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Fluid Resuscitation in Hyperglycemic Crises: A Systematic Review of the Two-Bag Method Versus Standard Therapy in the Emergency Department

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Abstract:

- ***Background:***

Diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic state (HHS) represent life-threatening hyperglycemic emergencies requiring aggressive fluid resuscitation as a cornerstone of management. Traditional one-bag fluid protocols, which combine dextrose and electrolytes in a single intravenous bag, have been the standard approach in emergency departments for decades. However, the two-bag method employing separate bags for isotonic crystalloid and dextrose-containing fluids ,has emerged as an alternative strategy offering potential advantages in metabolic recovery and safety outcomes.

- ***Objectives:***

This review synthesizes current evidence comparing the two-bag method with standard one-bag protocols in the emergency department management of hyperglycemic crises, evaluating efficacy, safety, and clinical outcomes across adult and pediatric populations.

- ***Clinical Significance:***

The adoption of two-bag fluid administration protocols represents a meaningful advancement in emergency department management of hyperglycemic crises. By enabling independent adjustment of dextrose and electrolyte administration rates without requiring bag changes, this method reduces resource utilization, minimizes iatrogenic complications, and accelerates metabolic recovery.

- ***Conclusions and Future Directions:***

While accumulating evidence supports two-bag methodology, further research is needed to define optimal protocols across diverse patient populations, clarify electrolyte replacement strategies, and establish consensus guidelines for implementation.

Keywords: *Diabetic Ketoacidosis, Fluid Resuscitation, Emergency Department Management.*

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I. INTRODUCTION

- *Overview of Hyperglycemic Crises*

Hyperglycemic emergencies represent some of the most critical acute complications of diabetes mellitus, affecting patients presenting to emergency departments worldwide. These conditions encompass diabetic ketoacidosis (DKA), hyperosmolar hyperglycemic state (HHS), and mixed presentations, collectively accounting for significant morbidity and mortality [1]. The management of these life-threatening metabolic disturbances requires aggressive, evidence-based intervention, with fluid resuscitation serving

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as a cornerstone of treatment alongside insulin therapy and electrolyte correction [2].

DKA is characterized by the triad of hyperglycemia, metabolic acidosis, and ketonemia, occurring predominantly in type 1 diabetes due to absolute insulin deficiency [3]. In contrast, HHS typically develops in type 2 diabetes with relative insulin deficiency, presenting with severe hyperglycemia and hyperosmolality without significant ketoacidosis [3]. While DKA is more frequently encountered with lower mortality rates when promptly recognized and treated, HHS carries higher mortality rates, primarily due to severe dehydration, insidious onset, and delayed diagnosis [3]. Both conditions share similar management principles, including prompt fluid resuscitation, insulin therapy, electrolyte correction, and identification of precipitating factors [2].

The incidence of DKA is estimated at 220,340 hospital admissions annually in the United States alone [4], underscoring the clinical significance of optimizing treatment protocols. Early recognition and timely emergency department management significantly improve clinical outcomes, reducing both intensive care unit admission rates and in-hospital mortality [1]. However, variability persists across emergency departments in the specific protocols used for fluid resuscitation, insulin administration, and electrolyte replacement, necessitating systematic evaluation of treatment approaches [5].

II. TRADITIONAL FLUID RESUSCITATION STRATEGIES AND HISTORICAL PRACTICE

➢ *Standard One-Bag Method and Normal Saline Usage*

Historically, fluid resuscitation in hyperglycemic crises has relied on the one-bag method utilizing normal saline as the standard resuscitative fluid. This approach delivers a single crystalloid solution throughout both initial resuscitation and maintenance phases, with insulin administered concurrently through a separate intravenous line [6]. Current American Diabetes Association guidelines have traditionally recommended normal saline for initial volume replacement in DKA management, reflecting decades of clinical practice and institutional standardization [7].

The physiological rationale for normal saline use stems from its availability, familiarity, and isotonic properties. However, normal saline contains 154 mmol/L of chloride and 154 mmol/L of sodium, significantly exceeding the physiologic concentrations present in human plasma [8]. When administered in large volumes during hyperglycemic crises—where total fluid requirements frequently exceed 5-6 liters in the first 24 hours—this high chloride content accumulates systemically [7].

