RESEARCH ARTICLE

Prescription pattern and utilization of crystalloid intravenous fluids in inpatient pediatric department in a tertiary care hospital

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ABSTRACT

Background: Crystalloid intravenous fluids (IVFs) are the mainstay method to maintain homeostasis when a child is unable to uptake the necessary fluids and electrolytes. Recent literature describes the context-dependent use of IVFs, which should be prescribed, ordered, dosed, and delivered like any other drug as they have adverse effects just like drugs.

Aims and Objectives: To study the utilization, identify adverse drug reactions (ADRs), conduct cost minimization analysis, and check the appropriateness of the crystalloid IVFs prescribed in the inpatient pediatric department.

Materials and Methods: Data were collected prospectively from 240 children aged 2 months to 18 years requiring maintenance IVFs in the inpatient pediatric department from August 2021 to December 2022. Children with known cardiac or renal disorders and those refusing to give consent or assent were excluded from the study. Demographic details, clinical profile, details of IVF, including type, cost, and treatment outcome, were recorded. ADRs reported were also analyzed.

Results: In this study, the most common diseases were respiratory illnesses (20.42%), pyrexias (17.50%), central nervous system disorders (17.50%), gastrointestinal disorders (10.83%), and poisoning (10%). The average days of admission were 5.15 days. Dextrose-Normal Saline (DNS) was prescribed 77.57% of the time, Normal Saline (NS) 17.97% of the time, and Ringer’s Lactate (RL) 4.47% of the time. ADRs were encountered in 2.5% of cases.

Conclusion: The prescribed pattern was in accordance with the AAP guidelines. DNS was most commonly prescribed, whereas RL was more commonly prescribed in acute gastroenteritis. The cost minimization showed that the crystalloid IVF cost can be lowered by 46.32%.

KEY WORDS: Intravenous Fluid; Drug Utilization; Cost Minimization

INTRODUCTION

Intravenous fluids (IVFs) are the mainstay of therapy to maintain the delicate fluid-electrolyte balance when a child is unable to uptake fluids orally.[1] Fluid resuscitation is divided into four stages: rescue, optimization, stabilization, and de-escalation. The stabilization stage is also called the maintenance phase. In this phase, apart from the daily fluid and caloric requirements, deficits in fluids and electrolytes are also corrected.[2]

The American Academy of Pediatrics has recommended that ‘patients aged 28 days–18 years requiring maintenance IVFs should receive isotonic solutions with appropriate potassium chloride (KCl) and dextrose. The guideline does not apply to patients in the neonatal intensive care unit or those with neurosurgical disorders, cardiac disease, hepatic disease, cancer, renal dysfunction,'
diabetes insipidus, voluminous watery diarrhea, or severe burns.”[3]

Crystalloid IVFs as interventions have their indications, a recommended dosage, expected outcomes, and unexpected side effects, just like modern drugs.[4]

Recent literature has emerged in which researchers describe and support context-dependent use, which should be prescribed, ordered, dosed, and delivered like any other drug.[5]

Drug utilization research is defined as research on “the marketing, distribution, prescription, and use of drugs in a society, with special emphasis on the resulting medical, social, and economic consequences” and has the principal aim of facilitating the rational use of drugs. Reports of adverse drug reactions (ADRs) can be correlated with drug utilization data to determine whether ADRs are common within certain groups, certain situations, or at certain quantities.[6]

Crystalloid IVFs of various brands are available in the Indian market. Different brands of IVFs with different prices and equivalent efficacy and potency provide an opportunity to carry out pharmaco-economic studies such as a cost-minimization study, which is one of the objectives of this study.[7]

The common IVF preparations used in pediatric wards are: normal saline (NS), dextrose in NS (DNS), half NS (1/2 NS), 5% Dextrose with half NS (5% D+1/2 NS), dextrose 5% in water (D5W), Ringer’s lactate (RL), isolyte P (Iso P), and isolyte M (Iso M).[8]

Despite the high prevalence of IVFs for maintenance therapy, there is a difference in fluid choice across geographies and concrete administration and monitoring protocols.[9]

Some recent studies in both developing and developed countries have shown the inappropriate use of crystalloid IVFs for maintenance therapy.[10-13]

In view of the high prevalence of IVF use, there is an urgent need to study their utilization. Knowledge on how IVFs are being prescribed and used will be of immense help in initiating a discussion on their rational use and suggesting measures to improve prescribing rationale and reduce costs.

