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Title of Master's Thesis:

FLUID THERAPY ASSOCIATED MORTALITY AND OTHER ADVERSE EFFECTS IN PAEDIATRIC PATIENTS

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1. SUMMARY

Author name: William Sollin

Research title: Fluid Therapy Associated Mortality and Other Adverse Effects in Paediatric Patients

Aim: To analyze and review recommendations to fluid therapy and their association with mortality and other adverse effects in paediatric patients

Objectives:

1. To assess current recommendations on fluid therapy
2. To assess fluid therapy associated mortality
3. To assess fluid therapy associated hyponatremia

Methodology: This is a literature review where searches were conducted using a single database. The database used was Medline (PubMed) and searches were conducted using key terms: Fluid therapy, mortality, adverse effects, pediatrics, and hyponatremia. Articles published from 2008 and forward were included with no more than 10 years search criteria used. Keywords were matched to database indexing terms (MESH). In PubMed, related articles were also retrieved and added to this review. Search limitations were set to humans and age 1 month -18 years. Studies with relatively low quality of evidence or strong bias were excluded.

Results: Routine bolus administration in resource-limited areas, low-molecular weight hydroxyethyl starch (HES) administration for volume expansion and fluid overload (FO%) were associated with increased mortality. The use of solutions of various tonicities showed insignificant association with mortality. Meta-analyses show that hypotonic solutions provide a larger relative risk (2.24 and 2.37) of the development of hyponatremia.

Conclusions: Following recommended guidelines on pediatric fluid therapy, in regards to tonicity and rate of administration, will likely decrease the incidence of mortality and certainly hyponatremia if compared to conventional clinical approaches. Balanced solution therapy might prove to be a safer alternative in the future. Physicians' compliance with and education on up-to-date guidelines will likely limit the incidence of mortality and various adverse effects relate to fluid therapy. Guidelines should be made easily noticeable to all physicians treating pediatric patients.

2. SANTRAUKA

Pavadinimas: Vaikams Skiriamos Skysčių Terapijos Sąlygotas Mirštamumas ir Kitas Pašalinis Poveikis

Literatūros apžvalgoje analizuojama ir apžvelgiama skysčių terapijos sąsaja su vaikų mirštamumu ir hiponatremija. Nustatyta, kad mirštamumo ir hiponatremijos atvejų sumažėja, kai yra laikomasi dabartinių skysčių terapijos rekomendacijų remiantis ESPGHAN, ESPEN, ESPR and CSPEN.

3. ACKNOWLEDGEMENTS

I dedicate this thesis to my beloved mother, father, brother and friends for their continuous support and faith in my ability to succeed during this time of great personal struggle.

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4. CONFLICTS OF INTEREST

The author declares no conflicts of interest.

5. TERMS AND ABBREVIATIONS

D5 – 5% dextrose

FO% – Fluid overload expressed in percentage

Half-NS – 0.45% saline solution

HES – Low-molecular weight hydroxyethyl starch

IV – Intravenous

LR – Lactated Ringer

NS – 0.9% normal saline solution

PICU – Pediatric intensive care unit

RCT – Randomized controlled trial

Third-NS – 0.3% saline solution

6. INTRODUCTION

Intravenous (IV) fluid administration is among the most used therapies in modern pediatric medicine. Hirschfeld et. al. introduced the practice of maintenance fluids administration via intravenous “drip” already in 1930(1). This was followed by Karelitz’s and Shick’s. introduction of sugar added in the solution, in the form of glucose, to resolve the complication of hypoglycemia in 1931(2). IV administration of maintenance fluids in modern days are credited to Holliday and Segar(3) as they introduced the 4:2:1 rule with the role of electrolytes being more understood. Their research is based on the link between energy expenditure and water requirements. They stated that for every 100 kcal of energy spent for the first 10 kg of body mass 100 ml of water was required, 50 ml of water per 100 kcal per kg ranging from 11 to 20 and 20 ml per 100 kcal per kg exceeding 20 kg (see Figure 1)

Figure 1. Calculations of maintenance fluid requirements for pediatric patients.(3)

Weight	mL/kg/d	mL/kg/h
A: the first 10 kg	100	4
B: weight between 10 and 20 kg	+50 ml/extra kg/d	+2 ml/extra kg/h
C: weight above 20 kg	+25 ml/extra kg/d	+1 ml/extra kg/h
Sum total requirements	A + B + C	A + B + C

