NaHCO₃ Plus Hydration Decreases Acute Kidney Injury After EVAR: Based On A Pilot RCT (The HYDRA-P Trial) Comparing It To Hydration Alone: Why Is It Different From Other Negative NaHCO₃ RCTs

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On behalf of the HYDRA-P TRIAL INVESTIGATORS

Implications of AKI in EVAR
Series of 950 EVARs with long-term FU

Incidence: 20 - 25%
Saratzis et al. EJVES 2016
Saratzis et al. CJASN 2015

AKI after EVAR associated with:
Short-term survival
Long-term survival
Long-term cardiovascular events
£4.2 million extra treatment costs
5,180 bed days

FEN-EVAR 2010
THORACO-ABDOMINAL BRANCH 2016
FEN-TEVAR 2018
Incidence of AKI following complex EVAR ranges from ~ 22.7% - 32%

SODIUM BICARBONATE TO PREVENT CONTRAST INDUCED NEPHROPATHY (CIN)

Mechanisms of Action
- Reduces renal tubular ischaemia caused by Contrast (Endothein-1)
- Alkalination of urine reduces free radical formation

No high-quality evidence for AKI prevention in EVAR
NO EVAR PATIENTS

SERUM HCO₃ AND URINE pH NOT REPORTED

Another Meta-Analysis

COMPARING HCO₃ WITH NaCl. NO COMBINATIONS

LOW eGFR

Bolus Upfront NaHCO₃ is Better Than Infusion

Amount of NaHCO₃ Matters

Summary of the strength of evidence: IV sodium bicarbonate versus IV saline

Contrast-induced Nephropathy
Comparative Effectiveness of Preventive Measures 2016
Comparative Effectiveness Reviews, No. 156
Investigators: Rathan M Subramaniam, MD, PhD, Renee F Wilson, MS, Sharon Turban, MD, MHS, Catalina Suarez-Cuervo, MD, Allen Zhang, BS, Cheryl Sherrod, MD, MPH, Jonathan Aboagye, MD, MPH, John Eng, MD, Michael J Choi, MD, Seven.

Another Meta-Analysis

Bin Zhang et al. BMJ Open 2015;5:e006989

COMPARING HCO₃ WITH NaCl. NO COMBINATIONS

LOW eGFR 15-45/ml/min

Bolus Upfront NaHCO₃ is Better Than Infusion

Amount of NaHCO₃ Matters

Sodium Bicarbonate for the Prevention of Contrast-induced Nephropathy: The Efficacy of High Concentration Solution
Nozomu Tamai, MD
Shigenori Ito, MD
Kosuke Nakasuka, MD
Kotaro Morimoto, MD
Kazuyuki Miyata, MD
Masahiko Inomata, MD
Takayuki Yoshida, MD
Shin Suzuki, MD
Yoshimasa Murakami, MD
Koichi Sato, MD

J INVASIVE CARDIOL 2012;24(9):439-442
USE OF HIGH DOSE RAPID INFUSION OF SODIUM BICARBONATE COMBINED WITH HYDRATION WOULD REDUCE RISK OF AKI MORE THAN USE OF AGGRESSIVE HYDRATION ALONE IN EVAR PATIENTS ONLY WITH ANY BASELINE RENAL FUNCTION

AIM:
1. Recruitment
2. Safety and efficacy of novel AKI prevention strategy
3. Help design the definitive RCT

STUDY INTERVENTIONS

STANDARD HYDRATION
HARTMANN’S SOLUTION
10ml/kg/hr at induction & 2ml/kg/hr for 12 hours
AND
BOLUS HIGH DOSE SODIUM BICARBONATE
8.4% (1mmol/ml) x1mmol/Kg OVER 1 HOUR at induction

KEEP MAP WITHIN 80% OF BASELINE 90% OF THE TIME (INTRA- AND POST-OP)

SURVEY OF ANAESTHETISTS IN UK

- 113 responders (vascular anaesthetists) across the country
- Asked on: hydration regime, HCO₃, NAC, AKI
- Fluids: 86% prefer “Hartmann’s”
- Aggressive hydration: 86% @ 10ml/kg/hour
- All agree HCO₃ is safe
- 73% believe AKI is important in EVAR
- Would adopt if AKI rate drops to 5% with HCO₃
- 92% prefer bolus HCO₃