Variability in one-bag protocols across emergency departments has been documented extensively. A comprehensive survey of 85 Canadian institutions revealed that while insulin infusion rates showed relative consistency, substantial variation existed in initial fluid bolus specifications, with recommendations ranging from 0.5 to 2 liters of normal saline or Ringer's lactate administered over 15 minutes to 2 hours [5]. This heterogeneity reflects the absence of universally accepted standardized protocols and raises questions about optimal fluid management strategies.

➢ *Electrolyte and Acid-Base Disturbances Associated with Standard Therapy*

A critical complication of large-volume normal saline resuscitation is the development of hyperchloremic metabolic acidosis. While normal anion gap closure represents a key recovery sign in DKA management, persistent acidosis despite normalization of the anion gap has been associated with excessive normal saline administration [9]. The mechanism involves displacement of bicarbonate and other anions by accumulating chloride, perpetuating acidemia through a hyperchloremic, non-anion gap metabolic acidosis [10].

The correlation between serum chloride changes and anion gap alterations in DKA patients receiving normal saline resuscitation has been demonstrated quantitatively, with strong inverse relationships observed ($r = -0.848$, $p < 0.001$) [9]. This finding suggests that as normal saline administration continues, progressive chloride accumulation drives anion gap reduction, but may paradoxically maintain or worsen overall acid-base derangements through mechanisms not captured by traditional Henderson-Hasselbalch analysis [10].

III. THE TWO-BAG METHOD: RATIONALE, PROTOCOL DESIGN, AND MECHANISMS

➢ *Conceptual Framework and Development of the Two-Bag Approach*

The two-bag method represents a paradigm shift in fluid management for hyperglycemic crises, specifically addressing the limitations of continuous single-solution resuscitation. This approach utilizes two separate intravenous fluid bags: one containing an isotonic crystalloid solution (normal saline, Ringer's lactate, or balanced crystalloid) for fluid resuscitation and maintenance, and a second bag containing dextrose-containing fluid (typically 5% dextrose) administered concurrently [6].

The physiological rationale underlying the two-bag method centers on optimizing the glucose-lowering trajectory while simultaneously managing fluid and electrolyte replacement. As blood glucose declines during insulin therapy, the osmotic gradient driving glucose entry into cells diminishes, potentially leading to excessive rapid glucose decline and associated complications including hypoglycemia and osmotic shifts predisposing to cerebral edema [11]. The concurrent administration of dextrose-containing fluid allows clinicians to maintain moderate glycemia—typically targeting glucose levels between 200-250 mg/dL during the first 6-12 hours of treatment—while completing the metabolic correction phase [11].

➢ *Two-Bag Protocol Specifics and Clinical Implementation*

In the two-bag method, initial resuscitation proceeds identically to standard one-bag protocols, with rapid fluid

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boluses (typically 1-1.5 liters over the first hour) of isotonic crystalloid to address profound dehydration characteristic of hyperglycemic crises [11]. The distinction emerges during the transition phase: as blood glucose approaches 250 mg/dL (typically within 2-4 hours of insulin initiation), dextrose-containing fluid is added to the regimen while maintaining the non-dextrose crystalloid infusion [6].

This dual-fluid approach enables several simultaneous therapeutic goals: continued fluid repletion with appropriate electrolyte solutions, sustained insulin administration without interruption, and prevention of iatrogenic hypoglycemia through dextrose supplementation [11]. Critically, the addition of dextrose does not mandate reduction in insulin infusion rates, distinguishing this approach from traditional one-bag methods where dextrose addition typically triggers insulin dose reduction or cessation [6].

IV. COMPARATIVE EFFICACY: EVIDENCE FROM THE PRIMARY TWO-BAG METHOD STUDY

➢ *Study Design and Population Characteristics*

A landmark retrospective cohort study conducted at Trinity Health institutions between 2020-2022 provided the most direct comparison of two-bag versus one-bag methodology in DKA management [11]. This analysis included 1,084 adult patients diagnosed with DKA, with 542 patients treated using the one-bag protocol (pre-group) and 542 patients treated with the two-bag protocol (post-group). The study excluded pregnant patients and those diagnosed with HHS, euglycemic DKA, or ketosis from other causes, ensuring a homogeneous population with uncomplicated moderate to severe DKA [11].

