

JAMA Internal Medicine | [Original Investigation](#)

Risk of Overcorrection in Rapid Intermittent Bolus vs Slow Continuous Infusion Therapies of Hypertonic Saline for Patients With Symptomatic Hyponatremia The SALSA Randomized Clinical Trial

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Impact factor: 23.4



中重度低血鈉病人使用3%Saline快速
間歇輸注比慢速連續滴注較能提升治
療成效

2021.04.27
Journal Club

報告者：鍾家偉護理師



01

Background

02

Method

03

Result

04

CAT

A photograph of medical professionals in a clinical setting. In the foreground, a doctor in a white coat and stethoscope is partially visible, overlaid by a green diagonal graphic. In the background, another medical professional in a white coat and face mask is holding up a large white sheet, possibly a patient's chart or a specimen. The scene is brightly lit, suggesting a window in the background.

Background

01

BACKGROUND

- 低血鈉是常見的電解質不平衡疾病，具有高死亡率
- 高張溶液治療→osmotic demyelination syndrome (OSD)
- 本院急診→slow continuous infusion(SCI)治療。
美、歐洲治療指引→rapid intermittent bolus (RIB)治療。
- 缺乏高證據文獻比較SCI及RIB之效果及安全性。

RIB優點:

1. 快速達到局部矯正
2. 較少發生過度矯正
3. 減少繁瑣劑量計算流程



P

中重度低血鈉患者($sNa \leq 125$ mmol/L)

I

RIB

中度：
噁心、頭痛、昏沉、虛弱、偏頭痛

C

SCI

重度：
嘔吐、木僵、癲癇、 $GCS \leq 8$

O

發生過度矯正機率、安全性及效果



A photograph of medical professionals in a clinical setting. In the foreground, a person in a white lab coat is writing on a clipboard. In the background, another person in a white lab coat and a surgical mask is holding up a large white sheet, possibly a patient's chart or a medical specimen. The scene is brightly lit, likely by natural light from a window. A green diagonal overlay covers the right side of the image, containing the text 'Method 02'.

Method

02

RCT



Randomization

1:1 allocation with
Block size 2.4.6.8



Blind

No



Sample Size

Type I error :0.05

Power :0.8

Attrition rate :15%

Number :89 (each group)



Inclusion

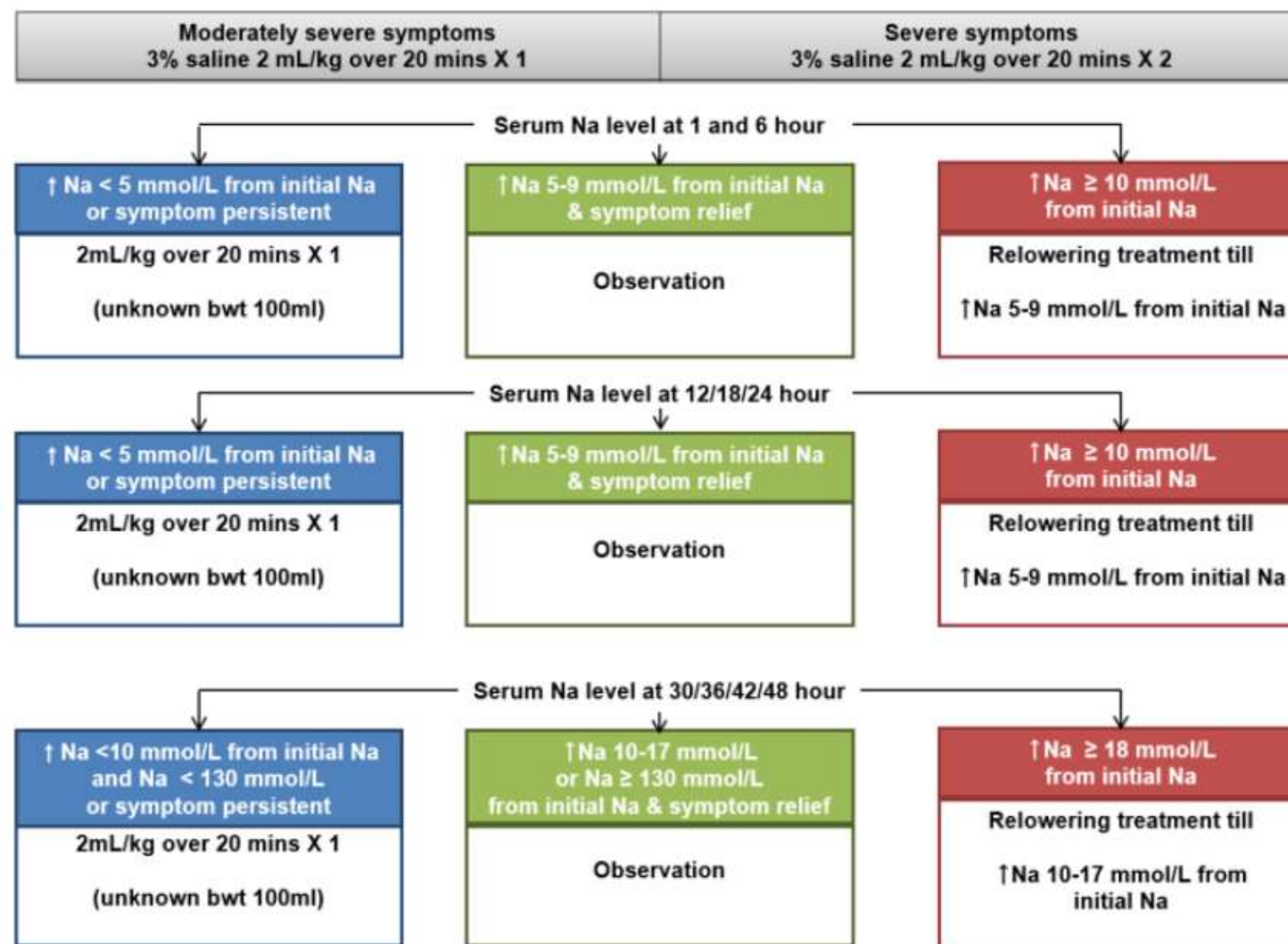
1. 18歲以上
2. 中重度低血鈉($sNa \leq 125\text{mmol/L}$)