Secondary Objectives
To compare whether the crystalloid IVF therapy is according to AAP guidelines.

MATERIALS AND METHODS
The study was conducted in accordance with the Declaration of Helsinki, ICMR research guidelines, and ICH-GCP. Institutional Ethics Committee approval was taken prior to the conduct of the study (N-EC/2021/SC/05/44, dated July 12, 2021).

Study Design
Prospective observational study.

Study Site
Inpatient pediatric ward in a tertiary care hospital.

Study Duration
From August 2021 to December 2022.

Sample Size
240. Using the formula $n = \frac{z^2 \times p \times q}{d^2}$.

Study Population
Children are admitted to the inpatient pediatric department.

Inclusion Criteria
i. Patients between the ages of 2 months and 18 years of either sex
ii. Patients requiring maintenance IVFs
iii. Parents willing to give written informed consent
iv. Patients between 12 and 18 years of age are willing to give written informed assent.

Exclusion Criteria
i. Patients below the age of 2 months and above 18 years of age
ii. Patients in the pediatric intensive care unit
iii. Patients with known renal or cardiac disorders
iv. Parents or LAR are unwilling to give consent
v. Patients aged 12–18 years of age are unwilling to give assent.

Evaluation Parameters in the Case Record Form
i. Patient details: Age, Gender.
ii. Clinical Profile: Diagnosis, Duration of Admission.
iii. Crystalloid IVF utilization: Type, dose, duration, frequency, total volume, average volume.

iv. ADRs: Severity—Modified Hartwig and Siegel Severity Scale, Causality—WHO-UMC scale.[14,15]

v. Cost minimization analysis: Cost of IVF borne by the patient; Minimum cost of IVF in the Monthly Index of Medical Specialties, November 2022 (MIMS, November 2022).[16]

vi. AAP 2018 Guidelines: Appropriate Dextrose, KCl Correction Prescribed

Statistical Tests
Data were entered in MS Excel, analyzed in SPSS v20.0, and expressed using descriptive statistics:

i. Actual numbers
ii. Mean with SD
iii. Percentage.

RESULTS
Among the 240 patients 132 (55%) were male and 84 (45%) were female. The mean age ± standard deviation was 8.675 ± 5.615 and the median age was 9.0 years with an age range of 0.3–17 years of age. The Mean ± SD duration of admission for the study subjects was 5.15 ± 4.77 days [Figures 1 and 2].

The diagnoses assigned to the patients were divided into disease groups. Top 5 disease groups were Respiratory illnesses (20.42%), central nervous system disorders (17.50%), Pyrexias (17.50%), Gastrointestinal disorders (10.83%), Poisoning (10%) [Table 1].

Overall, DNS was prescribed 816 times. NS was prescribed 189 times. RL was prescribed 47 times [Table 2]. Total IVF utilization in Litres/100 bed-days was calculated [Table 3].

There were six cases of ADRs seen, which included hyponatremia (3), chills (2), and chest pain (1). Hyponatremia and chest discomfort were considered to have moderate severity, and chills were considered to have mild severity. Out of the four categories of unlikely, possible, probable, and certain, all the ADRs were categorized as “possible.

The costs of acquisition for crystalloid IVFs observed in the study were recorded [Table 4]. This was compared with minimum cost of acquisition of various crystalloid IVFs in MIMS [Table 4].

Cost Minimization Analysis was done. Daily mean cost savings per patient would be ₹17.91 [Table 5]. The percentage average saving per patient is 46.32% [Figure 3].

