Fluid therapy for acute bacterial meningitis

Background

- Acute bacterial meningitis remains a disease with high mortality and morbidity rates. Many survivors sustain neurological deficits
- With prompt and adequate antimicrobial and supportive treatment, the chances for survival have improved

Background

- Careful management of fluid and electrolyte balance is an important supportive therapy
- Both over- and under-hydration are associated with adverse outcomes.
- There are potential risks from giving too much fluid (especially brain swelling) as well as too little fluid (especially shock).

Objectives

To evaluate treatment of acute bacterial meningitis with differing volumes of initial fluid administration (up to 72 hours after first presentation) and the effects on death and neurological sequelae.

Selection criteria

Randomised controlled trials (RCTs) of differing volumes of fluid given in the initial management of bacterial meningitis were eligible for inclusion.

Data collection and analysis

- Three trials eligible for inclusion (415 children)
- All trials were set in countries where death rates are high and where patients seek help late

Trước đây

- Biến chứng hạ Natri máu
- Có thể do tăng nồng độ hormon chống bài niệu – ADH
- Có sự liên quan giữa hạ Natri máu và co giật
 + bệnh trầm trọng hơn + di chứng thần kinh
- Có sự liên quan tới tỉ lệ tử vong cao do phù não
- Hạn chế dịch đế tránh làm phù não và cải thiện di chứng thần kinh

Trước đây

- Tỉ lệ tử vong cao còn ở những TH thiếu nước
- TH trẻ được duy trì lượng dịch cùng với lượng dịch mất, nồng độ cao ADH về bình thường sau 24h
- TH hạn chế dịch 2/3 nhu cầu, nồng độ ADH vẫn cao
- → ADH tăng trong viêm màng não vi khuẩn do giảm thể tích chỉ trở lại bình thường khi bù đủ dịch và Natri

Types of participants: All age groups with a diagnosis of acute bacterial meningitis (by clinical diagnosis or culture of cerebrospinal fluid)

Types of interventions:

- Fluid administered in the initial treatment of acute bacterial meningitis; irrespective of route of administration, type or volume of fluid.
- Comparisons of the initial volume of fluid administered in the treatment of acute bacterial meningitis, irrespective of route of administration, or type of fluid or duration of fluid restriction.

Types of outcome measures

Primary outcomes

- Death
- Short-term (within the first four weeks of illness) and long-term (persisting after the first four weeks of illness) neurological sequelae

Secondary outcomes

- Oedema (including cerebral)
- Total body water
- Extracellular water
- Serum and urinary sodium
- Plasma and urinary osmolality

a) Volume and constitution of fluid

- <u>Duke 2002</u> compared milk-based fluids delivered at 60% of that required for maintenance fluids with 100% of normal maintenance fluids.
- Maintenance fluids were defined: 100 ml/kg/day for the first 10 kg of BW, 50 ml/kg for the second 10 kg, and 20 ml/kg for over 20 kg
- The milk-based fluids comprised expressed breast milk or other milk feed given via a nasogastric tube for at least 48 hours, or longer with reduced conscious state, convulsions, impaired upper airway reflexes or persistent respiratory distress.
- Normal maintenance fluids of a solution: 0.45% NaCl and 5% dextrose plus 10 mmol/L of KCl per litre were delivered intravenously for at least the first 48 hours.

Powell 1990 compared two-thirds of required maintenance fluids with full maintenance fluids, plus replacement fluids for any estimated deficit over 24 hours

Maintenance fluids: 100 ml/kg for the first 10 kg of BW, plus 50 ml/kg for the next 10 kg (10 kg to 20 kg), plus 20 ml/kg for each kilogram in excess of 20 kg").

Rehydration was begun by administering 10 or 15 ml/kg by rapid intravenous infusion.

- Singhi 1995 compared restricted fluids at 65% of the calculated maintenance fluid requirement with maintenance fluid requirements, both given intravenously.
- Maintenance fluid: 110 ml/kg for first 10 kg, 50 ml/kg for next 10 kg and 25 ml/kg for subsequent weight
- The restricted fluids comprised one-fifth normal saline in 5% dextrose for 24 hours, followed by "a gradual liberalisation at a rate of 10 ml/kg over eight hours, if, after 24 hours of hospital stay, the serum sodium and plasma osmolality had returned to normal and there were no clinical signs of dehydration".

b) Duration of fluid therapy

One study administered fluids for 48 hours (<u>Duke 2002</u>); one study administered fluids for 24 hours (<u>Powell 1990</u>); and the third study administered fluid for 24 hours with a gradual increase thereafter until children in both arms received the full normal maintenance requirement after 48 hours (<u>Singhi 1995</u>).