Exclusion

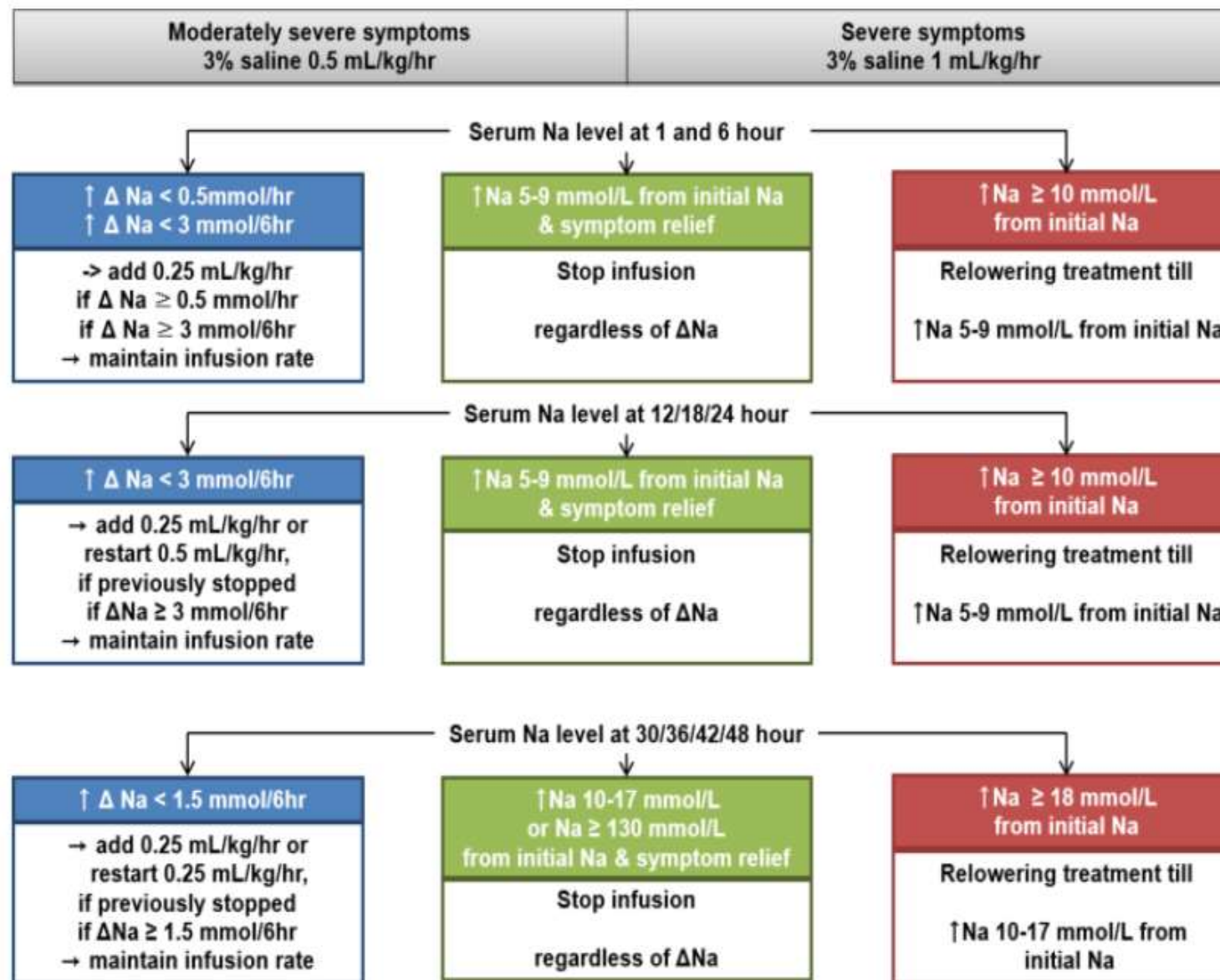
1. 多渴症、哺乳、無尿、低血壓、肝臟疾病、控制不佳糖尿病患者
2. 曾有心臟手術、AMI、VT、VF、ACS、腦部創傷、三個月內顱內壓升高病史者