In this study, it was observed that all 240 patients received appropriate dextrose. They also received appropriate potassium chloride for the correction and replacement of losses. This meets the requirements of the “American Academy of Pediatrics 2018 clinical practice guidelines.”

DISCUSSION
IVF usage is the preferred modality for maintenance rehydration therapy for children who can’t uptake fluids orally to maintain their fluid-electrolyte balance. They also offer a means to provide calories in terms of dextrose to
Table 1: Patient diagnoses organized into disease groups

<table>
<thead>
<tr>
<th>Disease group</th>
<th>Frequency (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory illnesses</td>
<td>49 (20.42)</td>
</tr>
<tr>
<td>CNS disorders</td>
<td>42 (17.50)</td>
</tr>
<tr>
<td>Pyrexias</td>
<td>42 (17.50)</td>
</tr>
<tr>
<td>Gastrointestinal disorders</td>
<td>26 (10.83)</td>
</tr>
<tr>
<td>Poisoning</td>
<td>24 (10.00)</td>
</tr>
<tr>
<td>Injuries</td>
<td>18 (7.50)</td>
</tr>
<tr>
<td>Postoperative cases</td>
<td>17 (7.08)</td>
</tr>
<tr>
<td>Blood disorders</td>
<td>14 (5.83)</td>
</tr>
<tr>
<td>Viral infectious diseases</td>
<td>5 (2.08)</td>
</tr>
<tr>
<td>Hypersensitivity/autoimmune conditions</td>
<td>3 (1.25)</td>
</tr>
</tbody>
</table>

CNS: Central nervous system

Table 2: Number of prescriptions of crystalloid IV fluids among patients

<table>
<thead>
<tr>
<th>Name of IV fluid</th>
<th>Number of IV fluid prescriptions (total=1052), n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNS</td>
<td>816 (77.57)</td>
</tr>
<tr>
<td>NS</td>
<td>189 (17.97)</td>
</tr>
<tr>
<td>RL</td>
<td>47 (4.47)</td>
</tr>
</tbody>
</table>

DNS: Dextrose-normal saline, NS: Normal saline, RL: Ringer’s lactate, IV: Intravenous

Table 3: Volume of crystalloid IV fluids prescribed to patients

<table>
<thead>
<tr>
<th>Name of IV fluid</th>
<th>Litres of IV fluid used</th>
<th>ATC code</th>
<th>Litres/100 bed-days</th>
</tr>
</thead>
<tbody>
<tr>
<td>DNS</td>
<td>557.5</td>
<td>B05XA30</td>
<td>2.334883</td>
</tr>
<tr>
<td>NS</td>
<td>26.4</td>
<td>B05XA03</td>
<td>0.110567</td>
</tr>
<tr>
<td>RL</td>
<td>23.5</td>
<td>B05XA30</td>
<td>0.098421</td>
</tr>
</tbody>
</table>

DNS: Dextrose-normal saline, NS: Normal saline, RL: Ringer’s lactate, IV: Intravenous

Table 4: Average cost of acquisition of various crystalloid IV fluids in current study

<table>
<thead>
<tr>
<th>Source of data</th>
<th>Name of IV fluid</th>
<th>Volume (mL)</th>
<th>Cost of acquisition (₹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current study (average cost)</td>
<td>DNS</td>
<td>500</td>
<td>34.5</td>
</tr>
<tr>
<td></td>
<td>NS</td>
<td>100</td>
<td>16</td>
</tr>
<tr>
<td></td>
<td>NS</td>
<td>500</td>
<td>33</td>
</tr>
<tr>
<td></td>
<td>RL</td>
<td>500</td>
<td>50</td>
</tr>
<tr>
<td>Monthly index of medical specialties (minimum cost)</td>
<td>DNS</td>
<td>500</td>
<td>17.85</td>
</tr>
<tr>
<td></td>
<td>NS</td>
<td>100</td>
<td>9.12</td>
</tr>
<tr>
<td></td>
<td>NS</td>
<td>500</td>
<td>22.02</td>
</tr>
<tr>
<td></td>
<td>RL</td>
<td>500</td>
<td>29.81</td>
</tr>
</tbody>
</table>

