Инфузионная терапия и гидроксиэтилкрахмалы: за и против

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План

- Причины неадекватной стратегии ИТТ
- Принципы восполнения ОЦК и гемодинамическая поддержка
- Рекомендации по тактике ИТТ
- ГЭК: за и против

- **Резюме**

Основные «причины» острой кровопотери (гиповолемии)

- Кровотечения из верхних отделов желудочно-кишечного тракта (ЖКТ), в том числе из варикозно расширенных вен пищевода
- Злокачественные и доброкачественные опухоли
- Расслаивающиеся аневризмы аорты и магистральных сосудов
- Наследственные заболевания крови
- Острый синдром диссеминированного внутрисосудистого свертывания крови
- Сепсис
- Травмы и ранения, в том числе травматические повреждения паренхиматозных органов

Проблемы неадекватной стратегии

- Неточная оценка объема кровопотери и (или) гиповолемии
- Несовременное начало ИТТ и ее мониторинга
- Отсутствие контроля за изменениями в системе гемостаза

Величина кровопотери должна оцениваться вместе с ее темпом!!!
+ преморбидный фон, вид патологии

Проблемы восполнения ОЦК и гемодинамической поддержки

- Гемодинамическая поддержка = ИТТ + вазоактивные препараты
- Кристаллоиды или коллоиды?
- Применение альбумина?
- Важно: соотношение 2:1-6:1, альбумин – менее 27 г/л
  - Объем инфузионной терапии?
- Важно: цель - АДср ≥ 65 мм рт.ст., ЦВД=7-8 мм рт.ст., диурез более 0,5 мл/кг/ч, SaO_2=95-98%
- Уровень гемоглобина? - (70-90 г/л, Ht ≥30%)
- Тромбоцитарная масса? - (менее $30x10^9$/л или менее $50x10^9$/л перед оперативным вмешательством
- Криопреципитат? - (при уровне фибриногена менее 1 г/л)

Тактика в предоперационный период (1)

- Цель: осуществление наиболее эффективных мер по возмещению кровопотери и (или) гиповолемии, улучшению центрального и периферического кровообращения, газообмена в легких и нормализации кислотно-основного состояния
- Сбор анамнеза в максимально короткие сроки
- Оценка сознания, определить АД, ЧСС, SaO_2 (по возможности), цвет кожных покровов (каждые 5 мин), оценка по SAPSII
- Респираторная поддержка (увлажненный кислород, ИВЛ)
- Надежный венозный доступ и оценка ЦВД
- Лабораторные исследования
- Почасовой диурез

Тактика в предоперационный период (2)

- Начать ИТТ (в зависимости от выраженности шока):
- Шок 1 степени - кристаллоиды – операционная
- Шок 2 степени и более – кристаллоиды (не менее 10 мл/кг) – операционная

- В процессе транспортировки – продолжение инфузионной терапии

Тактика действий во время операции (1)

- Дополнительные венозные доступы (при необходимости)
- Мониторинг за жизненно важными функциями организма
- Продолжение инфузионной терапии под контролем АД, ЧСС, ЦВД (при продолжающемся кровотечения, по возможности, необходимо добиться повышения уровня АДс до 90 мм рт.ст. и ЦВД до положительной величины) – **до обеспечения хирургического гемостаза преимущественно кристаллоиды**

Тактика действий во время операции (2)

- При кровопотере более 30% ОЦК объем переливания кристаллоидов может достигать 15 мл/кг, ГЭК – 10 мл/кг, СЗП – 10 мл/кг и эритроцитарной массы – 7-10 мл/кг.

- При объеме кровопотери, составляющей 50% ОЦК, целесообразно использовать кристаллоиды в дозе до 20 мл/кг, препараты ГЭК в дозе до 20 мл/кг, СЗП в дозе до 15-20 мл/кг и эритроцитарной массы в дозе до 10 мл/кг.

- Если объем кровопотери составляет 100% ОЦК, то необходимо применять кристаллоиды в дозе до 25-30 мл/кг, препараты ГЭК в дозе до 20 мл/кг, СЗП в дозе до 15-20 мл/кг и эритроцитарной массы в дозе до 10 мл/кг.

Тактика действий во время операции (3)

- **Важно:** темп инфузии должен опережать темп кровопотери на 700-1000 мл
- Критерии адекватности гемодинамической поддержки: АДср ≥ 65 мм рт.ст., ЦВД = 7-8 мм рт.ст., диурез более 0,5 мл/кг/ч, SaO_2= 95-98%.

Тактика послеоперационного периода (1)

- Предусматривает не только ИТТ и продолжение респираторной поддержки!!!

- Эффект терапии, проведенной до операции, в процессе оперативного вмешательства и анестезии (уровень АД, ЧСС, ЦВД, цвет кожи, SaO_2, почасовой диурез).
- Оценка тяжести состояния больного по SAPSII; повторно Hb, Ht, тромбоцитов, лейкоцитов, АВСК, развернутый гемостаз (ПТИ, АЧТВ, ОФТ, фибриноген, Д-димеры, тромбоциты и их агрегация).
- ИТТ = кристаллоиды, ГЭК, СЗП и эритроцитарную массу. Соотношение кристаллоидов и коллоидов обычно 2:1 - 6:1 без учета СЗП и эритроцитарной массы.