PATIENT POPULATION

INCLUSION CRITERIA
Any patient undergoing EVAR for infra-renal AAA

EXCLUSION CRITERIA
- Cardiac failure NYHA stage 4
- Allergy to sodium bicarbonate
- Contrast <48 hours before EVAR
- Metabolic/Respiratory Alkalosis
- SP-200mmHg
- ACE Inhibitors or NSAIDs within 48 hours
- Patient on Dialysis

OUTCOME MEASURES

PRIMARY
- RECRUITMENT (AIM OF 50% OF SCREENED PATIENTS)

SECONDARY
- AKI DEFINED BY NICE (Minimum Stage 1 KDIGO and AKIN)
  - SC rise of >26 micromol/l within 48 hrs of surgery
  - >50% rise in SCr
  - Fall of Urine output <0.5ml/kg/hr for more than 6 consecutive hours
- ADEQUACY OF HYDRATION
- ADEQUACY OF ALKANISATION
- ADVERSE EVENTS AND COMPLICATIONS
Thrombus (>50%) 4 (14.3%) 3 (10.0%) 7 (12.1%)
Significant proximal neck length
Proximal aneurysmal neck
Maximal diameter 6.2 (5.9, 6.6) (5.6, 8.9) 6.7 (5.8, 8.1) (3.8, 9.7) 6.3 (5.8, 6.9) (3.8, 9.7)

Abdominal Aortic Aneurysm
Sex
Age 75.5 (70, 80) (57, 89) 74.5 (73, 80) (66, 89) 75 (71, 80) (57, 89)

DEMOGRAPHICS AND AAA MORPHOLOGY
Demographics Standard Hydration (n = 28) Standard Hydration + Bolus Bicarbonate (n = 30) Total (N = 58)
Age
Male 25 (89.3%) 27 (90.0%) 52 (89.7%)
Female 3 (10.7%) 3 (10.0%) 6 (10.3%)

CARDIOVASCULAR AND RENAL INJURY RISK
Risk Factors Standard Hydration (n = 28) Standard Hydration + Bolus Bicarbonate (n = 30) Total (N = 58)

RECRUITMENT
HOW MANY STARTED WITH CKD?
CKD STAGE 3 OR WORSE (eGFR<60)
Standard Hydration (n=28) Standard Hydration + Bolus Bicarbonate (n=30)

2 (17%) 4 (13%)
OUTCOME

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Number (%) or mean (SD)</th>
<th>Standard hydration (n=30)</th>
<th>Standard hydration + bolus bicarbonate (n=28)</th>
<th>Effect size (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Kidney Injury (AKI)*</td>
<td>10 (33.3) 2 (7.1)</td>
<td>0.21 (0.05 to 0.89)</td>
<td>Adequacy of standardized hydration regime*</td>
<td>16 (53.3) 7 (25.0)</td>
</tr>
<tr>
<td>Serum bicarbonate (difference)*</td>
<td>-1.5 (1.8) 0.6 (1.8)</td>
<td>2.1 (1.1 to 3.0)</td>
<td>At start of procedure</td>
<td>24.3 (1.6) 24.6 (1.5)</td>
</tr>
<tr>
<td>PH (difference)*</td>
<td>0.0 (0.1) 0.0 (0.5)</td>
<td>0.0 (0.0 to 0.1)</td>
<td>At end of procedure</td>
<td>7.4 (0.7) 7.6 (0.4)</td>
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PERIOPERATIVE DETAILS

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<td>Median (IQR) duration of EVAR (min)</td>
<td>154 (130–185) 150 (120–180)</td>
<td>5 (−16 to 30)</td>
<td>154 (130–185) 150 (120–180)</td>
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<td>Median (IQR) duration of post-operative inotropic support</td>
<td>12 (8–17) 10 (1–16)</td>
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SUMMARY

**PREVIOUS RCTS OF NaHCO3**

- Have compared NaHCO3 with saline
- Lack of combination studies
- Involve mostly coronary and peripheral procedures, NOT EVAR
- Mostly include only patients with low eGFR
- Novel regime using a high dose bolus of sodium bicarbonate combined with standard hydration shows promise in reducing AKI after EVAR
- This is a EVAR specific pilot RCT
- Unlike previous trials using bicarbonate, 90% of the patients had normal/mildly impaired renal function
- Unlike previous trials, there was more aggressive management of MAP

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