In order to meet the requirements of electrolytes, Holliday and Segar(3) matched the concentrations of sodium (Na), potassium (K) and chloride (Cl) of that of cow and breast milk. They found that the requirements of Na were 3 mEq per 100 kcal per day and that of K were 2 mEq per 100 kcal per day. These findings resulted in 2 maintenance solutions, as compared to serum are hypotonic: 0.22 % normal saline (NS) + 20 mEq per liter of KCl and 0.45% NS + 20 mEq per liter of KCl. A few variations have been developed since to be used in clinical practice ranging from hypotonic to isotonic and varying composition of electrolytes, such as 5 % dextrose (D5) in 0.22% NS and D5 in 0.45% NS(4) which were highly used until isolated reports of severe hyponatremia resulting in death started arising in the 1980s and a studies suggesting physicians to avoid the use of hypotonic fluids(5). This caused questions regarding these solutions legitimacy in pediatric health care. Several warnings in regards to the use of hypotonic solutions were issued in the 1990s in response to research findings(6)(7)(8), showing a relation between the uses of hypotonic solutions and severe hyponatremia. Hyponatremia is classified according to severity: Mild hyponatremia (serum Na 130-135 mmol/L), moderate (Na 120-129 mmol/L) and severe (Na < 120 mmol/L).

Symptoms vary with severity and severe hyponatremia is associated with coma, respiratory arrest and death. Pediatric patients are at higher risk of developing hyponatremia complications such as death due to their skulls being small in relation to their brain size until the age of 16, resulting in a lesser ability cope with excessive accumulations of free water (9). They also cope worse due to children's lesser amount of spinal fluid which acts as a buffer to brain swelling (9) and their intracellular concentration of Na being 27% higher than in adults (8). Due to these findings, it is of clinical significance to analyze and review the association between fluid therapy and mortality as well as hyponatremia.

7. AIM AND OBJECTIVES

Aim: To analyze and review recommendations to fluid therapy and their association with mortality and other adverse effects in pediatric patients

Objectives:

1. To assess current recommendations on fluid therapy
2. To assess fluid therapy associated mortality
3. To assess fluid therapy associated hyponatremia

8. LITERATURE REVIEW

8.1 The current approaches to fluid therapy

Consensus has been hard to find in the scientific community on administration of fluids and electrolytes in pediatric patients until recently, so in this section we will review recent literature aiming at providing recommendations and guidelines as to the use of fluid therapy in pediatric medicine. Studies will be presented, including those preceding most current guidelines, such as independent review as well as the most up to date guidelines published by authorities in the pediatric medicine field.

Study 1, a review article published by I. Murat and M. Dubois in 2008 (10), analyzed approaches to perioperative fluid therapy. They found that for the intraoperative period, as it is aimed primarily at substituting deficits from preoperative fasting or third-space losses, isotonic dextrose-free solutions are to be used in most children over the age of 5 years and to avoid hypotonic solutions as they were found to be risk factors for mortality and hospital-acquired hyponatremia. In cases of absolute or relative blood volume loss NS or Ringer's acetate (both isotonic) should be used as other fluids were argued not to have any significant advantages. Holliday and Segar's 4:2:1 rule for maintenance fluids(3) were not challenged as they found good results regarding its capability of maintaining vascular osmotic pressure(10). It was also stated that the recommendation were only just that and that it is important for clinicians to individualize their approach to fluid therapy.