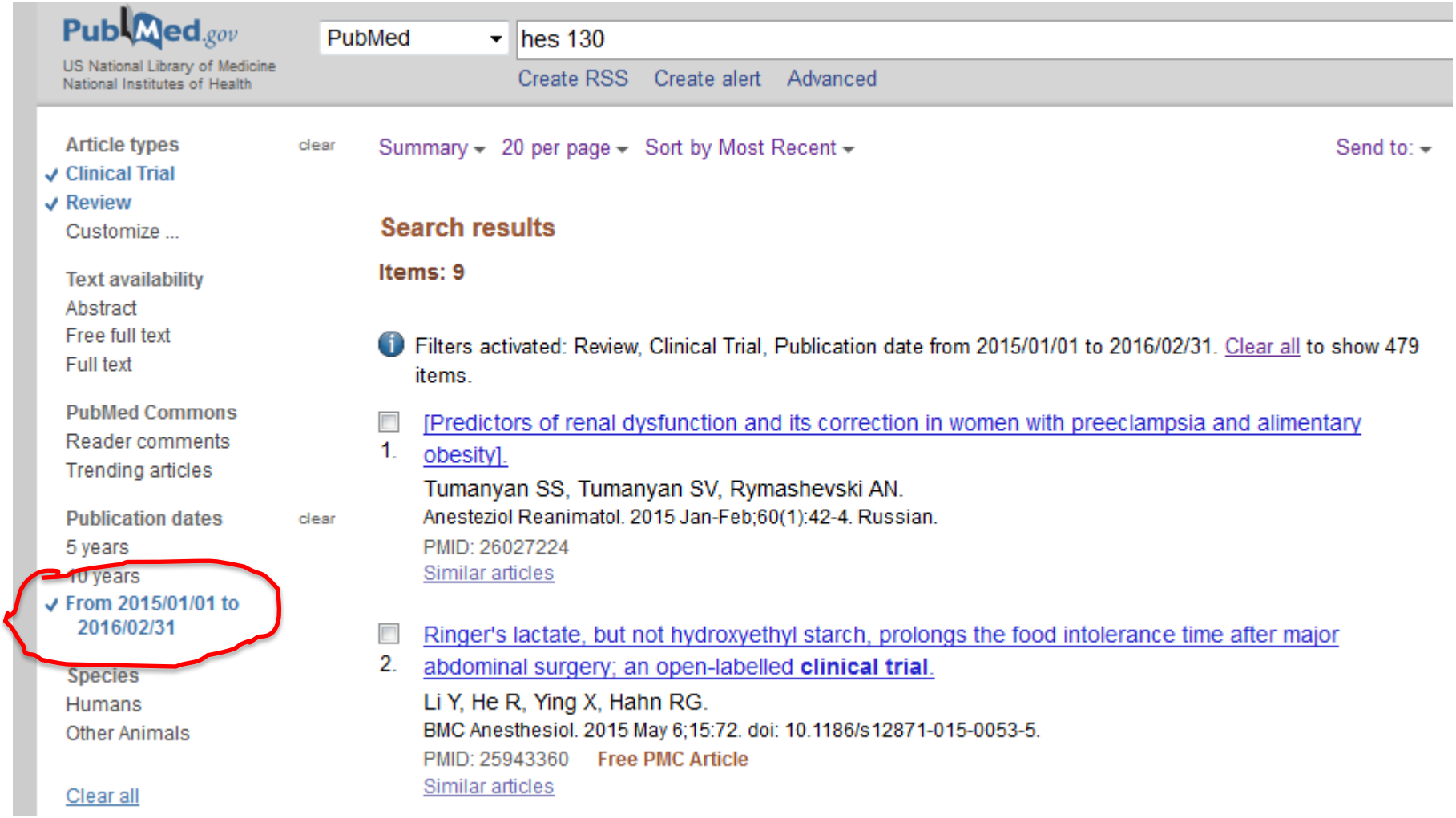
Тактика послеоперационного периода (2)

- Общий объем инфузионно-трансфузионной терапии за сутки варьирует в пределах 35-40-45 мл/кг
- Критическим значением гемоглобина, при котором необходима гемотрансфузия, является его уровень, равный 65-70 г/л - отмытые эритроциты
- СЗП = дефицит факторов свертывания крови (ежедневный контроль : ПТИ, АЧТВ, ОФТ, фибриноген, тромбоциты) Коагулопатическое кровотечение или недостаточно СЗП - криопреципитат
- Альбумин - снижение общего белка менее 45 г/л и снижение уровня альбуминов менее 27 г/л.

Тактика послеоперационного периода (3)

- При сохранении на фоне ИТТ артериальной гипотонии (АДср <65 мм рт.ст.) - продолжить (или начать) титрование вазоактивных препаратов
- **Цель:** АДср = 70-100 мм рт.ст., ЦВД = 7-12 мм рт.ст., диурез – более 0,5 мл/кг/ч
- Через 6-8 ч после операции при наличии надежного хирургического гемостаза, отсутствии выраженных расстройств в системе гемокоагуляции, для снижения тромбинемии и профилактики тромбоэмболических осложнений необходимо назначить нефракционированные гепарины в стандартной дозировке

ГЭК: за и против



Острая почечная недостаточность

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SPECIAL ARTICLE

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CONTRA: Hydroxyethyl starch solutions are unsafe in critically ill patients

Abstract *Purpose:* To describe the risk–benefit profile of hydroxyethyl starch (HES).
Methods: Narrative review.
Results: (1) Efficacy: no single clinical study or systemic review has shown that administration of any HES solution confers a clinically relevant benefit compared to crystalloids in critically ill patients or surgical patients in need of volume replacement. Contrary to beliefs expecting a ratio of 4:1 or more for crystalloid to colloid volume need, recent studies of goal-directed resuscitation observed much lower ratios of between 1 and 1.6. (2) Safety: HES administration is associated with coagulopathy, nephrotoxicity, pruritus and increased long-term mortality. Clinical studies claiming that modern HES 130/0.4 is safe have serious methodological drawbacks and do not adequately address the safety concerns. *Conclusions:* Given the complete lack of superiority in clinical utility studies and the wide spectrum of severe side effects, the use of HES in the ICU should be stopped. The belief that four times as much crystalloid as colloid fluid volume is needed for successful resuscitation is being seriously questioned.