eFigure 1. Treatment



A. Rapid intermittent correction with hypertonic saline in patients with moderately severe or severe symptomatic severe hyponatremia

eFigure 1. Treatment



B. Slow continuous correction with hypertonic saline in patients with moderately severe or severe symptomatic severe hyponatremia

A photograph of medical professionals in a clinical setting. In the foreground, a doctor in a white coat and stethoscope is partially visible, overlaid by a green diagonal graphic. In the background, another medical professional in a white coat and face mask is holding up a large white sheet, possibly a lab result or X-ray. The scene is brightly lit, likely from a window on the left.

Result

03

Figure 1. Flowchart of SALSA Study

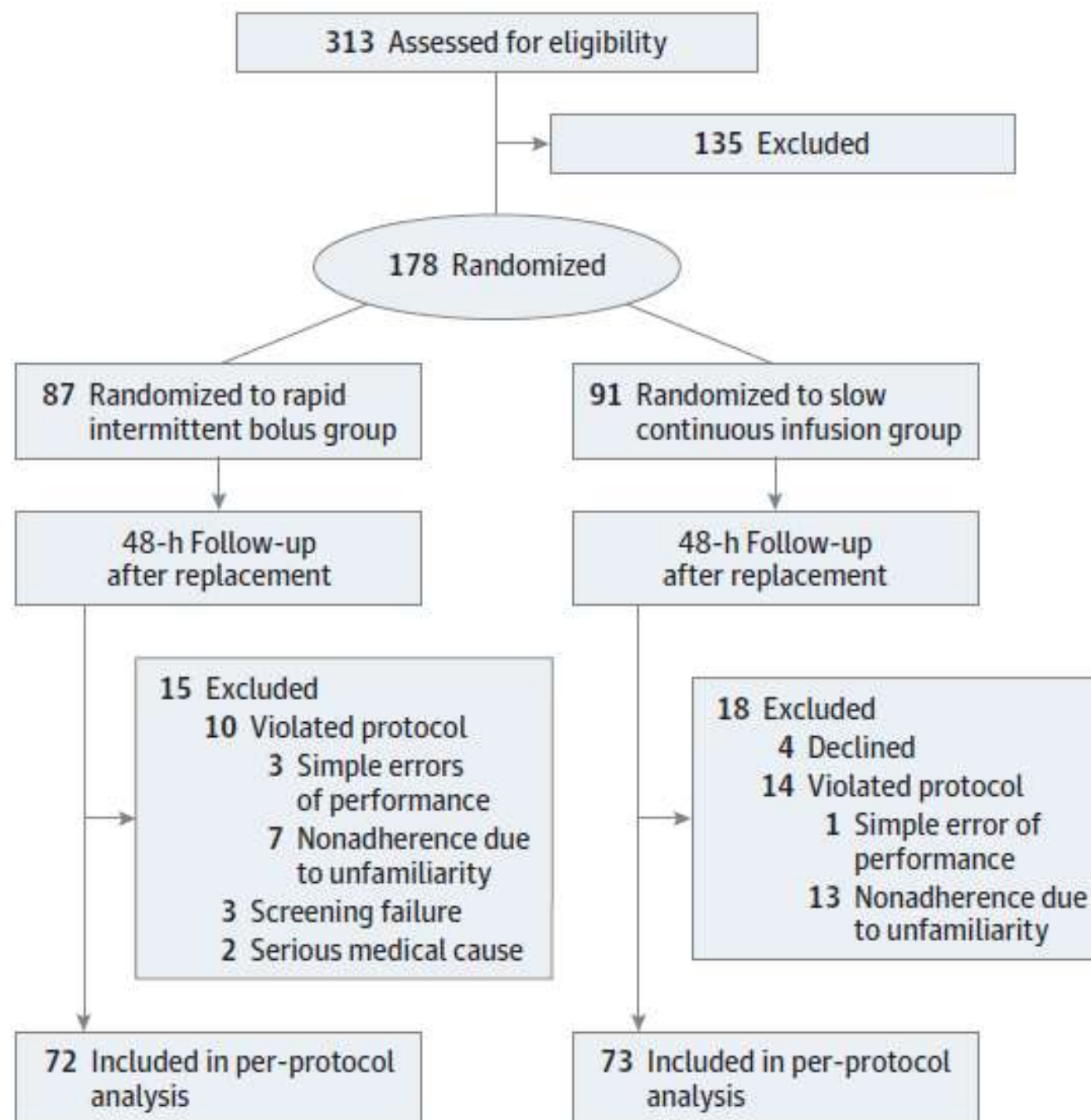


Table 1. Baseline Characteristics of Intention-to-Treat Population

Characteristics	Patients, No. (%)		P value
	Rapid intermittent bolus (n = 87)	Slow continuous infusion (n = 91)	
Demographics			
Male	42 (48.3)	38 (41.8)	.38
Age, mean (SD), y	72.9 (12.4)	73.2 (12.1)	.85
Weight, mean (SD), kg	56.6 (10.9)	57.5 (12.2)	.52
Body mass index, mean (SD)	22.2 (4.3)	22.9 (4.2)	.09
Causes of hyponatremia			
Thiazide use	21 (24.2)	32 (35.2)	.34
Decreased extracellular fluid due to nonrenal sodium loss	15 (17.2)	10 (11.0)	
Increased extracellular fluid	8 (9.2)	11 (12.1)	
Adrenal insufficiency	17 (19.5)	12 (13.2)	
Syndrome of inappropriate antidiuresis	26 (29.9)	26 (28.6)	