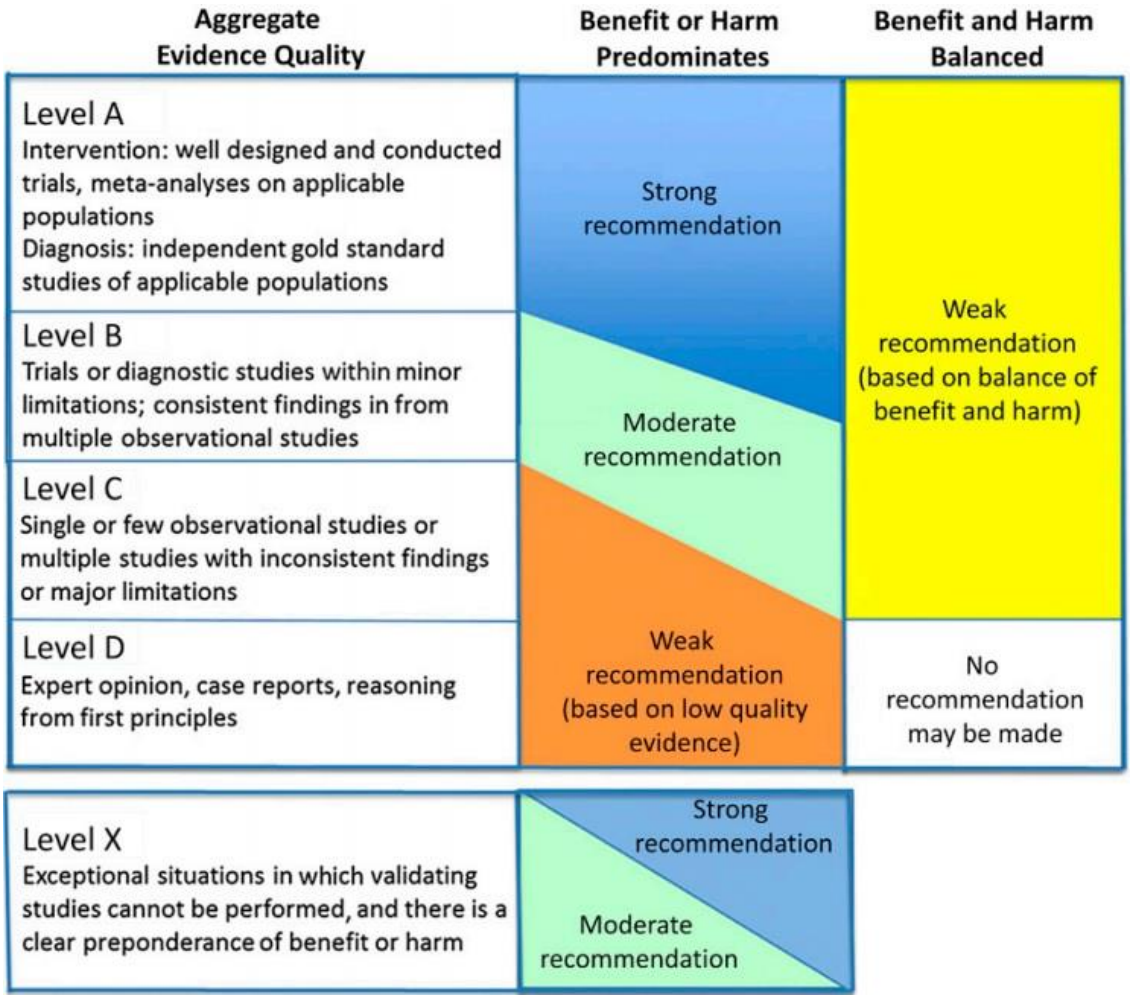
Study 2, published as an educational review by A. Friedman in 2010(11), aimed to provide knowledge as to the rationale of different approaches to fluid therapy by analyzing literature on the topic. He acknowledged previous incidents of hospital-acquired hyponatremia with the use of hypotonic solution and stated that fluid therapy targeted as maintaining fluid and electrolyte balance, is to be done by administration of isotonic solutions using Holliday and Segar's calculations(3), but to cater to individual needs and circumstances. A physician should not only follow recommendations, but also use knowledge about physiology in order to administer appropriate fluid therapy regrading volume and content and especially if to restore loss of fluid volume(11).

Study 3, a review by E. Hoorn in 2017(12), discussed the topic of fluid therapy as simply (reverse nephrology) and provides specific recommendations to pediatric patients. He found that use of isotonic solution did not increase the risk of hypernatremia or fluid over-load as well as decreasing the risk, compared to hypotonic solutions, of adverse effects such

as hyponatremia and seizures. He concluded to promote the use of isotonic solutions along with the classical calculations of volume requirements by Holliday and Segar(3).