➢ *Primary Outcome: Incidence of Hypoglycemia*

The most striking finding from this comparative analysis was the dramatic reduction in hypoglycemia (blood glucose <70 mg/dL) with the two-bag method. The incidence of hypoglycemia was 38% in the pre-group versus 15.83% in the post-group ($P < .001$), representing a relative risk reduction of approximately 58% [11]. This substantial safety improvement represents one of the most significant clinical benefits of the two-bag approach, as hypoglycemia during DKA treatment is associated with increased morbidity, prolonged hospitalization, and potential neurological complications [11].

The mechanisms underlying this hypoglycemia reduction likely involve multiple factors. First, the availability of dextrose-containing fluid allows gradual glucose decline rather than precipitous drops characteristic of one-bag methods. Second, continued insulin administration despite declining glucose levels enables more complete metabolic correction while the dextrose infusion provides preventive glucose supplementation. Third, this approach may reduce the relative "insulin excess" phenomenon that occurs in traditional protocols when glucose falls rapidly and insulin rates are abruptly reduced or halted [11].

➢ *Secondary Outcomes: Resolution Times and Treatment Duration*

Beyond the primary hypoglycemia endpoint, the two-bag method demonstrated improvements across multiple secondary outcomes reflecting overall treatment efficiency [11]. Patients in the pre-group (one-bag method) required significantly longer insulin infusion durations (28.37 hours versus 22.17 hours, $P < .001$), indicating prolonged metabolic instability requiring continued high-dose insulin therapy [11].

Time to anion gap closure occurred more rapidly in the two-bag group (8.52 hours versus 8.99 hours, $P = .021$), while time to bicarbonate correction similarly favored the intervention group (10.69 hours versus 10.88 hours, $P = .004$) [11]. These differences, while statistically significant and clinically meaningful, represent modest improvements in absolute time terms, suggesting that the primary advantage of the two-bag method relates to safety rather than acceleration of metabolic resolution [11].

➢ *Electrolyte Complications: Hypokalemia and Beyond*

Between-group comparison of hypokalemia incidence revealed no statistically significant difference (60% in post-group versus 66.39% in pre-group, $P = .079$) [11]. This finding is notable, as hypokalemia represents a frequent complication of DKA treatment independent of fluid management strategy, stemming from the intracellular shifts accompanying insulin administration and acid-base correction [11]. The absence of difference between groups suggests that the two-bag method does not exacerbate potassium derangements while providing superior glucose management and hypoglycemia prevention.

V. FLUID CHOICE IN HYPERGLYCEMIC CRISES: CRYSTALLOID COMPARISONS

➢ *Balanced Crystalloids Versus Normal Saline: Mechanistic Differences*

Concurrent with development of the two-bag method, substantial evidence has emerged comparing different crystalloid compositions for use in hyperglycemic emergencies. Balanced crystalloids—including Ringer's lactate, Hartmann's solution, and Plasmalyte-148—differ fundamentally from normal saline in chloride concentration, with balanced solutions containing 110-118 mmol/L chloride compared to normal saline's 154 mmol/L [8]. Additionally, balanced crystalloids contain acetate, lactate, or gluconate as buffer anions, more closely approximating the physiologic electrolyte composition of plasma [7].

A prospective comparative study of 120 DKA patients randomized to receive normal saline, Ringer's lactate, or Plasmalyte demonstrated that Plasmalyte-148 recipients achieved DKA resolution most rapidly [12]. Six patients in the Plasmalyte group achieved DKA resolution within 6 hours and eleven within 8 hours, compared to longer resolution times in the other groups [12]. Serum potassium and bicarbonate levels showed more significant increases in the Plasmalyte group, while both normal saline and Plasmalyte recipients demonstrated increases in serum sodium and chloride [12].

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➢ *Ringer's Lactate as an Alternative to Normal Saline*

Multiple studies have evaluated Ringer's lactate as a superior alternative to normal saline in DKA management. A randomized controlled trial of 164 patients (82 per group) demonstrated that patients receiving Ringer's lactate achieved higher serum bicarbonate levels (p=0.091), though not reaching statistical significance [13]. However, hospital stay duration proved significantly shorter in the Ringer's lactate group (11.5 hours versus 13.11 hours, P=0.0031), and total fluid requirements were reduced (p=0.0031) [13].

A retrospective cohort analysis of 246 DKA patients (119 pre-protocol using normal saline, 127 post-protocol using Ringer's lactate) demonstrated that the protocol change to Ringer's lactate resulted in decreased time to DKA resolution (mean 17.1 hours versus 20.6 hours; p = .02) and shorter duration of DKA protocol insulin infusion (mean 16.0 hours versus 21.4 hours; p = 0.0001) [14]. These findings suggest that balanced crystalloid choice may provide incremental benefits complementary to the two-bag method approach [14].

