Scientific Rationale for a Change in the Composition of Oral Rehydration Solution

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Scientific Rationale for a Change in the Composition of Oral Rehydration Solution

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DIARRHEAL DISEASES REMAIN IMPORTANT CAUSES OF death and morbidity in developing countries, with an estimated 1.5 billion episodes and 1.5 million to 2.5 million deaths each year among children younger than 5 years.[1-4] Although the number of children currently dying from diarrhea continues to be unacceptably high, it is substantially lower than the 5 million deaths per year estimated 20 years ago.[5]

A critical factor in this reduction in diarrhea deaths has been the widespread adoption of oral rehydration solution (ORS) programs for the treatment and prevention of diarrhea-associated dehydration.[6,7] Indeed, ORS has been hailed as one of the most important medical advances of the past century,[8] at least in part because of its simplicity, low cost, and remarkable ease of use.

Oral rehydation solution works on the elegantly simple physiologic principle of solute cotransport across the gastrointestinal epithelium (FIGURE). Briefly, landmark studies published in 1968[9,10] among patients with *Vibrio cholera* infections demonstrated that although the secretory nature of the diarrhea causes massive stool losses of water and electrolytes, sodium-coupled glucose cotransport remains largely intact and continues to stimulate resorption of salt and water.[11] Clinical trials documenting the efficacy of ORS soon followed in the 1970s and 1980s.[12-14]

For nearly 3 decades, the World Health Organization (WHO) and the United Nations Children's Fund (UNICEF) have recommended a single formulation of glucose-based ORS to treat or prevent dehydration from diarrhea of any etiology and in individuals of any age.[15,16] The composition of the solution, which has proven both safe and effective in worldwide use, was based on its efficacy in replacing water and electrolytes in individuals with cholera infection, since these infections were in part the impetus behind the development of ORS. Concern that the sodium concentration of 90 mEq/L was too high for the lower salt losses of viral and other causes of childhood diarrhea[17] was invoked to explain its low acceptance among pediatricians in industrialized countries who were concerned about the possible occurrence of hypernatremia.[18] Some authors also noted that the standard WHO ORS was occasionally associated with hypernatremia in children in developing countries.[19]

In the hopes of actually reducing stool output, efforts to improve the efficacy of ORS were made in the 1970s through 1990s. These included the addition of other substrates for sodium cotransport (eg, the amino acids glycine,[20] alanine, and glutamine[21]) or substitution of complex carbohydrates for glucose (eg, cooked rice powder and other cereal powders).[22] With the exception of rice-based ORS, which significantly reduces stool output in cholera patients,[23] these new ORS preparations were not more effective than standard ORS and are more expensive.[24] Solutions with higher concentrations of cotransporters and higher osmolarity decrease rather than increase intestinal sodium and water absorption, and hypernatremia has been reported with their use.[25]

Recent efforts to improve the efficacy of ORS have focused on solutions of reduced osmolarity (eg, sodium ranges of 60-75 mEq/L and glucose ranges of 75-90 mmol/L), although some cereal-based ORSs may also be lower in osmolarity.[26] These solutions generally preserve the 1:1 M ratio of sodium to glucose that is critical for efficient cotransport of sodium but present a lower osmolar load to the intestinal tract than does the original WHO ORS. Animal[27] and

See also p 2632.

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human studies have indicated that such solutions may be better designed for optimal water and electrolyte transport into the bloodstream. In intestinal perfusion studies, solutions of reduced osmolarity have shown improved net water absorption and equivalent net sodium absorption compared with the standard WHO ORS.[28] In clinical trials, children treated with reduced-osmolarity ORS experience less vomiting, less stool output, shorter duration of illness, and less need for supplemental intravenous fluids than do those treated with the standard WHO ORS.[29-31]

Advantages of Reduced-Osmolarity ORS

A number of randomized controlled trials have been conducted comparing the standard (1975 WHO) and reduced-osmolarity (2002 WHO) solutions (TABLE). In a trial of 300 adult patients with cholera,[32] those who received reduced-osmolarity ORS had no differences in stool output, duration of diarrhea, or need for unscheduled intravenous therapy compared with those treated with the standard WHO ORS. Patients who received reduced-osmolarity ORS had an increased incidence of hyponatremia (serum sodium level <130 mmol/L) (odds ratio [OR], 2.1; 95% confidence interval [CI], 1.1-4.1). The mean difference in serum sodium at 24 hours of treatment between the 2 groups was 1.2 mEq/L, and none of the patients with hyponatremia in either group was symptomatic.