Keywords Colloids · Crystalloids · Hydroxyethyl starch · Efficacy · Safety · Critically ill

Safety of "new" HES 130/0.4

There are claims that the latest HES solution (HES 130/0.4) is safe in regard to coagulation and renal adverse effects. However, adverse effects may be an inherent side effect of the compound, and there are indications that the latest HES 130/0.4 may not be an exception to the rule. In patients with severe head injury who received HES 130/0.4 and HES 200/0.5 in high cumulative doses, cerebrovascular bleeding events were similar in both groups [34]. In cardiac surgical patients, HES 130/0.4 and HES 200/0.5 at maximum daily doses were associated with similar incidences of postoperative bleeding [35]. A recent pooled analysis derived that post-surgical blood loss is significantly less after HES 130/0.4 than after HES 200/0.5. However, the derived effects are marginal, and in the largest group of cardiac surgery patients, there was no difference in estimated blood loss, calculated red blood cell (RBC) loss, or transfusion of RBC, platelets or fresh frozen plasma [36].

HES 130/0.4 also raised sensitive markers of renal impairment [37] and led to a progressive increase of plasma accumulation in relation to pre-existing renal impairment [38]. In a retrospective, matched pair analysis of kidney transplants, HES 130/0.4 administration was associated with a similar incidence of delayed graft function as HES 200/0.62 [39].

In rats, HES 130/0.4 also led to long-term storage in organs and carcass, although in several-fold less amounts than HES 200/0.5. However, accumulation in the kidney occurred in similar amounts [40]. HES 130/0.4 is also associated with pruritus in healthy volunteers with a duration of 8–16 days [41] and with more frequent and longer lasting itching than HES 200/0.5 after hemodilution therapy for sudden hearing loss [11].

Claims that new HES 130/0.4 is devoid of severe side effects are based on clinical studies that have severe limitations on closer scrutiny. Our literature search yielded 26 clinical studies with HES 130/0.4 administration in surgery or sepsis. These were mostly volume efficacy studies with clinically irrelevant endpoints such as volume need, ex-vivo clotting parameters, postoperative creatinine clearance or interleukin-6 response. Twenty-two studies reported observation periods of 48 h or less. Nineteen studies used unsuitable comparators such as other HES solutions or gelatin. Only seven studies compared HES to albumin or crystalloid [42–48] with a mean of 39.3 study patients and a mean study period of 1.4 days. Six of these reported cumulative doses with a mean of 44.2 ml/kg, which is less than the recommended maximum dose for 1 day (50 ml/kg). Similar limitations also apply to the clinical studies that provided the data for approval of HES 130/0.4 in the US [11]. Data are derived from 21 mainly non-inferiority studies in low risk patients or volunteers with a mean study period of 2 days, mean cumulative dose of 41.9 ml/kg, and mostly other HES and gelatin as comparator fluids. There is no evidence on the safety of HES 130/0.4 in severe sepsis or intensive care patients with pre-existing renal impairment or risk for renal dysfunction. Hence, none of these studies are able to dispel concern about the safety of HES in critically ill patients.

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ORIGINAL

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Effects of a predominantly hydroxyethyl starch (HES)-based and a predominantly non HES-based fluid therapy on renal function in surgical ICU patients

Abstract *Purpose:* To compare the effects of predominantly hydroxyethyl starch (HES 6% 130/0.4)-based with predominantly gelatin 4%-based fluid therapy on renal function in surgical intensive care unit (ICU) patients. *Methods:* Before–after, retrospective, study of surgical ICU patients. All patients admitted from January to June 2005 formed the HES group, with HES 130/0.4 as the standard colloid of choice. All patients admitted from January to June 2006 formed the GEL group, with gelatin 4% as the primary colloid. Acute renal failure (ARF) was defined as new need for renal replacement therapy (RRT) or at least a two-fold increase in baseline creatinine. *Results:* There were 1383 patients in the HES group and 1528 in the GEL group; 118 and 87, in each group respectively, had severe sepsis. The incidence of ARF and ICU and hospital mortality rates were similar in the two groups. In a post-hoc multivariable analysis, cumulative doses >33 ml/kg of either HES (OR = 1.85, 95% CI: 1.01–3.41, $p < 0.001$) or gelatin (OR = 1.99, 95% CI: 1.05–3.79, $p = 0.035$) were associated with a higher risk of ARF. *Conclusions:* The incidence of ARF was similar in patients who received predominantly HES (6% 130/.04) fluid therapy and in those who received predominantly gelatin 4%. Moderate cumulative doses of modern HES or gelatin solutions may be associated with a higher risk of ARF.

Keywords Critical care · Sepsis · Hydroxyethyl starch · Gelatin · Renal failure

Table 3 Morbidity and mortality

	All patients (n = 2911)	HES group (n = 1383)	GEL group (n = 1528)	p-value
Mechanical ventilation, n (%)	1836 (63.1)	895 (64.7)	941 (61.6)	0.232
Renal replacement therapy (RRT), n (%)	133 (4.6)	63(4.6)	70 (4.6)	0.973
Duration of RRT, hours, median [IQ]	47 [18–133]	46 [17–178]	48 [21–105]	0.619
Renal failure, n (%)[a]	164 (5.6)	80 (5.8)	84 (5.5)	0.572
Sepsis syndromes at any time, n (%)				<0.001
SIRS	845 (29.0)	433 (31.3)	412 (27)	
Sepsis	250 (8.6)	74 (5.4)	176 (11.5)	
Severe sepsis/septic shock	205 (7.0)	118 (8.5)	87 (5.7)	
Severity scores, mean ± SD[b]				
SOFA max	5.8 ± 4.0	5.6 ± 4.0	6 ± 4.1	0.006
SOFA mean	4.8 ± 3.2	4.6 ± 3.1	5 ± 3.2	0.001
ICU mortality, n (%)	159 (5.5)	76 (5.5)	83 (5.4)	0.940
Hospital mortality, n (%)	297 (10.2)	140 (10.1)	157 (10.3)	0.892
ICU LOS, days, median [IQ]	2 [2–4]	2 [2–4]	2 [2–5]	0.639