DNS: Dextrose-normal saline, NS: Normal saline, RL: Ringer’s lactate, IV: Intravenous

Table 5: Cost minimization analysis

<table>
<thead>
<tr>
<th>Source of data</th>
<th>Parameters</th>
<th>Cost (₹), mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Our study</td>
<td>Total IV fluid cost of acquisition for patient</td>
<td>140.25±55.28</td>
</tr>
<tr>
<td></td>
<td>Daily IV fluid cost of acquisition for patient</td>
<td>38.61±20.07</td>
</tr>
<tr>
<td></td>
<td>Monthly index of medical specialties</td>
<td>75.29±31.07</td>
</tr>
<tr>
<td></td>
<td>Daily IV fluid cost of acquisition from website</td>
<td>20.7±11.11</td>
</tr>
<tr>
<td></td>
<td>Average cost savings per patient for duration</td>
<td>64.96</td>
</tr>
<tr>
<td></td>
<td>of admission</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Average cost savings for patient per day of</td>
<td>17.91</td>
</tr>
<tr>
<td></td>
<td>admission</td>
<td></td>
</tr>
</tbody>
</table>

SD: Standard deviation, IV: Intravenous

The AAP recommends that patients 28 days to 18 years of age requiring maintenance IVFs should receive isotonic solutions with appropriate potassium chloride (KCl) and dextrose because they significantly decrease the risk of on the collation of several randomized, controlled trials and meta-analyses. In this study, we studied the utilization of crystalloid IVFs, which are the most prevalent category of IVFs used in pediatric wards of a tertiary care hospital, where sick children are often unable to orally uptake the adequate volume of fluids, electrolytes, and calories for their maintenance needs that they should ideally consume. In this study, a total of 557.5 L of DNS was prescribed. A total of 26.4 L of 0.9% NS was prescribed. A total of 23.5 L of RL was prescribed. There were six cases of ADR seen in the current study, which included hyponatremia (3), chills (2), and chest pain (1). The severity of the ADRs was assessed using the modified Hartwig and Seigel scale. Out of the 6 ADRs, 4 were of level 4, which is moderate severity, and 2 were of level 1, which is mild severity. Hyponatremia and chest discomfort were considered to have moderate severity, and chills were considered to have mild severity. Hyponatremia was treated with fluid restriction in all cases, which led to the resolution of symptoms. Chills and chest discomfort were self-limiting. Causality assessment was done using the WHO-UMC scale. Out of the four categories of unlikely, possible, probable, and certain, all the ADRs were categorized as “possible” as per the WHO-UMC scale. This is the first study including cost minimization as a part of IVF utilization, to our knowledge. In the current study, the costs of crystalloid IVFs observed in the study were recorded. Total mean cost savings per patient per day of admission would be ₹17.91. The average percentage saving per patient would be 46.32%. These savings per patient can be a very important factor for the study participants, their parents, and legally authorized representatives, taking into consideration their socio-economic situation and per capita income as observed in the current study. In 2018, Feld et al., along with the “American Academy of Pediatrics,” published a clinical practice guideline that stated as follows: “The AAP recommends that patients 28 days to 18 years of age requiring maintenance IVFs should receive isotonic solutions with appropriate potassium chloride (KCl) and dextrose because they significantly decrease the risk of...
developing hyponatremia. In the current study, we observed the crystalloid IVF prescribing practices in the pediatric ward and posed the question of whether the AAP clinical practice guidelines criteria were satisfied. It was therefore observed that all 240 patients received appropriate dextrose and appropriate potassium chloride for correction and replacement of losses.