In a large multicenter trial of children with acute diarrhea not due to cholera,[33] 675 children aged 1 to 24 months from 5 countries were randomized to receive standard or reduced-osmolarity ORS. Although stool output and vomiting were not statistically different between the groups, the use of unscheduled intravenous fluids following initial rehydration was reduced in the group receiving reduced-osmolarity ORS (10% vs 15%) (OR, 0.6; 95% CI, 0.4-1.0). The occurrence of hyponatremia was not statistically different between the groups (11% in the reduced-osmolarity group vs 9% in the standard group) (OR, 1.3; 95% CI, 0.2-2.2).

In a meta-analysis that evaluated the effects of reduced-osmolarity ORS in 15 randomized trials of nearly 2400 children,[31] use of a reduced-osmolarity ORS was associated with less frequent use of unscheduled intravenous fluids (combined OR, 0.61; 95% CI, 0.47-0.81) and less vomiting (combined OR, 0.71; 95% CI, 0.55-0.92). In addition, a statistically significant reduction in stool output was noted (standardized mean difference, –0.21; 95% CI, –0.31 to –0.12). The incidence of hyponatremia was not significantly elevated among children who received reduced-osmolarity ORS in these trials (OR, 1.45; 95% CI, 0.93-2.26).

Based on these and other relevant data, WHO and UNICEF convened a meeting in 2001 to review all published studies comparing standard and reduced-osmolarity ORS.[34] The conclusions were as follows:

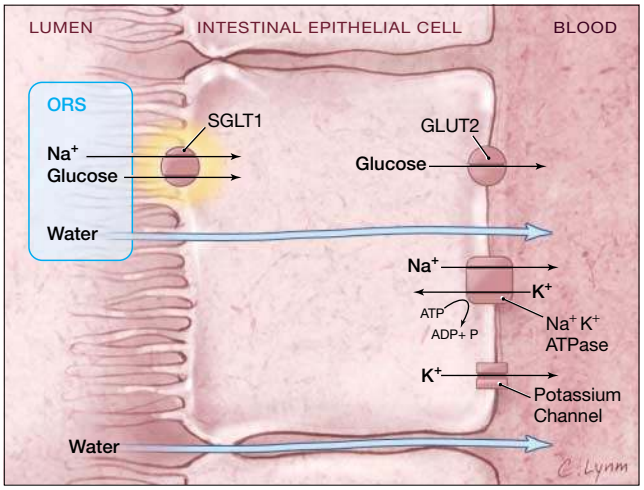
1. Reduced osmolarity ORS was more effective than standard ORS for acute noncholera diarrhea in children, as measured by clinically important outcomes such as reduced stool output, reduced vomiting, and reduced need for supplemental intravenous therapy. Although data were more limited, reduced-osmolarity ORS also appeared safe and effective for children with cholera;

2. Among adults with cholera, clinical outcomes were not different among those treated with reduced-osmolarity ORS compared with standard ORS, although the risk of transient asymptomatic hyponatremia was noted;

3. Given the programmatic and logistical advantages of using a single ORS composition globally, it was recommended that this be a reduced-osmolarity ORS (Table); and

4. Further monitoring, including postmarketing surveillance studies, were strongly encouraged to better assess any risk of symptomatic hyponatremia in cholera-endemic parts of the world.[34]

Figure. Coupled Transport of Sodium and Glucose in Intestinal Epithelial Cells



Although nutrient-independent sodium absorption across the brush border membrane of intestinal epithelial cells is impaired in patients with diarrhea, coupled transport of sodium and glucose is preserved, allowing absorption of salt and water provided by oral rehydration solutions (ORSs). Sodium-glucose transporter type 1 (SGLT1) mediates the transport of glucose against its concentration gradient by coupling it to sodium transport. Sodium that enters the cell is pumped into the blood by the Na^+K^+ATPase (adenosine triphosphatase) pump in the basolateral membrane, maintaining the sodium electrochemical gradient that drives the sodium-glucose cotransport mechanism. Transport of glucose into the blood is facilitated by glucose transporter type 2 (GLUT2).