SIRS systemic inflammatory response syndrome, *SOFA* sequential organ failure score, *LOS* length of stay

[a] Defined as 2-fold increase in serum admission creatinine levels and/or the use of renal replacement therapy

[b] Within 28 days of admission to the ICU

По существу, это первое исследование по изучению потенциальных неблагоприятных влияний на функцию почек общего количества (суммы доз), либо ГЭК (130/0.4) либо Желатина у пациентов ОРИТ, в том числе с тяжелым сепсисом.

Основные выводы:

(1) изменение стандартной практики с использованием преимущественно ГЭК 6% (130/0.4) или Желатина 4% не влияет на частоту возникновения ОПН, потребность в ЗПТ, а также летальности в ОРИТ.

(2) Высокие суммарные дозы (более 33 мл / кг массы тела) либо ГЭК либо Желатина связаны с высоким риском возникновения почечной недостаточности в ОРИТ и у пациентов с тяжелым сепсисом.

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EXPERT PANEL

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Prevention of acute kidney injury and protection of renal function in the intensive care unit

Expert opinion of the working group for nephrology, ESICM

Volume expansion

Recommendations

1. We **recommend** controlled fluid resuscitation in true or suspected volume depletion (grade 1C).
2. There is little evidence-based support for the preferential use of crystalloids, human serum albumin, gelatine-derived colloids or the lowest-molecular-weight hydroxy-ethyl starches (HES) for renal protection as long as derangements of serum electrolytes are prevented.
3. We **recommend** avoiding 10% HES 250/0.5 (grade 1B) as well as higher-molecular-weight preparations of HES and dextrans in sepsis (grade 2C).
4. We **recommend** prophylactic volume expansion by isotonic crystalloids in patients at risk of contrast nephropathy (grade 1B). We **suggest** using isotonic sodium bicarbonate solution, especially for emergency procedures (grade 2B).
5. We **suggest** prophylactic volume expansion with crystalloids to prevent AKI by certain drugs (specified below) (grade 2C).

Рекомендации

1. Мы рекомендуем проводить контролируемую инфузионную терапии с учетом потребности и или дефицита (степень 1С).
2. Существует мало доказательств того, что ИТ преимущественно на основе кристаллоидов, человеческого сывороточного альбумина, препаратов желатина, ГЭК с низкой молекулярной массой является эффективной для защиты почек до тех пор, пока необходимо корригировать гиповолемию и электролитные расстройства.
3. Мы рекомендуем избегать применения10% ГЭК 250/0.5 (степень 1В), а также препараты более высокого молекулярного веса ГЭК и декстраны при сепсисе (степень 2С).
4. Мы рекомендуем профилактическое увеличение объема изотонических кристаллоидов у пациентов с риском нефропатии (степень 1В). Мы предлагаем использовать изотонический раствором бикарбоната натрия, только в экстренных ситуациях (класс 2В).
5. Мы предлагаем профилактическое увеличение объема кристаллоидов для предотвращения ОПН при применении некоторых лекарств (степень 2С).

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ORIGINAL

The Crystalloid versus Hydroxyethyl Starch Trial (CHEST) Management Committee

The Crystalloid versus Hydroxyethyl Starch Trial: protocol for a multi-centre randomised controlled trial of fluid resuscitation with 6% hydroxyethyl starch (130/0.4) compared to 0.9% sodium chloride (saline) in intensive care patients on mortality

Abstract *Purpose:* The intravenous fluid 6% hydroxyethyl starch (130/0.4) (6% HES 130/0.4) is used widely for resuscitation but there is limited information on its efficacy and safety. A large-scale multi-centre randomised controlled trial (CHEST) in critically ill patients is currently underway comparing fluid resuscitation with 6% HES 130/0.4 to 0.9% sodium chloride on 90-day mortality and other clinically relevant outcomes including renal injury. This report describes the study protocol. *Methods:* CHEST will recruit 7,000 patients to concealed, random, parallel assignment of either 6% HES 130/0.4 or 0.9% sodium chloride for all fluid resuscitation needs whilst in the intensive care unit (ICU). The primary outcome will be all-cause mortality at 90 days post-randomisation. Secondary outcomes will include incident renal injury, other organ failures, ICU and hospital mortality, length of ICU stay, quality of life at 6 months, health economic analyses and in patients with traumatic brain injury, functional outcome. Subgroup analyses will be conducted in four predefined subgroups. All analyses will be conducted on an intention-to-treat basis. *Results and conclusions:* The study run-in phase has been completed and the main trial commenced in April 2010. CHEST should generate results that will inform and influence prescribing of this commonly used resuscitation fluid.

Keywords Hydroxyethyl starch · Fluid therapy · Resuscitation · Colloids · Randomised controlled trials

Trial registration

This trial has been registered with the Australian New Zealand Clinical Trials Registry (ACTRN1260900024 5291) as well as clinicaltrials.gov (NCT00935168).

Инфузионная терапия, повсеместно используемая, является одновременно краеугольным камнем в лечение пациентов в критическом состоянии, но, несмотря на это, есть ограниченная информация об эффективности различных типов инфузионных сред и их влиянии на летальность и другие показатели эффективности лечения.