Gunnell et al. conducted an audit studying IVFs prescribed to post-operative children in the UK in 2019–2020 and found that all participants received isotonic crystalloid IVFs.[17] Chaudhari et al. in their study in a pediatric population with diarrhea, found that 97.14% of participants received crystalloid IVFs, out of which 5% received DNS, 62.85% received isolyte P, 47.86% received RL, and 5.71% received NS.[18] These studies showed similar crystalloid IVF utilization compared to the current study. Gamage et al. conducted a study in Sri Lanka in 2015 looking at crystalloid IVF utilization and found that the most common fluid used was 0.45% NaCl + 5% Dextrose.[20] Venkateswaran et al. found in their study regarding drug utilization in a pediatric ward that 19% of the participants received crystalloid IVFs for maintenance therapy.[21] These studies showed a varied and different crystalloid IVF utilization pattern compared to the current study. Chandrakumara et al. in their study regarding maintenance fluids used in infants over three audit periods. They found that 12 infants had hyponatraemia in the first audit cycle. 11 out of the 12 were on hypotonic crystalloid IVFs. In the second and third audit cycles, two infants developed hyponatraemia; one was given a mixture of isotonic crystalloid IVF and total parenteral nutrition, and the other was given hypotonic crystalloid IVFs. Another case had an episode of hypernatremia with a serum sodium of 146 and was given 10% dextrose.[13] Evans et al. in their study investigating IVFs used in pediatric bronchiolitis, found that only 1 participant had hypernatremia with a serum level of 147 and was given isotonic saline. There was no statistical significance found between the isotonic and hypotonic crystalloid IVF groups. There was, however, a significant association between electrolyte disturbances and an increased duration of admission.[11] Walker et al. conducted a study in a UK pediatric ward investigating whether routine maintenance therapy using the crystalloid IVF “Plasmalyte” caused metabolic abnormalities and found that 3% of participants experienced hyponatremia when given “Plasmalyte” compared to 14% with other crystalloid IVFs used for maintenance therapy.[22] These studies showed a similar ADR profile as compared to our findings. Carandang et al. conducted a randomized controlled trial in 2013 investigating the association between hyponatremia and crystalloid IVFs used for maintenance therapy and found that 34.7% of the study participants had an episode of hyponatremia. 38.6% of these children were given hypotonic crystalloid IVFs, and 27.8% of the children were given isotonic crystalloid IVFs. It was observed that the participants developed hyponatremia at an earlier stage if they were given hypotonic crystalloid IVFs instead of isotonic crystalloid IVFs.[23] Shamim et al. conducted a randomized clinical trial in Aligarh, India, in 2014 comparing 0.9% NaCl IVF solution and 0.18% NaCl IVF solution in hospitalized children. Hyponatremia was seen in 24 h in 24% of participants in the isotonic group and 55% in the hypotonic group. Hyponatremia was seen in 14% of participants in the isotonic IVF group and in 45% of participants in the hypotonic IVF group.[24] These studies showed significant differences as compared to our findings.

The strength of our study is that we have conducted a rare study of the utilization, adverse effects, and appropriateness of crystalloid IVFs, which is critical in children as it is easy to overlook. The cost-minimization aspect of this study highlights the potential savings for an underserved population. The limitations of this study are that it was conducted in a single center and had a modest sample size. The sampling method used was convenient sampling, so some potential biases are possible. Cost minimization analysis was conducted instead of cost-effectiveness, which would require additional resources. Expanding this study to multiple centers, increasing the sample size, and using random sampling will improve the power of the study.

CONCLUSION

DNS was the most commonly prescribed IVF (77.57%), followed by NS (17.97%) and RL (4.47%). The incidence of ADRs was 2.5%. Hyponatremia, chills, and chest pain occurred in participants with longer stays, suggesting causes beyond crystalloid IVFs. A cost minimization analysis showed a 46.32% reduction in IVF acquisition costs for participants. All participants received adequate dextrose.
and potassium chloride as per the 2018 guidelines of the American Academy of Pediatrics.

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