]. Potassium levels must be closely monitored and hyperkalaemia treated with a glucose and insulin infusion.

11.4.6 Anticoagulants

In developed countries many victims of trauma are increasingly elderly patients with significant comorbidities requiring anticoagulation. Many of these patients are now taking Novel Oral Anticoagulants (NOAC) which are less detectable with standard laboratory tests, TEG/ROTEM may prove more useful in this group although clinical experience is still limited [64–66]. If, despite normal testing, the patient is clinically coagulopathic preceding use of a NOAC must be considered. The drugs are currently difficult to reverse but agents are starting to be approved for clinical use. Expert advice from a Haematologist is advised.

11.4.7 Factor Concentrates and Fresh Whole Blood

Whilst UK and US practice involves the use of FFP and cryoprecipitate for resuscitation European systems utilise factor concentrates such as prothrombin complex concentrate and fibrinogen concentrate to achieve similar goals [67]. This approach has been shown to reduce the need for allogenic blood transfusion and has the advantage of not requiring a cold chain for storage [68, 69].

Despite modern DCR techniques some casualties will continue to have a worsening coagulopathy. This may in part be due to the decreased red cell function and reduced levels of functioning clotting factors in stored blood products [70].

Fresh whole blood (FWB) overcomes these problems and has been used safely on recent military operations. It has shown a larger reduction in coagulopathy compared to component therapy [71]. Multiple retrospective analyses of mortality have however shown conflicting effects although none have shown harm [71–73]. There is now increasing interest in the use of both FWB and stored whole blood for resuscitation in trauma. This is likely to be an area of significant research in the immediate future [74].

11.4.8 Damage Control Surgery

DCS comprises of a range of surgical interventions targeted at halting deterioration of the patient's physiological condition rather than attempting definitive restoration of function. DCS allows rapid control of bleeding without which normal physiology in particular correction of coagulopathy cannot be achieved even with advanced fluid resuscitation techniques [44, 45]. This is discussed further in Chap. 13.

11.5 Considerations with Multiple Ballistic Casualties

DCR in severely injured hypovolemic casualties requires significant resources in terms of personnel, operating space and number of blood products [75, 76]. In the 2015 Paris terror attacks there were 76 high priority casualties that required emergency surgery or embolization to control bleeding [77]. Planning for the London Olympics estimated requirements of 10 units of PRBC, 6 Units FFP and 1 pool of platelets per T1 or high priority case [74].

An MTFA incident within the UK is likely to place significant pressure on blood stocks, particular group O [76]. Early use of group O positive blood in all males as well as females over 50 years will help to protect O neg. stocks. An earlier switch to group specific blood can be considered but this may well increase the risk of ABO incompatibility [74].

The use of pre-screened fresh whole blood donor panels may provide a means to meet surges in demand. This system is currently being implemented in Norway to increase blood supplies in times of emergency [74].

The large number of casualties requiring rapid access to surgery can provide significant pressures on theatre capability. Planning and preparation is key to being able to rapidly gain additional staff and generate increased theatre capacity.

Conclusion

Addressing all aspects of abnormal physiology as close to the point of injury as possible is vital for successful damage control resuscitation. Good organisation with the early involvement of senior clinicians and well-rehearsed teams are key to delivery, especially in the event of multiple casualties. Use of this approach is now well shown to improve outcome in severe ballistic injury [6].

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