Новое поколение 6% ГЭК 130/0.4, широко используется во всем мире, и начал использоваться в Австралии, но есть ограниченная информация о его эффективности и безопасности.

В настоящее время только одно большое РКИ изучает последствия применения 6% ГЭК 130/0.4 на летальность и возникновение ОПН.

Это исследование на 800 пациентах в ОРИТ с сепсисом может быть недостаточно и не может информировать об использовании крахмала в других важных подгруппах пациентов.

Поэтому оценка кристаллоидных против коллодидных растворов позволит получить важные данные о качественном составе инфузионной терапии.

Острый респираторный дистресс-синдром

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ORIGINAL

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Do hypooncotic fluids for shock increase the risk of late-onset acute respiratory distress syndrome?

Abstract *Objective:* In patients with shock, late-onset acute respiratory distress syndrome (ARDS) carries poor prognosis. Hypooncotic fluids may improve kidney function preservation, whereas hyperoncotic fluids may in theory decrease the risk of late-onset ARDS. Our objective was to determine whether predominant or exclusive use of crystalloids and/or hypooncotic colloids for shock resuscitation influenced the risk of late-onset ARDS. *Participant and settings:* International prospective cohort of consecutive adults who were free of ARDS on admission and who received fluid resuscitation for shock in 115 intensive care units (ICUs) during a 4-week period. *Measurements and results:* Severity scores, hemodynamic status, indication for fluids, risk factors for ARDS, plasma expander use, transfusions, and late-onset ARDS were recorded prospectively. Logistic regression models were tested to determine whether predominant or exclusive use of hypooncotic fluids was associated with higher incidence of late-onset ARDS. Of 905 patients, 81 [8.9%; 95% confidence interval (CI) 7.2–11.0] developed ARDS, with no difference between patients given only hypooncotic fluids (10.4%; 95% CI 7.6–13.7) and the other patients (7.7%; 95% CI 5.5–10.5; $p = 0.16$). Late-onset ARDS was significantly associated with sepsis [odds ratio (OR) 1.90; 95% CI 1.06–3.40], worse chest X-ray score at fluid initiation (1.55; 95% CI 1.27–1.91), positive fluid balance (1.06 per l; 95% CI 1.02–1.09), and greater transfusion volume (1.14 per l; 95% CI 1.01–1.29). The proportion of hypooncotic fluids in the plasma expander regimen was not associated with late-onset ARDS (1.01 per %; 95% CI 0.99–1.01). *Conclusions:* Based on this observational study, there is no evidence that in patients with shock the use of hypooncotic fluids increases the risk of late-onset ARDS. This finding needs to be confirmed.

Patients were divided into two groups according to whether they received hypooncotic fluids for shock resuscitation. Patients were classified into the hypooncotic fluid group if they received crystalloids, and/or gelatines, and/or 4% albumin only. Patients were classified into the hyperoncotic fluid group if they received hyperoncotic colloids (starches, dextrans) and/or 20% or 25% albumin.

Влияние на систему гемостаза

Intensive Care Med (2011) 37:1725–1737
DOI 10.1007/s00134-011-2385-z

SYSTEMATIC REVIEW

Christiane S. Hartog
Dorit Reuter
Wolfgang Loesche
Michael Hofmann
Konrad Reinhart

Influence of hydroxyethyl starch (HES) 130/0.4 on hemostasis as measured by viscoelastic device analysis: a systematic review

Abstract *Purpose:* Hydroxyethyl starch solutions (HES) are plasma volume expanders which affect hemostasis. Newer HES 130/0.4 is said to be safer. Reevaluation of published evidence is necessary after the recent retraction of studies. *Methods:* Systematic review of studies assessing HES 130/0.4 effects on hemostasis by thrombelastography (TEG, ROTEM) or Sonoclot (SCR) in comparison with crystalloid or albumin control fluids was performed. Only studies which provided statistical comparisons between study fluids were analyzed. Studies were divided into in vitro or in vivo hemodilution studies. We assessed study quality, HES effects which differed significantly from controls, values outside normal range, degree of hemodilution, and cumulative HES dose. *Results:* Seventeen in vitro and seven in vivo hemodilution studies were analyzed. Four studies reported quality control measures. Nineteen studies (all 15 ROTEM studies, 3 of 5 in vitro TEG, and 1 of 2 SCR studies) showed a significant hypocoagulatory effect of HES 130/0.4 on clot formation, while clotting time was not uniformly affected. Three in vivo TEG studies with low HES doses or cancer patients found mixed or non-significant results. In studies which provided normal ranges ($n = 9$), more values were outside normal ranges in the HES than in the control groups (87/122 vs. 58/122, $p < 0.001$). Dose effects were apparent in the in vitro studies, which investigated higher dilutions up to 80%. In vivo studies were fewer and did not investigate doses >40 ml/kg. *Conclusions:* HES 130/0.4 administration results in a weaker and smaller clot. Until results from well-designed clinical trials are available, safer fluids should be chosen for patients with impaired coagulation.

Keywords Plasma volume expanders · Thrombelastography · Coagulopathy · Colloids

Выводы: Применение ГЭК 130/0.4 приводит к образованию более «слабого» сгустка крови. До получения результатов хорошо спланированных клинических испытаний **для пациентов с нарушениями в системе гемостаза** должны быть выбраны другие инфузионные среды.