Study 4, issued by the American Academy of Pediatrics and authored by L. Feld et. al. 2018(13), is a clinical practice guideline focused on the proper use of intravenous maintenance fluids in pediatric patients regarding tonicity. Their goal was to issue guidelines on how to administer maintenance IV fluids in a wide range of pediatric patients of age 1 month to 18 years. Regarding IV maintenance fluids, they recommended (Recommendation strength: A; see Fig. 2) the use of isotonic solutions with an appropriate balance of K and Cl to postoperative patients in PICU setting and on general wards, excluding patients with neurosurgical disease, cardiac disease, hepatic disease, cancer, renal dysfunction, diabetes insipidus, large volume watery diarrhea, or with burns of great severity. They could not find any evidence for the development of any other adverse effects using isotonic solutions. No recommendations as to the appropriate volumes of fluids or to the use of isotonic buffered crystalloid solutions was issued in this review(13).

Figure 2. AAP rating of evidence and recommendations(13).



Study 5, clinical guidelines, by F Jochum et. al. 2018(14), presented after reviewing evidence on parenteral nutrition, fluid and electrolytes needs for pediatric patients for ESPGHAN, ESPEN, ESPR and CSPEN. They argue against the use of hypotonic solutions for maintenance use as they found scientific evidence for the risk of developing hyponatremia. Although they acknowledged concerns of inducing hyperchloremic acidosis by the use of isotonic solutions, as there will be an increased load of Cl in accordance with the calculations of electrolyte needs by Holliday and Segar's(3), they went on to promote the use of isotonic solutions. Holliday and Segar's recommendations for fluids(3) were also accepted as a convenient way of calculating maintenance requirements since there was not enough evidence to be found. Jochum et al.(14) concluded their research by providing a table with more specific recommendations for parenteral fluid therapy, including electrolytes, for pediatric patients beyond the neonatal period (> 28 d.); (see fig 3), but that various clinical situations will require adjustments of fluid therapy based on altered needs for energy and water.

Figure 3. Parenteral fluid and electrolytes need for patients beyond neonatal age(14)

	<1 y [a]	1–2 y	3–5 y	6–12 y	13–18 y
Fluid (ml/kg/d)	120–150	80–120	80–100	60–80	50–70
Na (mmol/kg/d)	2–3	1–3	1–3	1–3	1–3
K (mmol/kg/d)	1–3	1–3	1–3	1–3	1–3
Cl (mmol/kg/d)	2–4	2–4	2–4	2–4	2–4

8.2 Fluid therapy associated mortality

Study 6, by Kathryn Maitland et. al. as published in 2011 (15), performed a randomized controlled trial in order to analyze the relationship between fluid bolus and mortality at 48 hours and four weeks. They enrolled 3141 children in means-limited areas with critical febrile illnesses along with impaired perfusion and assigned them to receive boluses of 20 to 40 ml per kg of NS or 5% albumin solution, as well as a control group receiving no bolus infusion. All children with severe hypotension were at random assigned to either of the bolus groups. Proper antimicrobial treatment, maintenance fluids and care otherwise were provided, following guidelines. Malnourished and patients suffering from gastroenteritis were not enrolled.

Results showed that the 48-hour mortality amongst the children, without severe

hypotension, were 10.5% with NS, 10.6% with albumin solution and 7% in the control group. Mortality at 4 weeks were 12.0%, 12.2% and 8.7% respectively, even though the clinical severity was comparable among all three groups and results corresponded across all subgroups in regard to status, shock, malaria, coma, etc. The authors of the study could therefor conclude that the mortality after 48 hours was notably larger amongst critically ill children in these settings, but that no other statistically significant adverse effects could be singled out.

Study 7, a prospective observational study, performed in a South African pediatric intensive care unit (PICU) including 100 patients, analyzed the association between fluid overload expressed in percentage (FO%), defined as fluid in minus fluid out/ PICU admission weight x 100%, and mortality at 28 days (16). 10 patients were categorized as non-survivors at 28 days (referred to as mortality) and 90 as survivors. The non-survivors showed higher mean FO% at 4.9, compared to survivors at 3.4, leading the authors to conclude that there was a significant association between FO% and mortality at 28 days thought to be contributed to by excessive maintenance fluid administration.

Study 8, conducted by L. Li et. al. in 2016 (17), is a meta-analysis evaluating the safety of using low-molecular weight hydroxyethyl starch (HES) for volume expansion. They used 13 randomized controlled trials (RCT), published before January 2014, including 1156 pediatric patients. Four of the RCTs had reported on overall mortality. Out of 160, four died out of the group that had received isotonic fluids other than HES for volume expansion whilst eight died out of 150 of those who received HES. They also found that the use of HES decreased the platelet count significantly and increased the duration at which they had to stay in PICU. This led the authors to conclude that the approach of HES had no significant impact on mortality.