Baseline characteristics of participants a) Age

Duke 2002 between 1 month and 12 years

Powell 1990 between three months and 16 years

Singhi 1995 between two months and 7 years

b) Health status

- Duke 2002: chidren were from a population in which 25% were undernourished at the time of their presentation.
 - In regard to the meningitis symptoms, the mean duration of symptoms was 6 days, with two-thirds of children having convulsions, before presentation; 20% of the children were hypoglycaemic.
- Powell 1990 : previously healthy children
- Singhi 1995: Malnourished children were excluded study and children had a duration of symptoms ranging from one to 10 days on presentation.

- c) Diagnostic techniques used to establish a diagnosis of bacterial meningitis
- <u>Duke 2002</u>: clinical signs of meningitis and a cloudy or turbid cerebrospinal fluid (CSF) with a moderate or large number of leucocytes and amount of protein, determined by dipstick testing.
- Powell 1990: clinical examination, CSF cytology and chemical studies.
- Singhi 1995: suggestive history, physical examination and CSF findings of hypoglycorrhachia, increased protein concentration and polymorphonuclear leucocytosis.

Main results

The meta-analysis found no significant difference between the maintenance-fluid and restricted-fluid groups in number of deaths (RR 0.82, 95% confidence interval (CI) 0.53 to 1.27; 407 participants) (moderate trial quality)

Review: Fluid therapy for acute bacterial meningitis Comparison: 1 Maintenance fluids versus restricted fluids Outcome: 1 Death

Study or subgroup	Maintenance fluids n/N	Restricted fluids n/N	Risk M - H, Fixe	k Ratio 6d,95% Cl	Weight	Risk Ratio M - H, Fixed, 95% Cl	
1 All participants Duke 2002	29/181	31/176	-		83.6 %	0.91 [0.57, 1.44]	
Singhi 1995	2/22	7/28	-	-	16.4 %	0.36 [0.08, 1.58]	
Subtotal (95% CI) Total events: 31 (Mainten Heterogeneity: Chi ² = 1.3 Test for overall effect: Z =	17, df = 1 (P = 0.24);	ricted fluids)	•		100.0 %	0.82 [0.53, 1.27]	
2 Participants with hypon Singhi 1995	atraemia 0/11	4/15		_	100.0%	0.15 [0.01, 2.50]	
Subtotal (95% CI) Total events: 0 (Maintena Heterogeneity: not applic Test for overall effect: Z =	able			-	100.0 %	0.15 [0.01, 2.50]	
3 Participants without hy Singhi 1995	ponatraemia 2/11	3/13	-	F	100.0%	0.79 [0.16, 3.90]	
Subtotal (95% CI) Total events: 2 (Maintena Heterogeneity: not applic Test for overall effect: Z =	able		•		100.0 %	0.79 [0.16, 3.90]	
			1 1 1	l i	1		
	F	avours maintenanc	0.001 0.01 0.1 1 :e	. 10 100 Favours restricte	1000 d		

Main results

The meta-analysis found no significant difference between the maintenance-fluid and restricted-fluid groups in acute severe neurological sequelae (RR 0.67, 95% CI 0.41 to 1.08; 407 participants) (very low trial quality); or in mild to moderate sequelae (RR 1.24, 95% CI 0.58 to 2.65; 357 participants) (moderate trial quality)

Review: Fluid therapy for acute bacterial meningitis Comparison: 1 Maintenance fluids versus restricted fluids Outcome: 2 Severe neurological sequelae

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Study or s		nce fluids f /N	Restricted fluids n/N	Risk Ratio M - H, Fixed, 95% C	Weight I	Risk Ratio M - H, Fixed, 95% CI	
1 Acute (w Duke 2	ithin the first 4 weeks) 002	17/181	26/176	-	75.0 %	0.64 [0.36, 1.13]	
Singhi	1995	6/22	10/28		25.0 %	0.76 [0.33, 1.78]	
Total even Heterogen	(95% CI) its: 23 (Maintenance fluids) eity: Chi ² = 0.12, df = 1 (P verall effect: Z = 1.66 (P =	$= 0.72); I^2$		•	100.0 %	0.67 [0.41, 1.08]	
2 Chronic Duke 2	(after the first 4 weeks) 002	9/177	21/174		100.0%	0.42 [0.20, 0.89]	
Total even Heterogen	(95% CI) ts: 9 (Maintenance fluids), eity: not applicable verall effect: Z = 2.25 (P =		174 ted fluids)	•	100.0 %	0.42 [0.20, 0.89]	
3 Participa Singhi	ants without hyponatraemii 1995	a 2/11	4/13		100.0%	0.59 [0.13, 2.64]	
Total even Heterogen	(95% CI) its: 2 (Maintenance fluids), eity: not applicable verall effect: Z = 0.69 (P =		13 d fluids)		100.0 %	0.59 [0.13, 2.64]	
4 Participa Singhi	ants with hyponatraemia 1995	4/11	6/15	_	100.0%	0.91 [0.34, 2.47]	
Total even Heterogen	(95% CI) ts: 4 (Maintenance fluids), eity: not applicable verall effect: Z = 0.19 (P =		15 d fluids)	•	100.0 %	0.91 [0.34, 2.47]	
			0.1	005 0.1 1	10 200		_
		Fav	ours maintenance		urs restricted		