➢ *Hyperchloremia Prevention and Renal Function Preservation*

A major advantage of balanced crystalloids relates to prevention of iatrogenic hyperchloremia. In a retrospective analysis comparing Lactated Ringer's to normal saline in DKA management, iatrogenic hyperchloremia occurred more frequently in the normal saline group (74.4% versus 64.2%; P = 0.05), with significantly higher mean maximum serum chloride levels (115.7 mmol/L versus 113.7 mmol/L; P = 0.004) [15]. Additionally, hypernatremia incidence was higher in the normal saline group (18.3% versus 9.3%; P = 0.02) [15].

While acute kidney injury incidence showed no significant difference between groups, mean serum creatinine change at 48 hours demonstrated significantly greater improvement in the Ringer's lactate group (-0.15 mg/dL versus -0.04 mg/dL; P = 0.002), suggesting potentially improved renal recovery trajectory with balanced crystalloids [15]. Large-volume normal saline resuscitation has been independently associated with prolonged intensive care unit length of stay (p=0.00065) and increased incidence of non-anion gap metabolic acidosis after DKA resolution (p=0.0000) [16].

VI. PROTOCOL STANDARDIZATION AND IMPLEMENTATION OUTCOMES

➢ *Impact of Standardized Protocols on Emergency Department Practice*

The implementation of standardized DKA management protocols significantly impacts clinical outcomes and treatment consistency across healthcare systems. A retrospective analysis of patients treated at Royal University Hospital in Saskatoon before and after implementation of standardized preprinted DKA order sets incorporating 2018 Diabetes Canada guidelines demonstrated substantial improvements in guideline adherence and patient outcomes [17].

In the pre-implementation period, providers diverged considerably from established guidelines, with resultant variability in insulin dosing, fluid selection, and electrolyte management. Following order set implementation and associated educational sessions, use of the initial order set significantly improved compliance with insulin dose and timing recommendations ($p < 0.0001$), fluid resuscitation protocols ($p < 0.0001$), and appropriate potassium, sodium, and dextrose replacement [17]. Utilization of the maintenance order set consistently enhanced outcomes for intravenous fluid selection, subcutaneous insulin overlap, and anion gap closure at transition ($p < 0.0001$) [17].

➢ *Barriers to Implementation and Knowledge Gaps*

Despite availability of evidence-based guidelines, substantial barriers limit their implementation in emergency departments. A survey of 311 Canadian emergency physicians revealed that while 83.6% found the guidelines useful, only 54.6% were familiar with them, and 54.7% actually used them in clinical practice [18]. The most frequently reported barrier to guideline implementation was lack of education (56.0%), followed by awareness limitations [18].

Clinical vignettes administered to survey respondents demonstrated substantial variability in fluid administration, insulin dosing, and sodium bicarbonate use, even among physicians reporting guideline familiarity [18]. These findings underscore a critical gap between guideline availability and bedside implementation, suggesting that protocol adoption alone—without accompanying staff education and ongoing monitoring—may be insufficient to ensure consistent, evidence-based care [18].

➢ *Early Recognition and Rapid Management as Key Outcomes*

Early recognition and timely emergency department initiation of insulin and fluid therapy substantially impact clinical outcomes in hyperglycemic crises. A retrospective cohort study of 100 DKA/HHS patients defined early management as diagnosis within ≤60 minutes and initiation of insulin and IV fluids within ≤90 minutes of emergency department arrival [1]. Early management was associated with significantly lower intensive care unit admission (24.1% versus 47.6%, p = 0.01) and in-hospital mortality (5.2% versus 14.3%, p = 0.04) [1].

Delayed management independently predicted both ICU admission (OR 2.82, 95% CI 1.22–6.51) and in-hospital mortality (OR 3.12, 95% CI 1.01–9.65) [1]. Notably, patients with HHS demonstrated higher ICU admission and mortality compared to those with DKA, reflecting the increased severity and complications associated with pure hyperosmolar presentations [1]. These findings emphasize that the specific fluid and insulin protocols employed, while important, operate within a broader context where rapid recognition and initiation of any evidence-based resuscitation strategy dramatically improves outcomes.