Comorbidity			
Diabetes mellitus	31 (35.6)	28 (30.8)	.53
Hypertension	62 (71.3)	61 (67.0)	.63
Table 1. Baseline Characteristics of Intention-to-Treat Population (continued)			
			.70
			.82
Characteristics	Rapid intermittent bolus (n = 87)	Slow continuous infusion (n = 91)	P value
Laboratory values			
			.94
Sodium, mean (SD), mmol/L	118.2 (5.0)	118.2 (5.0)	.94
Serum osmolality, mean (SD), mOsm/kg	251.8 (27.0)	250.3 (14.7)	.69
Creatinine, mean (SD), mg/dL	0.98 (0.8)	0.92 (0.9)	.23
Potassium, mean (SD), mmol/L	4.1 (0.8)	3.9 (0.7)	.10
Total carbon dioxide, mean (SD), mmol/L	22.7 (3.7)	23.7 (6.0)	.58
Urine, mean (SD)			
Osmolality, mOsm/kg	442.7 (170.7)	406.8 (156.9)	.19
Sodium, mmol/L	74.5 (50.7)	69.7 (48.1)	.63
Potassium, mmol/L	36.5 (23.9)	32.8 (21.1)	.22

Table 1. Baseline Characteristics of Intention-to-Treat Population (continued)

Characteristics	Patients, No. (%)		P value	.70
	Rapid intermittent bolus (n = 87)	Slow continuous infusion (n = 91)		.82
Laboratory values				>.99
Sodium, mean (SD), mmol/L	118.2 (5.0)	118.2 (5.0)	.94	.08
Serum osmolality, mean (SD), mOsm/kg	251.8 (27.0)	250.3 (14.7)	.69	.81
Creatinine, mean (SD), mg/dL	0.98 (0.8)	0.92 (0.9)	.23	.48
Potassium, mean (SD), mmol/L	4.1 (0.8)	3.9 (0.7)	.10	>.99
Total carbon dioxide, mean (SD), mmol/L	22.7 (3.7)	23.7 (6.0)	.58	.66
Urine, mean (SD)				
Osmolality, mOsm/kg	442.7 (170.7)	406.8 (156.9)	.19	
Sodium, mmol/L	74.5 (50.7)	69.7 (48.1)	.63	
Potassium, mmol/L	36.5 (23.9)	32.8 (21.1)	.22	