Intensive Care Med (2013) 39:2126–2134
DOI 10.1007/s00134-013-3111-9

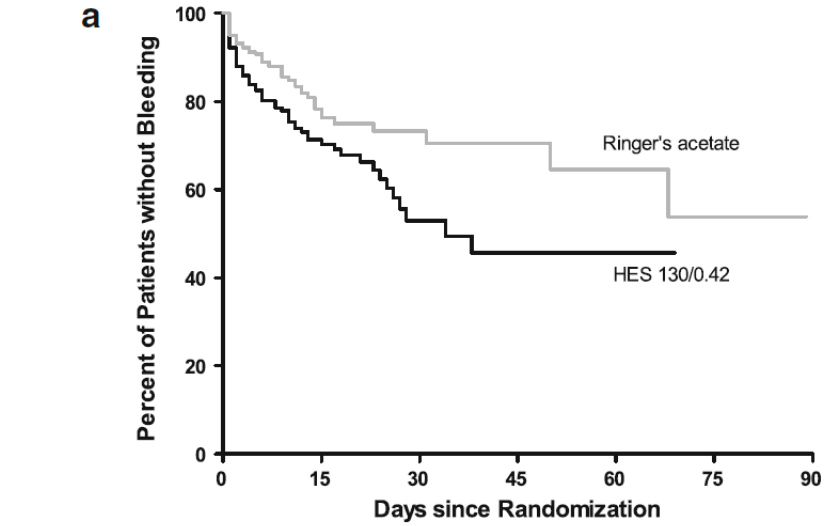
ORIGINAL ARTICLE

Nicolai Haase
Jørn Wetterslev
Per Winkel
Anders Perner

Bleeding and risk of death with hydroxyethyl starch in severe sepsis: post hoc analyses of a randomized clinical trial

tively. *Conclusions:* In post hoc analyses of patient with severe sepsis, treatment with HES increased the risk of bleeding which was associated with increased risk of death. HES-induced bleeding complications may negatively affect outcome in patients with severe sepsis.

Выводы: Постфактум, анализ пациентов с тяжелым сепсисом, у которых использовался ГЭК, **увеличивался риск кровотечения** и связанный с этим повышенный риск смерти. ГЭК индуцированной кровотечения могут негативно повлиять на исход у пациентов с тяжелым сепсисом.



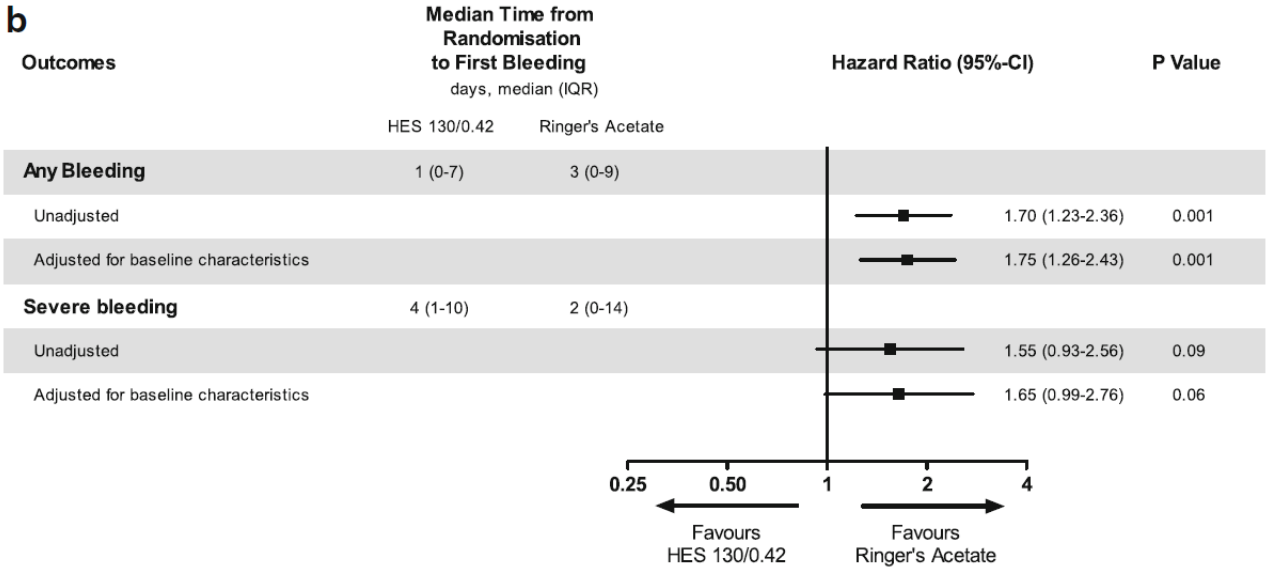


Fig. 1 Time to bleeding and hazard ratio for bleeding and severe bleeding according to trial fluid assignment. **a** Kaplan–Meier curves of time to bleeding censored at death, discharge from the intensive care unit, or at 90 days whichever came first for the two intervention groups. Kaplan–Meier analysis showed that the time to bleeding differed significantly between the groups ($P = 0.001$). **b** Hazard ratios with 95 % confidence intervals for bleeding and severe bleeding according to trial fluid assignment. Severe bleeding was defined as an intracranial bleeding or bleeding with concomitant transfusion with three units of red blood cells

Intervention

Overall, 779 patients (98 %) received trial fluid. Most trial fluid was given in the first 3 days (Table S1 in the supplementary material). The median cumulative volume during the entire ICU admission was 3,000 ml (IQR 1,507–5,100) in the HES group and 3,000 (IQR 2,000–5,750) in the Ringer's group ($P = 0.20$) corresponding to 44 and 47 ml/kg ideal body weight, respectively ($P = 0.18$).