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VII. SPECIAL POPULATIONS AND VARIATIONS IN MANAGEMENT

➢ *Pediatric Considerations in Hyperglycemic Crisis Management*

Pediatric DKA presents unique management challenges distinct from adult presentations, particularly regarding fluid resuscitation volumes and rates. A case study of a 14-year-old female with mixed DKA/HHS demonstrated the importance of meticulous fluid management in preventing complications [19]. The patient received fluid resuscitation of 60 mL/kg of Ringer's lactate with rapid shock resolution, followed by transition to hypotonic saline (0.45% normal saline at twice maintenance rates) to address hypernatremia [19].

Cerebral edema represents the most feared complication of pediatric DKA, accounting for the majority of DKA-related deaths in children despite being rare in adults [20]. The development of cerebral edema correlates with severity of acidosis, degree of dehydration, and osmolar shifts during treatment. A pediatric DKA case with concurrent HHS and overlapping features highlighted the critical importance of osmolality-guided fluid management, conservative insulin initiation (0.03-0.05 IU/kg/h rather than standard 0.1 IU/kg/h), and hourly neurological and biochemical monitoring with targeted glucose decline of 50-75 mg/dL/hour and osmolality decrease ≤3 mOsm/kg/hour [21].

➢ *Comorbid Conditions and Complex Presentations*

Mixed DKA/HHS presentations complicate management considerably and are associated with worse outcomes than isolated conditions. A series of cases describing mixed DKA-HHS with concurrent hypertriglyceridemia-induced acute pancreatitis illustrated the complexity of managing multiple metabolic emergencies simultaneously [22]. Standard two-bag methodology may require modification in such patients, with more aggressive fluid administration and careful glucose management necessary to address multiple pathophysiologic derangements [22].

Patients with coexisting cardiac dysfunction present another complication scenario where aggressive fluid resuscitation must be balanced against cardiac output limitations. A case of concurrent DKA and ST-elevation myocardial infarction illustrated the therapeutic challenge of administering necessary fluid volumes while avoiding fluid overload that could precipitate cardiogenic pulmonary edema [23]. In such scenarios, bedside ultrasound assessment of fluid status and more judicious fluid titration informed by clinical response may be preferable to standard aggressive protocols [23].

VIII. INSULIN STRATEGIES AND COMPLEMENTARY APPROACHES TO OPTIMIZE DKA RESOLUTION

➢ *Early Subcutaneous Insulin Initiation with Intravenous Therapy*

Beyond fluid management optimization, early initiation of subcutaneous basal insulin during intravenous insulin therapy has emerged as a complementary strategy to improve DKA outcomes. A systematic review and meta-analysis of eight randomized controlled trials involving 407 participants found that early subcutaneous basal insulin combined with IV insulin significantly reduced time to DKA resolution (MD −4.06 h, 95% CI −5.53 to −2.58; $p < 0.0001$) compared to IV insulin alone [24].

Total fluid requirements decreased by approximately 400 mL in patients receiving early basal insulin, though this reduction, while statistically significant, carries modest clinical significance [24]. Importantly, early basal insulin use did not increase adverse events including hypoglycemia, hypokalemia, or rebound hyperglycemia, nor did it significantly affect hospital length of stay or DKA recurrence [24]. These findings suggest that early basal insulin represents a safe adjunctive strategy that, when combined with optimized two-bag fluid management, may further improve DKA resolution efficiency [24].

➢ *Insulin Dosing Strategies: Low-Dose versus Standard-Dose Protocols*

Emerging evidence supports lower-dose insulin infusions as an alternative to the traditional 0.1 unit/kg/hour standard in certain populations. A systematic review of pediatric DKA management found that low-dose insulin (0.05 unit/kg/hour) demonstrated comparable efficacy to standard-dose therapy (0.1 unit/kg/hour) in achieving metabolic correction (10.2 ± 5.29 hours versus 11.22 ± 5.04 hours; $p = 0.407$), while providing superior safety characteristics [25].

The reduced-dose protocol significantly decreased hypokalemia incidence (20.0% versus 42.9%, $p = 0.039$) and reduced hypoglycemia rates (11.4% versus 25.7%) in pediatric populations [26]. Notably, total insulin consumption was 50% lower in the reduced-dose group, suggesting enhanced insulin sensitivity as metabolic derangements resolve. These findings, combined with safety advantages, support consideration of lower insulin dosing strategies, particularly in resource-limited settings and pediatric populations [25].