Main results

When neurological sequelae were defined further, there was a statistically significant difference in favour of the maintenance-fluid group for spasticity (RR 0.50, 95% CI 0.27 to 0.93; 357 participants); seizures at both 72 hours (RR 0.59, 95% CI 0.42 to 0.83; 357 participants) and 14 days (RR 0.19, 95% CI 0.04 to 0.88; 357 participants)

Review: Fluid therapy for acute bacterial meningitis Comparison: 1 Maintenance fluids versus restricted fluids Outcome: 5 Spasticity

Study or subgroup	Maintenance fluids n/N	Restricted fluids n/N		Risk Ratio M-H,Fixed,95% CI						Risk Ratio M-H,Fixed,95% CI	
1 At 14 days Duke 2002	14/181	27/176		_	-	_				0.50 [0.27, 0.93]	
	Fi	avours maintenanc	0.1 e	0.2	0.5	1	2 Favours	5 restric	10 ted		

Review: Fluid therapy for acute bacterial meningitis Comparison: 1 Maintenance fluids versus restricted fluids Outcome: 6 Seizures

Study or subgroup	Maintenance fluids n/N	Restricted fluids n/N			k Ratio ed,95% Cl		Risk i M - H, Fixed		
1 Within the first 72 hours Duke 2002	s 38/181	63/176		+			0.59[0	.42, 0.83]	
2 At 14 days Duke 2002	2/181	10/176	—				0.19[0	.04, 0.88]	
			ī	1		ī	1		
	E	avours maintenanc	0.05 e	0.2	1 Favour:	5 restricted	20		

Review: Fluid therapy for acute bacterial meningitis

Comparison: 1 Maintenance fluids versus restricted fluids

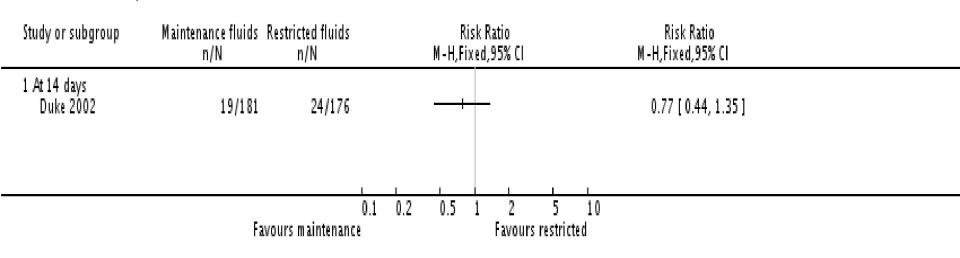
Outcome: 4 Hemiparesis/hemiplegia

Study or subgroup	Maintenance fluids Re: n/N	trictive fluids n/N	M - H,	Risk Ratio Fixed,95% Cl		Risk Ratio M-H,Fixed,95% CI	
1 At 14 days Duke 2002	18/181	18/176				0.97 [0.52, 1.81]	
		Ī	ī		Ī		
		0	0.5 0.7	1 1	.5 2		
	Favours maintenance				Favours restricted		

Review: Fluid therapy for acute bacterial meningitis

Comparison: 1 Maintenance fluids versus restricted fluids

Outcome: 7 Visual impairment



Main results

There was a statistically significant difference in favour of the maintenance-fluid group for chronic severe neurological sequelae at three months follow-up (RR 0.42, 95% CI 0.20 to 0.89; 351 participant

Main results

An adverse effect in children with restricted fluid intake was that they
were less likely to have low levels of sodium in their blood and
therefore they would experience greater reductions in body fluids.

 An adverse effect of unrestricted fluid administration was reported in one study as short-term swelling of the face and low blood sodium levels one to two days after fluids were started, although the largest study found no difference in blood sodium levels

Authors' conclusions

- Some evidence supports maintaining intravenous fluids rather than restricting them in the first 48 hours in settings with high mortality rates and where children present late.
- Where children present early and mortality rates are lower, there is insufficient evidence to guide practice

THANK YOU



FOR PAYING ATTENTION