Circulation Journal
Official Journal of the Japanese Circulation Society
http://www.j-circ.or.jp

Effect of Hydroxyethyl Starch 130/0.4 on Blood Loss and Coagulation in Patients With Recent Exposure to Dual Antiplatelet Therapy Undergoing Off-Pump Coronary Artery Bypass Graft Surgery

Jeong Soo Lee, MD; So Woon Ahn, MD; Jong Wook Song, MD;
Jae Kwang Shim, MD, PhD; Kyung-Jong Yoo, MD, PhD; Young Lan Kwak, MD, PhD

Background: Hydroxyethyl starch (HES) solutions are often used for maintaining intravascular volume and improving microperfusion, while a large amount of HES can cause adverse effects on coagulation. As the indications for clopidogrel expand, an increasing number of patients undergoing off-pump coronary artery bypass surgery (OPCAB) are also undergoing dual antiplatelet therapy (DAPT), with its higher risk of bleeding complications. The aim of the present study was to determine whether a moderate dose of 6% HES 130/0.4 significantly increases perioperative blood loss in patients with continued DAPT within 5 days of OPCAB.

Methods and Results: Patients who received clopidogrel and aspirin within 5 days of OPCAB were randomly allocated to receive HES 130/0.4 (≤30 ml/kg) followed by crystalloid infusion (HES group, n=53), or crystalloid only (crystalloid group, n=53) perioperatively. The amount of perioperative blood loss (sum of bleeding during the intraoperative and postoperative 24-h period), transfusion requirements, modified thromboelastography and coagulation variables, hemodynamic parameters, and fluid balance were recorded. Perioperative blood loss and coagulation profiles were similar between the groups, but the postoperative hemoglobin level was higher in the crystalloid group.

Conclusions: Up to 30 ml·kg^{-1}·day^{-1} of 6% HES 130/0.4 did not increase the perioperative blood loss compared to crystalloid in patients with recent exposure to DAPT undergoing OPCAB. HES 130/0.4 caused a similar degree and duration of coagulation impairment as observed when only crystalloid was given. (*Circ J* 2011; **75:** 2397–2402)

До 30 мл/кг/день 6% ГЭК 130 / 0,4 не привело к увеличению периоперационной кровопотери по сравнению с кристаллоидами....
ГЭК 130 / 0,4 вызвало такую же степень и продолжительность нарушения коагуляции, как и когда применяли только кристаллоиды

British Journal of Anaesthesia **107** (5): 693–702 (2011)
Advance Access publication 19 August 2011 · doi:10.1093/bja/aer229

BJA

Resuscitation with hydroxyethyl starch improves renal function and lactate clearance in penetrating trauma in a randomized controlled study: the FIRST trial (Fluids in Resuscitation of Severe Trauma)

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Background. The role of fluids in trauma resuscitation is controversial. We compared resuscitation with 0.9% saline *vs* hydroxyethyl starch, HES 130/0.4, in severe trauma with respect to resuscitation, fluid volume, gastrointestinal recovery, renal function, and blood product requirements.

Methods. Randomized, controlled, double-blind study of severely injured patients requiring>3 litres of fluid resuscitation. Blunt and penetrating trauma were randomized separately. Patients were followed up for 30 days.

Results. A total of 115 patients were randomized; of which, 109 were studied. For patients with penetrating trauma (n=67), the mean (SD) fluid requirements were 5.1 (2.7) litres in the HES group and 7.4 (4.3) litres in the saline group (P<0.001). In blunt trauma (n=42), there was no difference in study fluid requirements, but the HES group required significantly more blood products [packed red blood cell volumes 2943 (1628) *vs* 1473 (1071) ml, P=0.005] and was more severely injured than the saline group (median injury severity score 29.5 *vs* 18; P=0.01). Haemodynamic data were similar, but, in the penetrating group, plasma lactate concentrations were lower over the first 4 h (P=0.029) and on day 1 with HES than with saline [2.1 (1.4) *vs* 3.2 (2.2) mmol litre^{-1}; P=0.017]. There was no difference between any groups in time to recovery of bowel function or mortality. In penetrating trauma, renal injury occurred more frequently in the saline group than the HES group (16% *vs* 0%; P=0.018). In penetrating trauma, maximum sequential organ function scores were lower with HES than with saline (median 2.4 *vs* 4.5, P=0.012). No differences were seen in safety measures in the blunt trauma patients.

Conclusions. In penetrating trauma, HES provided significantly better lactate clearance and less renal injury than saline. No firm conclusions could be drawn for blunt trauma.
Study registration: ISRCTN 42061860.

Выводы. При проникающих ранениях, ГЭК обеспечили значительно лучший клиренс лактата и меньшее повреждение почек, чем физиологический раствор.

Intensive Care Med (2014) 40:160–170
DOI 10.1007/s00134-013-3156-9

SYSTEMATIC REVIEW

Накопление в тканях

Christian J. Wiedermann
Michael Joannidis

Accumulation of hydroxyethyl starch in human and animal tissues: a systematic review

Abstract *Purpose:* To systematically review clinical and preclinical data on hydroxyethyl starch (HES) tissue storage. *Methods:* MEDLINE (PubMed) was searched and abstracts were screened using defined criteria to identify articles containing original data on HES tissue accumulation. *Results:* Forty-eight studies were included: 37 human studies with a total of 635 patients and 11 animal studies. The most frequent indication for fluid infusion was surgery accounting for 282 patients (45.9 %). HES localization in skin was shown by 17 studies, in kidney by 12, in liver by 8, and in bone marrow by 5. Additional sites of HES deposition were lymph nodes, spleen, lung, pancreas, intestine, muscle, trophoblast, and placental stroma. Among major organs the highest measured tissue concentration of HES was in the kidney. HES uptake into intracellular vacuoles was observed by 30 min after infusion. Storage was cumulative, increasing in proportion to dose, although in 15 % of patients storage and associated symptoms were demonstrated at the lowest cumulative doses (0.4 g kg^{-1}). Some HES deposits were extremely long-lasting, persisting for 8 years or more in skin and 10 years in kidney. Pruritus associated with HES storage was described in 17 studies and renal dysfunction in ten studies. In one included randomized trial, HES infusion produced osmotic nephrosis-like lesions indicative of HES storage ($p = 0.01$) and also increased the need for renal replacement therapy (odds ratio, 9.50; 95 % confidence interval, 1.09–82.7; $p = 0.02$). The tissue distribution of HES was generally similar in animals and humans. *Conclusions:* Tissue storage of HES is widespread, rapid, cumulative, frequently long-lasting, and potentially harmful.