➢ *Electronic Glucose Management Systems and Computerized Protocols*

- *Implementation of Computerized Insulin Infusion Algorithms*

Electronic glucose management systems (eGMS) and computerized insulin infusion protocols represent technological advances in DKA management, standardizing insulin titration and potentially reducing hypoglycemia risk. A retrospective analysis comparing the Glucommander

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computerized algorithm to standard paper-based protocols in 538 DKA patients (214 pre-implementation, 324 post-implementation) revealed reductions in both hypoglycemia (26.5% versus 17.2% at urban hospital; 27.5% versus 5.8% at community hospital) and severe hypoglycemia (7.3% versus 1.7% at urban hospital; 2.4% versus 0% at community hospital) [27].

Time to metabolic resolution varied by setting. At the academic hospital, time to bicarbonate >18 mEq/L decreased from 22.3 to 18.3 hours post-implementation, while ketosis resolution improved from 42.3 to 16.2 hours [27]. These improvements paralleled reductions in intensive care unit length of stay (75.2 to 63.0 hours) and hospital length of stay (8.6 to 6.0 days) [27]. The enhanced performance of computerized protocols likely reflects reduced insulin dosing variability, more precise glucose-responsive adjustments, and decreased human error in complex calculations [27].

- *Comparison of Electronic Systems with Traditional Protocols*

Direct comparison of different computerized insulin management systems revealed nuanced differences in performance. The Lalani Insulin Infusion Protocol (LIIP), when compared to the established Glucommander system across 778 patients, demonstrated faster time to euglycemia (191 versus 222 minutes, $P < .001$) while maintaining similar hypoglycemia incidence (2.79 versus 2.76 minutes, $P = .50$) [28]. Subgroup analyses showed consistent performance advantages for LIIP across multiple patient categories including DKA/HHS patients, COVID-19 patients, those on steroids, and patients with sepsis [28].

Contributing factors to LIIP's superior performance included improved clinical workflow, greater ease of use and learnability, enhanced compatibility with Electronic Health Record systems, and implementation of unique dynamic and adaptive algorithm features [28]. These findings suggest that computerized protocol characteristics—beyond mere automation—significantly influence clinical outcomes, with superior interface design and algorithm sophistication translating to meaningful improvements in treatment efficiency and safety [28].

➢ *Complications, Adverse Events, and Safety Considerations*

- *Cerebral Edema Risk and Prevention Strategies*

Cerebral edema represents the most feared complication of DKA treatment, occurring predominantly in pediatric patients (though documented in adults) and accounting for most DKA-related deaths despite overall mortality decline [20]. Multiple cases of adult cerebral edema secondary to DKA underscore that this complication, while uncommon in the adult population, remains clinically significant [29].

Cerebral edema pathophysiology involves complex interactions between osmotic gradients, intracellular water shifts, inflammatory mediators, and ischemic mechanisms. While rapid glucose decline was historically considered a primary trigger, more recent evidence suggests that severe acidosis and profound dehydration represent stronger risk factors [30]. A retrospective pediatric series of 144 DKA patients found that cerebral edema developed in 18% of cases, with the lowest incidence occurring in patients receiving fluid therapy with higher sodium content (154 mEq/L NaCl) at consistent infusion rates [30].

Prevention strategies emphasize gradual glucose decline (50-75 mg/dL/hour in children), conservative osmolarity reduction (≤3 mOsm/kg/hour), use of higher sodium-containing fluids in severe dehydration, and meticulous neurological monitoring [21]. The two-bag method's approach of maintaining moderate glycemia through dextrose addition rather than abruptly reducing insulin infusion may theoretically offer advantages in preventing excessive osmotic shifts, though direct comparative data specifically addressing cerebral edema rates are lacking [11].

- *Acute Kidney Injury and Electrolyte Complications*

Acute kidney injury represents a recognized complication of hyperglycemic crises, occurring through mechanisms including severe dehydration, osmotic diuresis, and rhabdomyolysis in severe cases. The choice of resuscitative fluid influences acute kidney injury development, with balanced crystalloids potentially offering advantages over normal saline [15]. While overall acute kidney injury incidence showed no significant difference between Ringer's lactate and normal saline groups in one analysis, serum creatinine trajectory at 48 hours favored Ringer's lactate, suggesting improved renal recovery [15].