Study 9, a meta-analysis by I. Machenocie and S. Bhaumik(18), evaluated the association between initial fluid administration volume on admission, mortality and neurological adverse effects in three RCTs. 420 patients diagnosed with acute bacterial meningitis were included. The definition of restricted fluid therapy was set to administration of lower than maintenance fluid therapy. The analysis showed no statistically significant difference in risk ratio regarding mortality when comparing the group which had received maintenance fluid therapy to that on a restricted-fluid therapy regimen. Spasticity and seizures on the other hand proved to be less prevalent among the patients receiving maintenance fluid therapy.

Study 10, a matched retrospective cohort study by S. Wiess et. al.(19), sought to analyze the 30-day mortality outcome, regarding the choice of either lactated ringer (LR) or NS, amongst 12529 pediatric patients diagnosed with either severe sepsis or septic shock. Patients were grouped as LR-any (received LR as well as other solutions), LR-only (received only LR) and NS as they found that LR was used favorably with less severely ill patients or as an accessory fluid in combination with large volume infusions. They found no significant difference on mortality outcome when matching the LR-any groups to NS as well as LR-only to NS when taking in account volume and the proportion of LR therapy applied.

Study 11, an observational cohort review to evaluate the association between balanced and unbalanced LR or NS fluid therapy in severe pediatric sepsis and mortality. Balanced solutions was defined as isotonic solutions with a strong ion difference (SID) resembling that of plasma. They found that, out of 36908 patients that met the analysis criteria for entry, 1641 had received exclusively balanced solutions for resuscitation at 72 hours and that this group showed a lesser mortality rate at 12.5 % compared to that of the unbalanced group at 15.9 % after matching for propensity.

8.3 Fluid therapy associated hyponatremia

Study 12, a cohort study from 2013 by Carandang et. al(20), evaluated fluid tonicity associated development of hyponatremia in hospitalized pediatric patients. Patients with normal plasma concentration of sodium at admission were enrolled in the study of which 674 received hypotonic solutions and 372 isotonic. Hyponatremia was defined as sodium < 135 mEq / L. After taking in to account the intergroup differences, hyponatremia was found in 38.6% patients that were administered hypotonic maintenance fluids and 27.8% in the isotonic group. They concluded that hyponatremia was a common finding in these hospitalized patients and that the risk ratio of developing hyponatremia was 1:1.63 if to compare isotonic to hypotonic solution. They also found that hyponatremia risk varied with reason of admission and was especially expressed in patients admitted to the hematology/oncology unit (1:2.37).

Study 13, a meta-analysis of 10 RCTs by J Wang et. al. in 2013(21), assed the safety of administering isotonic versus hypotonic fluids regarding plasma sodium levels. They analyzed the risk of developing hyponatremia as well as severe hyponatremia. They found that the relative risk of developing hyponatremia was significantly higher (RR=2.24) as well

as sever hyponatremia (RR=5.29) when administering hypotonic solutions in favor of isotonic. Isotonic fluids were concluded to be the safer alternative as to use of maintenance fluids.

Study 14, a meta-analysis performed in 2014 by Foster et. al.(22), aimed to determine the hyponatremia associated risk when using hypotonic versus isotonic maintenance fluids in PICU setting and postoperative wards. They included 10 RCTs which had selections of patients from various types of hospital units, studying a total of 893 patient cases. Statistical analysis found a general increased relative risk of hyponatremia (<135mmol/L) of 2.37, when receiving maintenance fluids, if the solution was hypotonic rather than isotonic. Patients which were administered hypotonic fluids at any point in during their hospital stay were at a relative risk of moderate hyponatremia of 6,1 compared to isotonic fluids. Patients receiving 0.45% Saline (half-NS) were at a relative risk of 2.42 of developing hyponatremia. Conclusions were made to recommend the use of isotonic fluid administration to avoid hyponatremia in any setting.

Study 15, a systematic review and meta-analysis of serum sodium's association with hypotonic versus isotonic solutions by G. Yang et. al. in 2015(23), including 8 RCTs with a total of 752 patients, found a significantly decreased risk ratio when using isotonic intravenous maintenance fluids, as compared to hypotonic, of 0.36:1. Conclusions were made as to recommend isotonic fluids as the maintenance fluid of choice and that hypotonic solutions had correlation with hyponatremia.