Table. Composition of Standard and Reduced-Osmolarity WHO ORS

	Standard WHO (1975)	Reduced-Osmolarity WHO (2002)
Glucose, mmol/L	111	75
Sodium, mEq/L	90	75
Potassium, mEq/L	20	20
Chloride, mEq/L	80	65
Citrate, mmol/L	10	10
Osmolarity, mOsm/L	311	245

Abbreviations: ORS, oral rehydration solution; WHO, World Health Organization.

Concerns About Use of Reduced-Osmolarity ORS

Some concerns have been raised regarding the revised formulation of ORS.[35-37] We believe, however, that the published literature does not support these concerns.

For example, concern has been raised that any reduction in the sodium concentration of ORS will increase the risk of hyponatremia, especially among cholera patients.[35] Cholera stool sodium losses can be as high as 120 to 150 mEq/L, and in fact the composition of the original WHO ORS (90 mEq/L) was a compromise between those who favored a solution with 120 mEq/L of sodium and those who proposed a lower concentration better suited for children with diarrhea due to causes other than cholera. Thus, even the former formulation of standard WHO ORS contains less sodium than some thought necessary for adequate sodium repletion in cholera.

Among subsets of children with cholera in 3 published clinical trials of ORS,[33,38,39] the mean serum sodium concentration at 24 hours was 136 mEq/L in those treated with standard ORS and only 0.8 mEq/L (95% CI, 0.2-1.4 mEq/L) lower in those treated with reduced-osmolarity ORS.[34] Although, as noted above, the incidence of hyponatremia was higher in adult cholera patients treated with a lower sodium solution, the clinical significance of this finding is unclear because all hyponatremic episodes in adults were transient and asymptomatic.[32]

Preliminary data concerning the incidence of hyponatremia in cholera-endemic areas of the world have been reassuring. A safety evaluation of reduced-osmolarity ORS was recently completed in Bangladesh among nearly 50 000 adults and children treated for diarrhea. Preliminary data analysis reveals that none of the adults had symptoms of hyponatremia during the 1-year study. Among close to 7000 children treated with reduced-osmolarity ORS, symptomatic hyponatremia was detected in only a small percentage of cases (0.2%), the majority of whom had another possible reason for hyponatremia (eg, severe pneumonia, dysentery) (N.H.A., unpublished data).

Other electrolyte abnormalities, including chronic sodium deficit and hypokalemia, have been hypothesized to occur with reduced-osmolarity ORS.[35] It is likely that cholera patients, especially adults, treated with either reduced-osmolarity or standard ORS are transiently sodium depleted, and that the deficit would be somewhat greater with the reduced-osmolarity solution. There is, however, no evidence that the deficit is clinically significant with either solution. It is also likely that sodium stores would be restored in the days following resumption of a normal salt-containing diet. It has been suggested that balance studies be performed in which patients are provided only standard or reduced-osmolarity ORS for 24 to 48 hours. The practice of withholding food (and therefore additional sodium) from patients with diarrhea is not in keeping with the past 15 years of standard diarrhea management, which recommends immediate nutrition after successful rehydration.[40-43] These balance studies would therefore be unethical to carry out and would have no relevance to current clinical care.

Likewise, hypokalemia has not been observed among patients treated with reduced-osmolarity ORS. In the CHOICE study,[33] mean (SEM) serum potassium at 24 hours was 4.0 (0.7) mEq/L in children treated with reduced-osmolarity ORS vs 3.9 (0.8) mEq/L in those treated with the WHO ORS (O.F. unpublished data, 2001).