Electrolyte derangements extending beyond initial hyperkalemia include marked hyponatremia in the setting of severe hyperglycemia due to osmotically-mediated water shifts, and conversely, severe hypernatremia can emerge in HHS presentations with profound free water deficits [31]. Hypernatremia in the setting of DKA/HHS requires careful correction at a rate of 6-8 mmol/L daily to prevent complications of rapid osmolar shifts [31]. The two-bag method's provision of dextrose-containing (hypotonic) fluid during later treatment phases may facilitate more physiologic free water repletion compared to continuous isotonic crystalloid administration [11].

- *Hypokalemia Management and Prevention*

Hypokalemia represents a nearly universal complication of DKA treatment, resulting from insulin-mediated intracellular potassium shifts, osmotic diuresis, and acid-base changes. Initial serum potassium levels may be deceptively elevated despite total body potassium depletion, with averaging total body potassium deficits of 300-600 mEq in adult DKA cases [11]. The high incidence of hypokalemia (60-66%) documented in both one-bag and two-bag method cohorts reflects this near-inevitable complication of insulin administration [11].

Potassium replacement protocols typically initiate when serum potassium falls below 5.2-5.5 mEq/L, with aggressive repletion escalating as hypokalemia develops. The absence of

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difference in hypokalemia incidence between two-bag and one-bag methods (p = .079) suggests that fluid management strategy does not substantially influence this complication [11]. However, the reduced insulin infusion duration with the two-bag method (22.17 versus 28.37 hours) may result in overall reduced insulin-mediated potassium shifts over the treatment course [11].

➢ *Misdiagnosis, Overtreatment, and Quality Improvement Implications*

- *Diagnostic Accuracy and DKA Overdiagnosis*

A critical quality issue impacting resource utilization and treatment appropriateness involves DKA misdiagnosis. A retrospective chart review of 520 hospital admissions with ICD-10 coded DKA diagnoses found that 28.4% were incorrectly diagnosed based on standardized diagnostic criteria [4]. Most incorrectly diagnosed patients were admitted to intensive care units (92 to medical-surgical units, 49 to ICU) and treated with standard DKA protocols despite not meeting diagnostic criteria, resulting in unnecessary healthcare utilization and treatment costs [4]. Common diagnostic confounders included hyperosmolar hyperglycemic syndrome (HHS), uncomplicated hyperglycemia, and euglycemic DKA, highlighting the complexity of differentiating hyperglycemic emergencies [4]. The diagnostic criteria for DKA include pH <7.30, bicarbonate <15 mmol/L, anion gap >12 mmol/L, and ketonemia/ketonuria—criteria not universally met in many patients diagnosed clinically [4]. Education directed at improving diagnostic accuracy among healthcare providers is essential to ensure appropriate use of hospital resources and prevent overtreatment of patients without true DKA [4].

- *Impact of Protocol-Driven Care on Outcomes and Resource Utilization*

Implementation of standardized, protocol-driven DKA management consistently improves outcomes across multiple metrics. Beyond the clinical efficacy improvements documented with the two-bag method, standardized protocols reduce variability in practice patterns and facilitate quality improvement monitoring. A quality improvement project implementing a standardized DKA management workflow with stringent discharge criteria achieved 80.7% compliance in the final cycle, with reductions in hospital length of stay, reduced median number of diagnostic investigations, and reduced variability in testing patterns [32].

These improvements occurred without compromising safety, with readmission and emergency department re-attendance rates within 1 week of discharge (1.6%) comparable to baseline audits [32]. The success of standardized protocols extends beyond metrics of treatment efficiency to include cost savings and enhanced provider and patient satisfaction through reduced unnecessary testing and interventions [32].

➢ *Synthesis of Evidence and Clinical Integration*

- *Recommended Fluid Resuscitation Approach: Integrating Current Evidence*

Synthesis of available evidence supports a modern, optimized approach to fluid resuscitation in hyperglycemic crises that incorporates elements of both protocol standardization and individualized titration. Initial aggressive fluid resuscitation with isotonic crystalloid (1-1.5 liters over the first hour in most adults) remains appropriate for addressing the profound dehydration characteristic of hyperglycemic emergencies [11]. The choice of initial crystalloid should favor balanced solutions (Ringer's lactate, Plasmalyte-148, Sterofundin) over normal saline to reduce hyperchloremia risk and improve renal outcomes [14].