Hyponatremic symptom			
Moderate	66 (75.9)	68 (74.7)	.86
Severe	21 (24.1)	23 (25.3)	
Nausea	29 (33.3)	27 (29.7)	.60
Headache	7 (8.0)	4 (4.4)	.31
Dizziness	3 (3.4)	7 (7.7)	.33
General weakness	39 (44.8)	44 (48.4)	.64
Drowsiness	6 (6.9)	2 (2.2)	.16
Vomiting	18 (20.7)	20 (22.0)	.83
Stupor	2 (2.3)	3 (3.3)	>.99
Seizure	2 (2.3)	0	.24
Bone fracture	1 (1.1)	2 (2.2)	>.99
Fall	1 (1.1)	1 (1.1)	>.99
Site to initiate hypertonic saline			
Emergency department	67 (77.0)	64 (70.3)	.41
General ward	20 (23.0)	26 (28.6)	
Intensive care unit	0	1 (1.1)	
IV route			
Peripheral	85 (97.7)	90 (98.9)	.59
Central	1 (1.1)	0	
Mixed	1 (1.1)	1 (1.1)	
Blood pressure, mean (SD), mmHg			
Systolic	141.6 (25.6)	136.9 (42.9)	.20
Diastolic	75.6 (12.3)	75.7 (15.2)	.97
Glasgow Coma Scale score, mean (SD)			
Pretreatment (n = 146)	14.3 (1.5)	14.0 (2.5)	.64