Concern has also been raised that reduced-osmolarity ORS may complicate the management of patients with severe protein-energy malnutrition. Children with severe protein-energy malnutrition are known to have significant alterations in fluid and electrolyte homeostasis, with an excess of extracellular fluid and resultant hyponatremia.[44] However, total body sodium is increased, and indeed sodium restriction is an important aspect of clinical management. Clinical trials using reduced-osmolarity ORS among malnourished children have actually shown improved clinical outcomes. Among 64 children younger than 4 years with weight for age less than 60% of the standard, a reduced-osmolarity ORS (224 mOsm/L) was compared in a double-blind fashion with the standard WHO ORS.[45] Stool output, duration of diarrhea, and intake of ORS were all significantly lower in the group receiving the reduced-osmolarity ORS compared with those given standard ORS, and mean serum sodium concentrations were normal in both groups at the end of therapy. No patient had symptoms of hyponatremia. In another trial of 180 infants with diarrhea (35 of whom had cholera infection), treatment with reduced-osmolarity ORS was associated with a significant reduction in stool frequency, an effect that was greatest in children with severe protein-energy malnutrition. Serum sodium levels in the 2 groups were not significantly different.[39]

Among infants with persistent diarrhea (duration >14 days), who are at risk of developing protein-energy malnutrition and early death, reduced-osmolarity ORS has also been shown to be more effective than standard ORS. In a study of 95 infants in Bangladesh hospitalized with persistent diarrhea, receipt of reduced-osmolarity ORS was associated with an approximate 40% reduction in stool output, a more prompt resolution of diarrhea, and no evidence of hyponatremia.[46]

Conclusions

A number of randomized controlled trials have established the superiority of reduced-osmolarity ORS over standard ORS in the management of diarrheal diseases in children. Concerns about the safety of reduced-osmolarity ORS center on its use in patients with cholera, especially adults. While the provision of 17% less sodium to patients with cholera may lead to a slightly greater negative sodium balance at the end of treatment, this deficit should be rapidly corrected when a normal diet is resumed. Experience to date provides no evidence that transient hyponatremia, which may also occur with standard ORS, has significant adverse clinical consequences for cholera patients.

The benefits of promoting the use of a single ORS solution for all patients with diarrhea, including cholera, are enormous, as has been clearly established with standard ORS. It is recognized, however, that any single ORS formulation, including standard ORS, that is promoted for use in patients of all ages and with diarrhea of any etiology must be a compromise that takes into consideration both the substantial differences in stool sodium losses that occur across the spectrum of diarrheal disease as well as substantial differences in the global burden of cholera vs noncholera diarrhea. It is estimated that acute noncholera diarrhea in children causes 1.5 million to 2.5 million deaths per year, whereas cholera causes significantly fewer deaths in all age groups (approximately 120 000 per year) (O.F., unpublished data). Reduced-osmolarity ORS has the potential to substantially reduce childhood deaths from noncholera diarrhea due to the reduced requirement for supplementary intravenous fluids. Although reduced-osmolarity ORS may not have the same benefit for cholera patients, clinical trials show it to be as effective as standard ORS. It is our view that the current evidence demonstrates the benefits of reduced-osmolarity ORS for the world's children, and that use of the revised formulation is fully justified.

Disclaimer: Drs Duggan, Fontaine, Pierce, Mahalanabis, Alam, Bhan, and Santosham were participants in the July 2001 WHO/UNICEF meeting on reduced-osmolarity ORS.

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改变口服补液盐配方的科学合理性

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腹泻一直是发展中国家高死亡率的原因。每年约有15亿儿童患病，有1.5百万-2.5百万5岁以下的儿童死于腹泻[1-4]。尽管目前因腹泻死亡的儿童的数量仍然高得不能接受，但是与20年前每年5百万左右的死亡率相比，已经有了根本性的下降[5]。

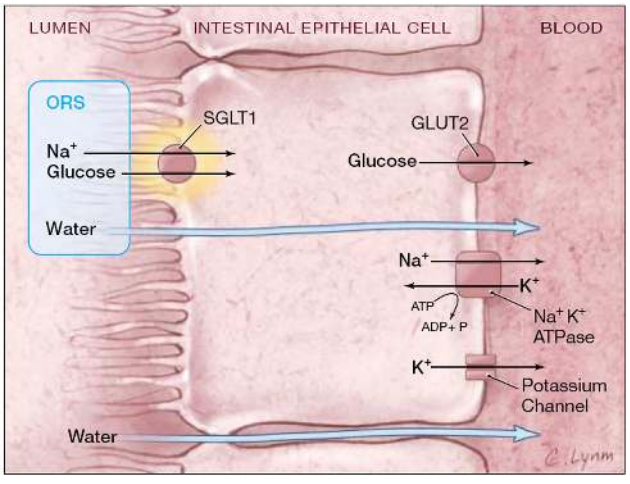
腹泻死亡率降低的主要原因是广泛给予口服补液治疗，以纠正和预防腹泻脱水[6,7]。实际上，ORS已被认为是上世纪最重要的药物进步之一[8]，部分原因基于其简单、低廉和易于应用。