Study 16, performed by J. Friedman et. al.(24), compared isotonic and hypotonic intravenous maintenance fluid therapies' association with hyponatremia as a secondary outcome. Findings showed, amongst the 110 patients enrolled, that there were no significant differences in mean sodium levels at 48 hours when comparing the randomized groups receiving either isotonic or hypotonic fluids.

Study 17, a double-blind RCT by S. McNab et. al in 2015(25), included all children admitted in need of intravenous fluid therapy lasting at least six hours . They set to analyze the risk of developing hyponatremia when using NS compared to 0.45% saline (half-NS) for patients of either group, matched 1:1, for at least 72 hours or when the maintenance fluid infusion rate was down to half of recommended maintenance rate. Results for the 690 enrolled patients showed that fewer patients developed hyponatremia (<135 mmol/L) with at least a decrease of 3 mmol/L from baseline plasma sodium concentration when infused with NS (4%) compared to 11% in the group receiving 0.45% saline solutions (hypotonic) giving

an odds ratio of 0.31:1. They went on to recommend using NS if to avoid the risk of hospital-acquired hyponatremia without increasing the risk of adverse effects.

Study 18, an RCT by F. Robles and C. Garcia published in 2016 (26), compared isotonic D5 in NS, hypotonic D5 in half-NS and hypotonic 3.3% dextrose (D3) in 0.3% saline solution (third-NS) in regard to their impact on serum sodium at 8 hours of maintenance fluid therapy. Paediatric patients from three months to 15 years of age admitted to hospital with medical or surgical needs were enrolled. Baseline serum sodium concentration characteristics were similar for all patients enrolled. Results of statistical analysis showed that incidence of hyponatremia was 1.9%, 22% and 20.4% for patients receiving D5 in NS, D5 in half-NS and D3 in third-NS respectively, thus leading the authors to recommend D5 in NS as a safer alternative to hypotonic solutions.

9. RESEARCH METHODOLOGY AND METHODS

Methodology: This is a literature review where searches were conducted using a single database. The database used was Medline (PubMed) using key terms: Fluid therapy, mortality, adverse effects, pediatrics, and hyponatremia. Articles published from 2008 and forward were included with no more than 10 years search criteria used. Keywords were matched to database indexing terms (MESH). In PubMed, related articles were also retrieved and added to this review. Search limitations were set to humans and age 1 month - 18 years. Studies with relatively low quality of evidence or strong bias were excluded.

Selection Criteria: This literature review was conducted to investigate how the use of current approaches to fluid therapy was associated with mortality and hyponatremia. Association was defined as measureable outcome of either mortality or hyponatremia. Hyponatremia was defined as serum sodium levels of < 135mmol/L or clinical findings of hyponatremia, mortality as fluid therapy associated fatal outcome and approaches as reviews or systematic reviews resulting in clinical recommendations or guidelines. Included studies should be performed by experts on the subject. Empirical studies were included and samples were taken from all over the world. Only search results relevant to the three objectives were included.

10. RESULTS AND THEIR DISCUSSION

Current recommendations: There was consensus, amongst ESPGHAN, ESPEN, ESPR, CSPEN, as well as the authors of the other studies, on isotonic solutions being the intravenous fluids of choice as maintenance fluid and to replace blood volume deficit amongst all studies as they were found to be safer in regards to mortality, hyponatremia and other adverse effects. The use of the classical 4:2:1 calculation of maintenance volume requirements and rate of infusion for maintenance therapy were found to be recommended by study 1-3, not assessed by study 4 and modified by study 5. Study 5 put forward aged-based guidelines to maintenance fluid therapy rates and electrolyte needs (Fig. 3). None of the studies put forward recommendations on fluid administration for specific diagnoses, but acknowledged that fluid administration is to be altered from recommendations on a case-to-case basis.