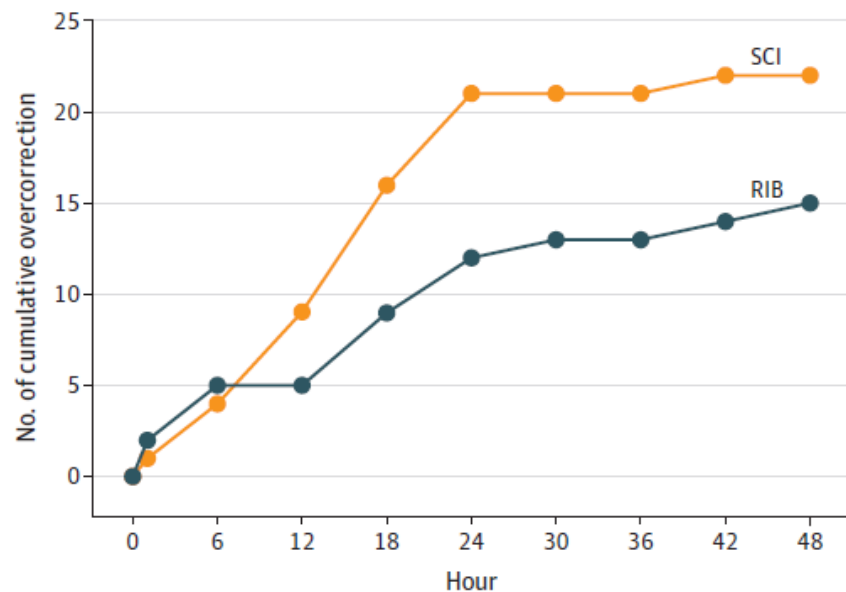
RESULT

Table 2. Outcomes and Progressions in Intention-to-Treat Population

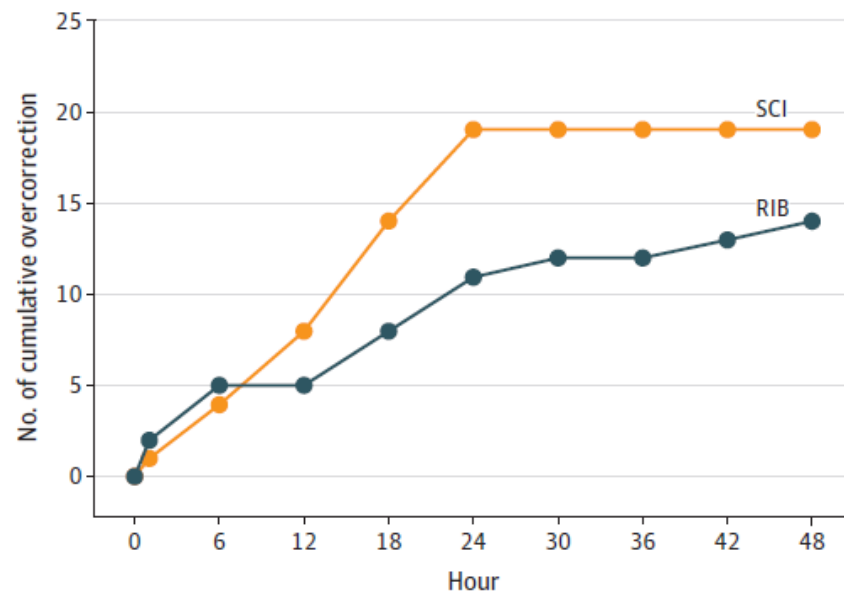
					Patients, No. (%)					
Variable					Rapid intermittent bolus (n = 87)	Slow continuous infusion (n = 91)	Absolute difference (95% CI)	P value		
Dropout					15 (17.2)	18 (19.8)	NA	.66		
Post hoc analysis (efficacy as incidence of target correction rate by the time frame)										
sNa 5-9 mmol/L					15 (17.2)	22 (24.2)	−6.9 (−18.8 to 4.9) ^a	.26		
Within 1 h	28 (32.2)	16 (17.6)	14.6 (2 to 27.2) ^a	.02						
Within 6 h	50 (57.5)	54 (59.3)	−1.9 (−16.4 to 12.6) ^a	.80						
Within 24 h	78 (89.7)	79 (86.8)	2.8 (−6.6 to 12.3) ^a	.56						
sNa 10-17 mmol/L or ≥130 mmol/L within 48 h	60 (69)	67 (73.6)	−4.7 (−17.9 to 8.6) ^a	.49	11 (13.1)	15 (16.9)	−3.8 (−14.4 to 6.8) ^a	.49		
Fluid type within 24 h except for saline, 3%					7 (8.8)	5 (6.5)	2.3 (−6.0 to 10.5) ^a	.60		
Isotonics only	31 (35.6)	28 (30.8)	NA	.40	an (SD), h	8.2 (8.7)	8.6 (6.9)	−0.4 (−2.7 to 2.0) ^b	.21	
Hypotonics only	52 (59.8)	62 (68.1)	NA			57 (65.5)	60 (65.9)	−0.4 (−14.4 to 13.5) ^a	.85	
Isotonics and hypotonics	3 (3.4)	1 (1.1)	NA		h (n = 96)	23.6 (12.4)	22.3 (13.4)	1.3 (−3.9 to 6.6) ^b	.56	
None	1 (1.1)	0	NA			11.3 (18.6)	7.5 (6.5)	3.8 (−0.3 to 7.9) ^b	.50	
Fluid amount within 24 h except for saline, 3%, mean (SD), mL	1563 (1160)	1641 (2165)	NA	.76		79 (90.8)	68 (74.7)	16.1 (5.3 to 26.9) ^a	.005	
Fluid type within 24-48 h except for saline, 3%							3.4 (1.8)	1.8 (1.7)	1.6 (1.0 to 2.3) ^b	<.001
Isotonics only	28 (32.2)	18 (19.8)	NA	.15	drome	0	0	0	NA	
Hypotonics only	23 (26.4)	26 (28.6)	NA			36 (41.4)	52 (57.1)	−15.8 (−30.3 to −1.3) ^a	.04	
Isotonics and hypotonics	22 (25.3)	22 (24.2)	NA							
None	14 (16.1)	25 (27.5)	NA			14.6 (1.2)	14.1 (2.4)	0.5 (−0.1 to 1.1) ^b	.50	
Fluid amount within 24-48 h except for saline, 3%, mean (SD), mL	1077 (895)	1152 (884)	NA	.54		14.6 (1.2)	14.2 (2.2)	0.4 (−0.2 to 1.1) ^b	.74	
Oral intake during 48 h, mean (SD), mL	1852 (1298)	1961 (1262)	NA	.40						
Cumulative amount of hypertonic saline, 3%, mean (SD), mL										
Within 1 h	220.4 (76.3)	38.6 (29.2)	NA	<.001						
Within 6 h	273.9 (102.3)	210.4 (119.2)	NA	<.001						
Within 24 h	362.6 (183.3)	440.6 (308.4)	NA	.22						
Within 48 h (total amount)	535.4 (322.1)	572.8 (371.8)	NA	.57						
Urine volume during 48 h, mean (SD), mL	3611 (2763)	4108 (2889)	NA	.27						
Neuroimage after correction of hyponatremia	5 (5.7)	10 (11.0)	NA	.21						
Phlebitis	0	2 (2.2)	NA	.50						
Mortality										
During admission	4 (4.6)	1 (1.1)	NA	.20						
At 30 d	3 (3.4)	1 (1.1)	NA	.36						