ORS的作用机制，出色地遵循了溶质转运通过胃肠上皮细胞协的简单生理原理（见图）：简单讲，1968年发表的标志性的研究显示[9,10]，霍乱弧菌感染的病例会因腹泻的分泌性质而大量排便，使体内水份和电解质丢失，但Na偶联的葡萄糖协同运输系统不会受到影响，且继续刺激盐和水的重吸收[11]。ORS的效果在20世纪70-80年代的临床研究已显现出来[12-14]。

30多年来，WHO和UNICEF同时推荐一个含有葡萄糖ORS的简单的配方，可用于治疗和预防任何年龄段的任何原因导致的腹泻性脱水[15,16]。经全球使用已证明该溶液的组成是有效和安全的，可以有效的补充霍乱感染的腹泻引起的水和电解质的丢失，因为早期因水和电解质引起的感染是开发ORS的动力之一。相对因病毒和其他感染的儿童较低的失钠量，90 mEq/L的钠浓度显得比较高[17]。所以这样高浓度的Na在发达国家中难以被儿科医生中接受，因为他们认为有引起高钠血症的可能[18]。许多研究人员也指出WHO标准ORS在发展中国家使用也会有高钠血症的情况发生[19]。

为了降低粪便量，从上世纪70年代到90年代，开展了改进ORS疗效的多种尝试。这些试验涉及与Na协同运输相关的其他物质（如：甘氨酸[20]，丙氨酸和

图. 钠－葡萄糖经小肠上皮细胞的同向转运



虽然腹泻患者与营养无关的经小肠上皮刷状缘的钠吸收被破坏，钠－葡萄糖偶联的转运被保留，因此患者可以从ORS液中吸收水和盐。

盐-糖转运载体I（SGLT1）通过捆绑葡萄糖和钠转运，介导的葡萄糖的逆着浓度梯度转运，钠进入细胞依靠嵌在细胞膜的Na^+K^+ATP酶泵钠入血，稳定Na电解质的梯度使得Na-葡萄糖的正常跨膜转运。葡萄糖转运至血液是由基底膜上葡萄糖转运载体II（GLUT2）完成的。

表. WHO标准ORS和低渗ORS的成份

	WHO标准ORS (1975)	WHO低渗ORS (2002)
葡萄糖, mmol/L	111	75
钠, mEq/L	90	75
钾, mEq/L	20	20
氯, mEq/L	80	65
枸橼酸盐, mmol/L	10	10
渗透压, mOsm/L	311	245

缩写：ORS，口服补液溶液；WHO，世界卫生组织

谷氨酸[21]）或复杂的碳水化合物（如：熟的米粉和其他谷类的粉末）[22]，除了含米粉的ORS可明显减少霍乱感染的病人的粪便排出量[23]，新处方ORS并不比传统的ORS来的有效，而且价格更高[24]。更高浓度协同运输载体和更高渗透压并不增加反而减少小肠Na和水的吸收，高钠血症也出现了[25]。

近期提高ORS疗效的尝试集中在减少渗透压上（如：钠浓度范围60～75 mEq/L，糖浓度范围75～90 mmol/L），尽管一些以谷物为基础的ORS的渗透压可以更低[26]。这些溶液通常保证1:1M的钠与糖的摩尔比例，这个比例有利于钠的协同运输， 与原来的WHO的标准ORS比，新的低渗ORS可实现更低的小肠渗透压。动物[27]和人的实验表明新的低渗ORS可更好地将水和电解质转运至血液。小肠灌注试验表明，与WHO标准ORS相比，低渗透压可以提高水的净吸收，钠的净吸收则与标准ORS相当[28]。临床研究显示，与WHO的标准ORS比，低渗ORS可明显减少儿童呕吐次数，粪便量，缩短病程，减少静脉补液的需要[29-31]