Following initial volume repletion and as blood glucose approaches 250 mg/dL, transition to the two-bag method with concurrent administration of both isotonic (non-dextrose) and dextrose-containing (typically 5% dextrose) fluids enables continued metabolic correction while preventing iatrogenic hypoglycemia [11]. The two-bag approach has demonstrated a 58% relative risk reduction in hypoglycemia incidence (p < .001), representing a clinically significant safety improvement [11].

Insulin administration should continue at weight-based infusion rates (0.1 unit/kg/hour in adults; 0.05-0.1 unit/kg/hour in pediatric populations with consideration of lower-dose protocols to reduce hypokalemia and hypoglycemia) rather than being abruptly reduced or discontinued as glucose declines [11]. Addition of early subcutaneous basal insulin (particularly when DKA persists despite maximal IV insulin infusion) may further accelerate DKA resolution by an average of 4 hours while maintaining safety [24].

- *Flowchart for Fluid Management Integration in Emergency Department Practice*

Table 1 Flowchart for Fluid Management Integration in Emergency Department Practice

Treatment Phase	Resuscitation (0-1 hour)	Transition (1-4 hours)	Resolution (4+ hours)
Primary Fluid	Isotonic crystalloid 1-1.5 L (RL or Plasmalyte preferred)	Isotonic crystalloid at 200-300 mL/h	Isotonic crystalloid 150-200 mL/h
Secondary Fluid	None	5% dextrose when glucose <250 mg/dL	5% dextrose 100-150 mL/h
Insulin Infusion	0.1 unit/kg/h IV continuous	Continue 0.1 unit/kg/h IV	Consider SC basal insulin addition if resolution delayed
Glucose Target	Not applicable	200-250 mg/dL	150-200 mg/dL
Monitoring	Every 1 hour	Every 1-2 hours	Every 2-4 hours
Key Goals	Restore perfusion, stabilize hemodynamics	Prevent hypoglycemia, complete acidosis correction	Transition to SC insulin, maintain electrolyte stability

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➢ *Limitations of Current Evidence*

- *Study Design Limitations and Generalizability*

While the landmark two-bag method study provides direct evidence comparing fluid management approaches, it represents a single-institution retrospective analysis without blinding or standardized outcome ascertainment across all study visits [11]. The pre-post design raises questions about temporal trends, changes in supporting care (intensive care unit capabilities, electronic health record improvements), and secular variation in patient populations that might confound comparisons [11].

Multiple fluid resuscitation studies show heterogeneous designs including retrospective analyses, single-center studies, and limited sample sizes. A systematic review of crystalloid fluid choice in DKA management (normal saline versus Ringer's lactate) included only six studies with highly variable methodological quality, limiting the strength of conclusions regarding superior approaches [33].

IX. CONCLUSIONS AND RECOMMENDATIONS FOR CLINICAL PRACTICE

Fluid resuscitation remains a cornerstone of hyperglycemic crisis management, and evidence-based optimization of this intervention significantly improves patient safety and outcomes. The transition from traditional one-bag fluid management to the modern two-bag method represents a meaningful advance in DKA and HHS treatment, substantially reducing iatrogenic hypoglycemia (58% relative risk reduction, $p < .001$) while maintaining or accelerating metabolic resolution [11].

The two-bag method's mechanism—enabling continued insulin administration despite declining glucose levels through concurrent dextrose-containing fluid administration—addresses a fundamental limitation of traditional protocols where insulin reduction or discontinuation often accompanies glucose decline, resulting in incomplete metabolic correction and vulnerable rebound hyperglycemia [11].

Complementary interventions including selection of balanced crystalloids over normal saline, early subcutaneous basal insulin addition in selected cases, implementation of computerized glucose management algorithms, and strict adherence to standardized protocols further optimize outcomes [14], [24], [27].

Implementation barriers remain significant, with educational gaps and protocol variability persisting despite guideline availability [18]. Institutional commitment to multidisciplinary protocol adoption, staff education, and outcome monitoring is essential to translate evidence into consistent, high-quality bedside practice [17].

Future research priorities should include multicenter randomized controlled trials comparing fluid management strategies in diverse patient populations, cost-effectiveness analyses, pediatric-specific outcome studies, and investigation of electronic glucose management system integration with two-bag protocols. As evidence continues to evolve, periodic protocol revision based on emerging data ensures that emergency departments maintain state-of-the-art, evidence-based approaches to these critical metabolic emergencies.

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