Figure 2. Cumulative Overcorrection and Relowering Treatment

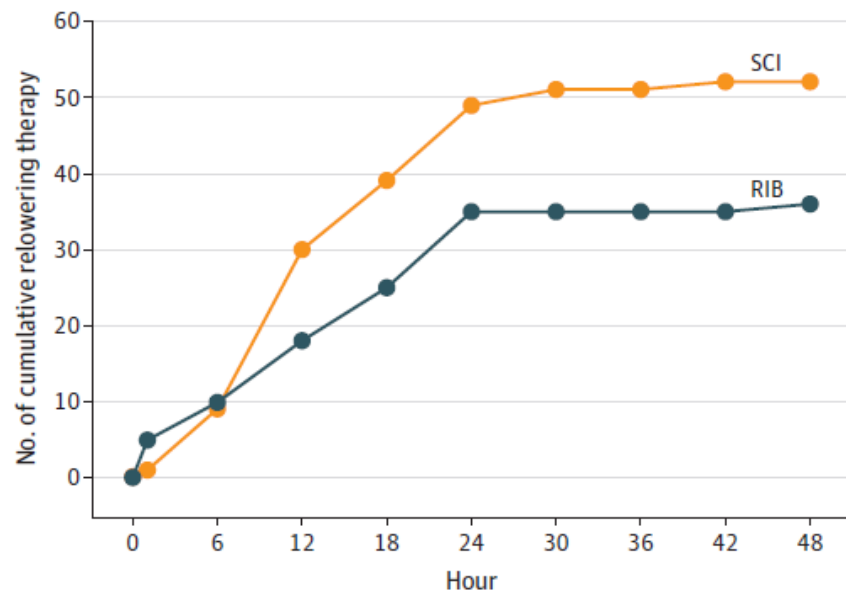
A Cumulative overcorrection in intention-to-treat analysis



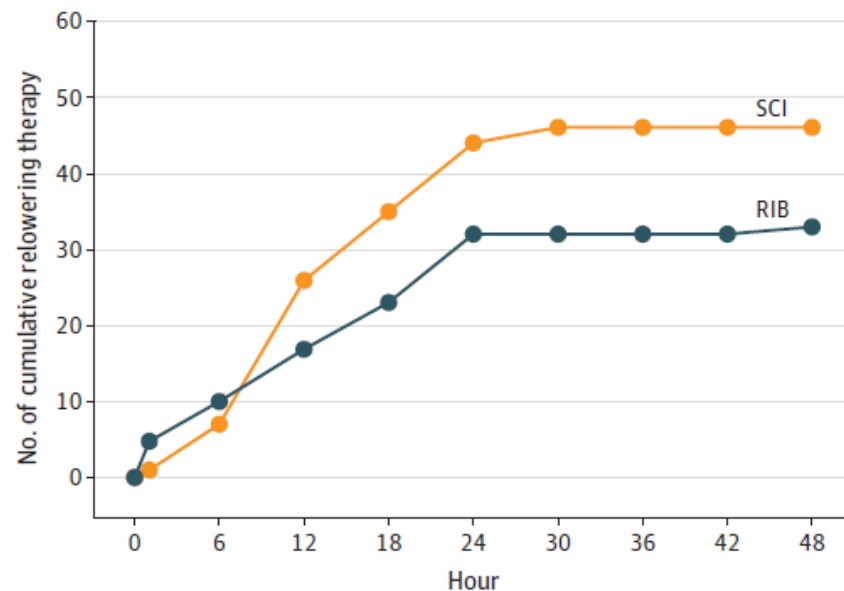
B Cumulative overcorrection in per-protocol analysis



C Cumulative relowering therapy in intention-to-treat analysis



D Cumulative relowering therapy in per-protocol analysis



A background image showing medical professionals in a clinical setting. In the foreground, a person in a white lab coat is writing on a clipboard. In the background, another person in a white lab coat and a surgical mask is holding up a large sheet of paper, possibly a medical chart or a diagnostic image. A green diagonal overlay covers the right side of the image, containing the text 'Critical Appraisal Tool' and the number '04'.