Fluid therapy associated mortality: Study 6 indicates an insignificant difference with approach to fluid therapy when assessing mortality of 10.5% with normal saline solution, 10.6% with albumin solution and 7% in the control group of patients receiving equal volume replacing bolus in all different kinds of diagnoses in resource-limit areas. Study 7 found that fluid overload of 4.9% could be found in non-surviving patients and 3.4% in survivors and suggested this to be due to excessive administration of fluid volumes. In study 8 when comparing HES to recommended isotonic solutions, mortality was found to be greater with use of HES in pediatric patients (8/150 vs 4/160). Study 9 showed that the use of recommended isotonic solution did not result in higher risk of mortality when given routinely on admission, compared to other solutions. Study 10 found that the use of 0.9% saline had no association, compared to other isotonic solutions, with mortality rates. Study 11 deviates by challenging older solutions by proposing the use of balanced solutions as a safer alternative. They found that mortality rates decreased by 12% with use of balanced LR

Fluid therapy associated hyponatremia: All studies except study 16, a study with significantly smaller sample size, showed higher occurrences of hyponatremia with use of non-recommended solutions as maintenance fluids. Study 12 and 17 (RCTs) found 38% vs 27.8% and 11% vs 4% risk of hyponatremia when using hypotonic solution vs isotonic 0.9% saline solution. Study 13 and 15 (meta-analyses) showed an increased relative risk when using isotonic fluids matched against hypotonic of 2.24 and 2.37. Study 18, the most recent RCT, showed increased risks of developing hyponatremia when using hypotonic

solutions. Results were 1.9%, 22% and 20.4% for D5 in NS, D5 in half-NS and D3 in third-NS respectively.

11. CONCLUSIONS

Following recommendations and guidelines on pediatric fluid therapy, with regards to tonicity and rate of administration, will likely limit the rate of fluid therapy associated mortality and certainly hyponatremia, but balanced solutions might prove to be a safer alternative if future studies find more such evidence.

1. Isotonic solutions at indicated rates are to be used in fluid therapy for most paediatric patients and most reasons of administration if to limit the incidence of various adverse effects. There were agreement amongst all studies that isotonic solutions should be the intravenous fluids of choice as maintenance fluids and if to replace blood volume deficits as they were found to be safer in regards to mortality and hyponatremia. The use of the classic 4:2:1 calculation for maintenance rates by Holliday and Segar based on weight are still widely accepted, but more specific guidelines have been presented by ESPGHAN, ESPEN, ESPR and CSPEN to specifically cater to the maintenance fluid requirements and electrolyte needs of children of various ages. It can also be concluded that guidelines are only put forward to be used in most cases, but that specific clinical circumstances may call for altercations in the approach to fluid therapy on a case-to-case basis.

2. Deviation by clinicians from recommended administration of intravenous solutions as to their volume and composition might have an impact on fluid therapy associated risk of mortality in paediatric patients based on the results of this review. Routine bolus administration of normal saline solution and 5% albumin solution are associated with higher mortality rates compared to a group receiving no bolus administration in resource-limited areas, but the reason for these results remain uncertain. Overloading of fluids is found to have an association with higher mortality rates as well as the administration of low-molecular weight hydroxyethyl starch solutions for fluid replacement purposes when put against well proven isotonic solutions, but this needs to be studied further to obtain stronger evidence. There was no difference to be found in mortality rates when comparing isotonic to hypotonic solutions. Balanced lactated Ringer’s solutions show to have decreased association with mortality rates when compared to unbalanced lactated Ringer’s solutions, but evidence is insufficient.

3. Deviation by clinicians from recommended administration of intravenous maintenance fluids, as to their tonicity, will significantly increase the fluid therapy associated risk of hyponatremia based on the results of this review. There is an increased risk, as well as a

larger relative risk, of development of hyponatremia in paediatric patients when hypotonic solutions are administered in favor of isotonic solutions as maintenance fluids.

12. PRACTICAL RECOMMENDATIONS

According to the results of this literature review, it is recommended to follow guidelines on fluid therapy if to avoid increased risk of mortality, hyponatremia and other adverse effects in pediatric patients of age >28 d. and <18 years. Isotonic solutions at indicated rates are to be used in fluid therapy for most paediatric patients and most reasons of administration. The use of the 4:2:1 rule is acceptable for fluid and electrolyte requirements, but a more specific guideline have been presented by ESPGHAN, ESPEN, ESPR and CSPEN to specifically cater to the maintenance fluid requirements and electrolyte needs of children according to age and is to be preferred. Specific clinical circumstances may call for altercations in the approach on a case-to-case basis and the clinician must use his understanding of fluid therapy to cater to every individual patient's need.

Clinicians should put great emphasis on following up-to-date guidelines on fluid therapy and these guidelines should be made easily noticeable to all physicians treating pediatric patients.

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