低渗ORS的优点

很多关于标准ORS（1975 WHO）和低渗ORS（2002 WHO）的随机对照临床试验已经完成（见表）。一项300名成人霍乱感染临床试验结果显示，与接受标准ORS治疗组比[32]，接受低渗ORS治疗组在粪便量、腹泻持续时间和计划外静脉补液率方面没有差异。接受低渗ORS的病人有低钠血症的倾向（血清Na的含量130 mmol/L，比值2.1，95%可信区间CI，1.1-4.1）。2组的24小时的血清Na均数差为1.2 mEq/L，两组的低血钠症患者均未出现症状。

一项大型多中心临床试验由来自5个国家的675名的年龄为1～24个月的急性非霍乱腹泻儿童随机接受标准ORS或者低渗ORS[33]。尽管两个组的呕吐次数和粪便排出量没有统计学差异，但低渗ORS组的计划外补液率明显降低（10% vs 15%，比值0.6; 95% CI，0.4-1.0）。两组的低血钠症发生率没有明显的区别（11% vs 9%，比值1.3; 95% CI，0.2-2.2）。

根据meta分析表明，15项随机对照由2400名儿童参与的临床实验表明低渗ORS可以降低计划外补液率（合并比例0.61; 95% CI，0.47-0.81）和减少呕吐次数（合并比例0.71; 95% CI，0.55-0.92）[31]。另外，粪便排出量也有统计学的差异（标准化均数差-0.21; 95% CI， -0.31 至 -0.12）。高钠血症发生率没有明显的增高（比值，1.45; 95% CI，0.93-2.26）。

基于上述相关数据，2001年WHO和UNICEF召开大会，回顾了所有公开发表的关于标准ORS和低渗ORS的临床效果的文献[34]，结论如下：

1. 用减少的粪便量，减少的呕吐次数和减少的静脉补液率这些重要的临床指标衡量，低渗ORS对于儿童急性非霍乱感染的腹泻的治疗效果优于标准ORS。尽管数据比较有限，但低渗ORS治疗儿童霍乱显示是有效、安全的。

2. 对于成年人腹泻，标准ORS和低渗ORS的临床效果没有显著区别，但是短暂的无症状的高血钠症有发生的可能。

3. 考虑到在全球推广一种ORS具有计划和逻辑的优势，这种ORS建议选择低渗ORS（见表）。

4. 为了更好评价有关全球霍乱流行地区的有症状的低血钠症的发生几率[34]，推荐开展进一步的检测，包括进入市场后的调查研究。

使用低渗ORS的注意事项

需要提的使用低渗ORS的注意点[35-37]，虽然目前的文献并不支持相关事项，但我们认为是必要的。

如，标准ORS中减少的Na的量会增加低钠血症的发生率，尤其霍乱病人[35]。霍乱病人因为粪便排出的Na高至120至150 mEq/L。实际WHO的标准ORS的钠量为90mEq/L，一个调和的浓度，介于某些适合钠浓度为120mEq/L的病人和某些认为低浓度适合非霍乱腹泻的儿童。因此，在霍乱患者中，甚至对于之前WHO推荐的ORS含有的Na对于补充Na仍然是不够的。

3篇发表的ORS临床试验文章提到[33,38,39]，接受标准ORS治疗的24小时的平均钠血清量为136 mEq/

L，接受低渗ORS治疗的仅降低0.8mEq/L（95% CI，0.2-1.4mEq/L）[34]，虽然在上文提到，但低血钠症在接受低钠溶液治疗的霍乱成年患者的发生率高，临床结果不甚明确，因为低钠血症的患病周期短暂，而且不典型[32]。

关于全球的霍乱感染区域的低血钠症发生率的基础数据仍在统计。50000名成人和儿童腹泻患者的低渗ORS的治疗效果已在孟加拉完成，结果显示低渗ORS是安全的。在一年的研究表明没有一例成年病人发生低血钠症。接近7000名儿童用低渗ORS治疗，典型的低血钠症只是在一小部分人群中有检测到（0.2%），低血钠症还可有其他原因造成（如，严重肺炎，痢疾）（N.H.A.，未发表数据）。