Critical Appraisal Tool

04

CASP 隨機對照試驗檢核表

(A)研究結果可信嗎?

篩選問題

1. 研究問題是否清楚且聚焦?



是

☐不明確☐否

考量點：一個聚焦的問題包括下列項目：

- 研究群體 中重度低血鈉($sNa \leq 125\text{mmol/L}$)患者
- 介入措施 RIB
- 比較措施 SCI
- 研究的結果 發生過度矯正機率、效果及安全性

2. 受試者是否確實被隨機分派到不同組別?



是

☐不明確☐否

考量點：

- 如何進行隨機分派?
- 研究者是否被隱匿分組訊息?

By an independent statistician, the randomization sequence was created using a computer-generated list of random numbers and was stratified by centers with a 1:1 allocation using random block sizes of 2, 4, 6, and 8. Study coordinators who were independent persons and responsible for screening and enrolling the participants allocated each patient to a group based on the randomized sequence. The allo-

本篇文獻是否值得繼續閱讀?



詳細問題

3. 受試者、健康相關工作人員及研究人員是否盲化?

☐是☐不明確☐否

考量點：

- 健康工作人員，如：醫師、護理師等
- 研究人員，特別指結果評估者

vere or severe) (Figure 1). Whereas patients and physicians were aware of the intervention received, the analysts were blinded to the intervention.

4. 各組研究對象在一開始進入試驗時的基本特性是否相似？ ☒ 是 ☐ 不明確 ☐ 否

Baseline 兩組間無達統計顯著差異

考量點：審視其他可能的影響因素，例如：年齡、性別、社會階層等，這些也被稱為基準值的特質

5. 除了實驗的介入措施之外，各組的所有對待是否相同？ ☒ 是 ☐ 不明確 ☐ 否

6. 是否所有進入試驗的受試者在研究結論當中均被適當的考量過？ ☒ 是 ☐ 不明確 ☐ 否

考量點：

- 試驗有提早結束嗎？
- 受試者是否一經隨機分派，均納入最後的分析？

統計結果皆以ITT進行分析

hours).^{3,23} The treatment goal, relowering treatment strategy, and cause-specific treatment of hyponatremia were equally applied to each group.

(B)研究結果為何？

7. 介入措施的效果有多大？

考量點：

- 測量那些結果？
- 主要結果是否有清楚界定？
- 每個研究結果有哪些發現？
- 是否有證據顯示有選擇性報告研究結果的情形？

- RIB發生過度矯正的人數比例與SCI並無顯著差異
- RIB需要額外治療的人數比例與治療項目多餘SCI
- RIB發生relowering treatment人數比較少於SCI
- RIB在一小時內達治療目標人數比例多於SCI
- RIB在一、六小時內累積的3%量多餘SCI

8. 介入措施的效果估計有多精確？

考量點：

- 信賴區間為何？
- 是否具有統計顯著性？

此研究主要結果雖沒有達顯著差異，但回到研究問題，此結果表示RIB與SCI並沒有發生OSD或過度矯正的差異

(C)研究結果對於當地病人有幫助嗎?

9. 研究結果是否可以應用在你的情境當中(或當地族群)?  ☒是 ☐不明確 ☐否

考量點：

- 你有理由相信你照顧的對象跟研究的受試者不同嗎?
- 如果是的話，在哪些方面不同?

10. 是否臨床上重要的結果均已被考量?  ☒是 ☐不明確 ☐否

考量點：

- 你希望看到其他有關結果的訊息嗎?
- 這篇試驗的需求有被清楚描述嗎?

OSD、Phlebitis、Mortality

11. 介入措施所帶來的效益是否值得付出傷害及成本的代  ☒是 ☐不明確 ☐否

價?

考量點：

- 即使這一點文章內沒有提到，你的看法呢?

RIB可以在短時間內達到治療目標，且發生relowering treatment的人數比例也較少於SCI，雖然本研究沒有提及到一小時後病人之症狀改善，但在本院急診曾使用RIB於低血鈉患者，在bonus後病人迅速緩解期頭暈、噁心等不適症狀。

ADD THE TITLE WORDS



同意：10票

仍有疑慮：20票

不同意：0票

QUESTION TIME

使用3% Saline治療中重度低血鈉患者時，你贊成使用rapid intermittent bolus (RIB) 方法來替代 slow continuous infusion(SCI)方法嗎？





THANK YOU

MEDICAL WORK REPORT

報告者：
鍾家偉護理師