其他的电解质不正常状况，包括慢性钠损失和低钾血症状况的病人被考虑用低渗ORS治疗[35]。霍乱患者，尤其是成年人，用低渗ORS和标准ORS治疗都会出现短暂的低钠，当用低渗ORS治疗时，低钠的发生率会更高。但这种区别在临床上没有显著意义。当含正常的钠的饮食恢复，体内钠储存很快会恢复正常。建议研究ORS的临床试验应持续到24或48小时。腹泻病人禁食（进食摄入更多的钠）和15年以来推荐的成功补液后立即增加营养摄入的标准腹泻指导准则不同步[40-43]，这些平衡研究的开展与现行的临床监护没有关联，是缺乏职业道德的。

同时，低血钾症的发生率在接受低渗ORS的病人中没有发现。CHOICE研究[33]病人接受低渗ORS在24小时的平均血清钾浓度4.0（0.7）mEq/L，WHO-ORS的研究（未发表，2001）在24小时的平均血清钾浓度3.9（0.8）mEq/L。

有人担心，低渗ORS用于蛋白－能量营养不良的患者，可能使问题更为复杂。儿童蛋白质-能量营养不良明显会扰乱体液和电解质稳态，细胞外液过多和相应的低血钠[44]，但整个身体的钠含量是增高的，绝对的钠限制是临床治疗最为重要的方面。临床试验对营养不良的儿童使用低渗ORS收到了良好的临床效果。对于64个小于4岁，体重低于标准60%的儿童使用低渗ORS（224 mOsm/L）和标准ORS进行双盲试验，低渗ORS组的粪便排除量，腹泻持续时间，ORS的摄入量都明显低于标准ORS组[45]。血清钠浓度在治疗末期两组之间没有差异。两组病人均没有出现低血钠症。在另外一项180名腹泻婴儿（其中35名为霍乱感染）参与的临床研究中，低渗ORS治疗组具有显著减少腹泻次数的效果。这种效果在严重蛋白质-能量营养不良的儿童群体更加明显。2个组别的血清钠水平没有显著的区别[39]。

对于顽固腹泻儿童（持续14天），有蛋白质-能量营养不良和早期死亡的高发率危险，低渗ORS进行治疗更具有积极意义。对于95名孟加拉的住院顽固腹泻婴儿接受低渗ORS，可以减少40%的粪便排出量，更高的腹泻治疗率，并无低血钠症状[46]。

结论

许多临床随机对照试验已经表明在儿童的腹泻疾病的控制和治疗中，低渗ORS优于标准ORS。对于低渗ORS安全性的担忧集中在霍乱患者，尤其是成人霍乱患者。

但减少的17%的钠对于腹泻病人可能会导致治疗末期的低钠症状，而这种症状可由正常饮食立即弥补。尽管标准ORS也会使得腹泻病人产生低血钠，目前的实验数据并没有显示，短暂的低钠血症是非常严重的临床反应。

与标准ORS相比，提倡单一ORS溶液治疗所有腹泻病人，包括霍乱感染的腹泻，好处是很多的。已经认识到，在全球对所有年龄、任何病因的腹泻患者推广一种ORS（包括标准ORS），必需在以下两方面取得折衷：所有腹泻均存在的钠丢失的关键差异，以及全球霍乱治疗和非霍乱治疗的负担的关键差异。全球每年1.5百万～2.5百万的儿童死于急性非霍乱腹泻，而霍乱在所有年龄组导致的死亡则要少得多（每年大约120000）（O.F.，未公开数据）。低渗ORS可以减少额外的静脉补液的需求，具有在降低非霍乱儿童死亡率方面发挥关键作用的潜力。 尽管低渗ORS对霍乱腹泻不能产生同样的效果，临床试验表明低渗ORS和标准ORS具有相同的功效。这是我们的观点，现在的证据显示出低渗ORS对于全球的儿童是有益处的，而且对于标准ORS的处方修改是正确的。

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