Keywords Hydroxyethyl starch · Hetastarch · Storage · Accumulation · Uptake · Deposit

Выводы:
Накопление ГЭК в тканях имеет место быть, накопление часто длительное и потенциально вредно.

Летальность
(риск повышения летальности)

Intensive Care Med (2013) 39:558–568
DOI 10.1007/s00134-013-2840-0

ORIGINAL

David J. Gattas
Arina Dan
John Myburgh
Laurent Billot
Serigne Lo
Simon Finfer
CHEST Management Committee

Fluid resuscitation with 6 % hydroxyethyl starch (130/0.4 and 130/0.42) in acutely ill patients: systematic review of effects on mortality and treatment with renal replacement therapy

Применение в программе ИТ при критических заболеваниях у взрослых 6% ГЭК 130 связано с увеличением риска летальности и частоты применения ЗПТ.

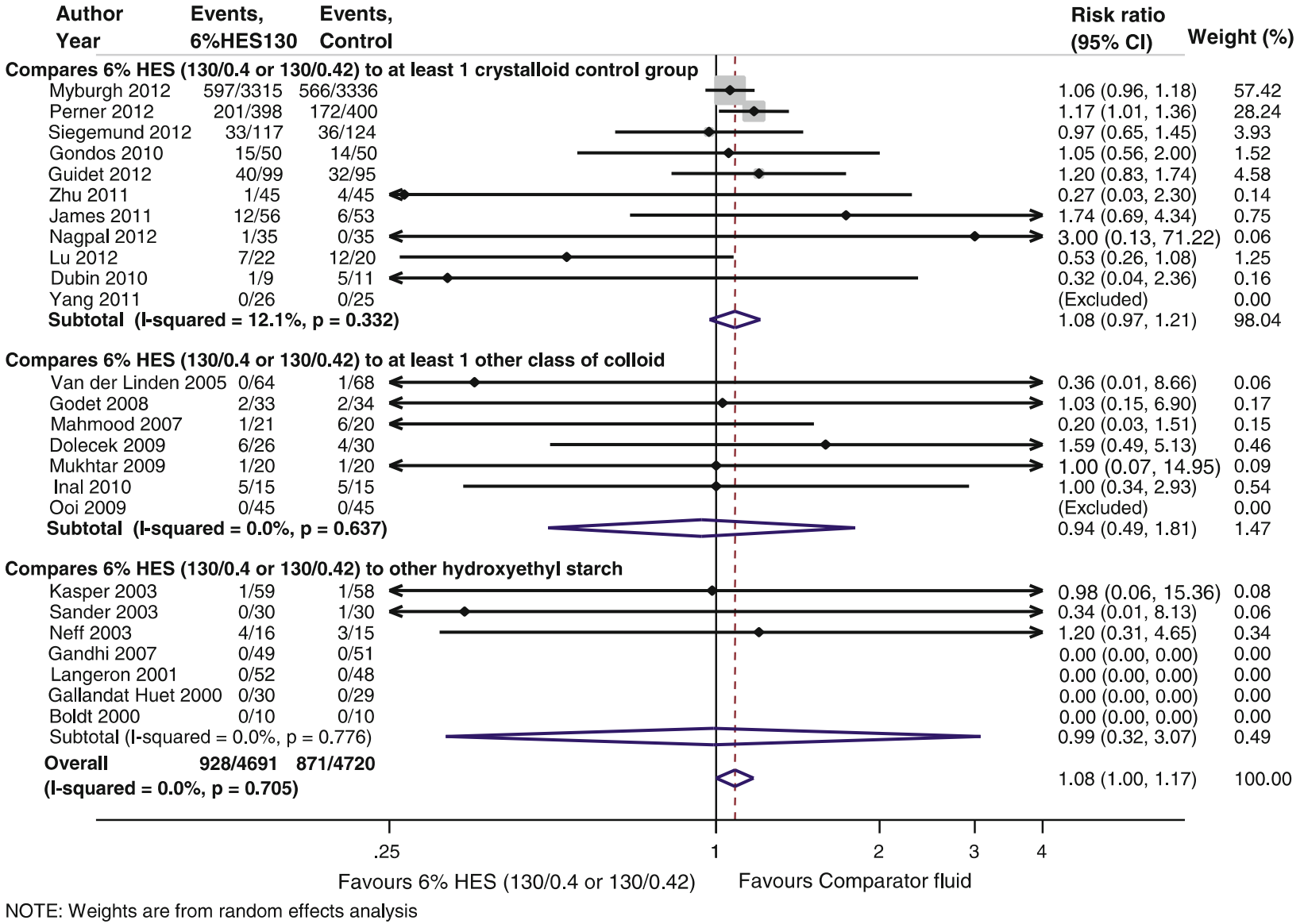


Fig. 2 Forest plot of pooled estimates for mortality. 6 % HES 130 = 6 % hydroxyethyl starch with a molecular weight of 130 kD and a molar substitution ratio of approximately 0.4. CI = confidence interval. Studies reporting at least one event in each group are arranged in ascending year of publication. Weights are from random effects analysis

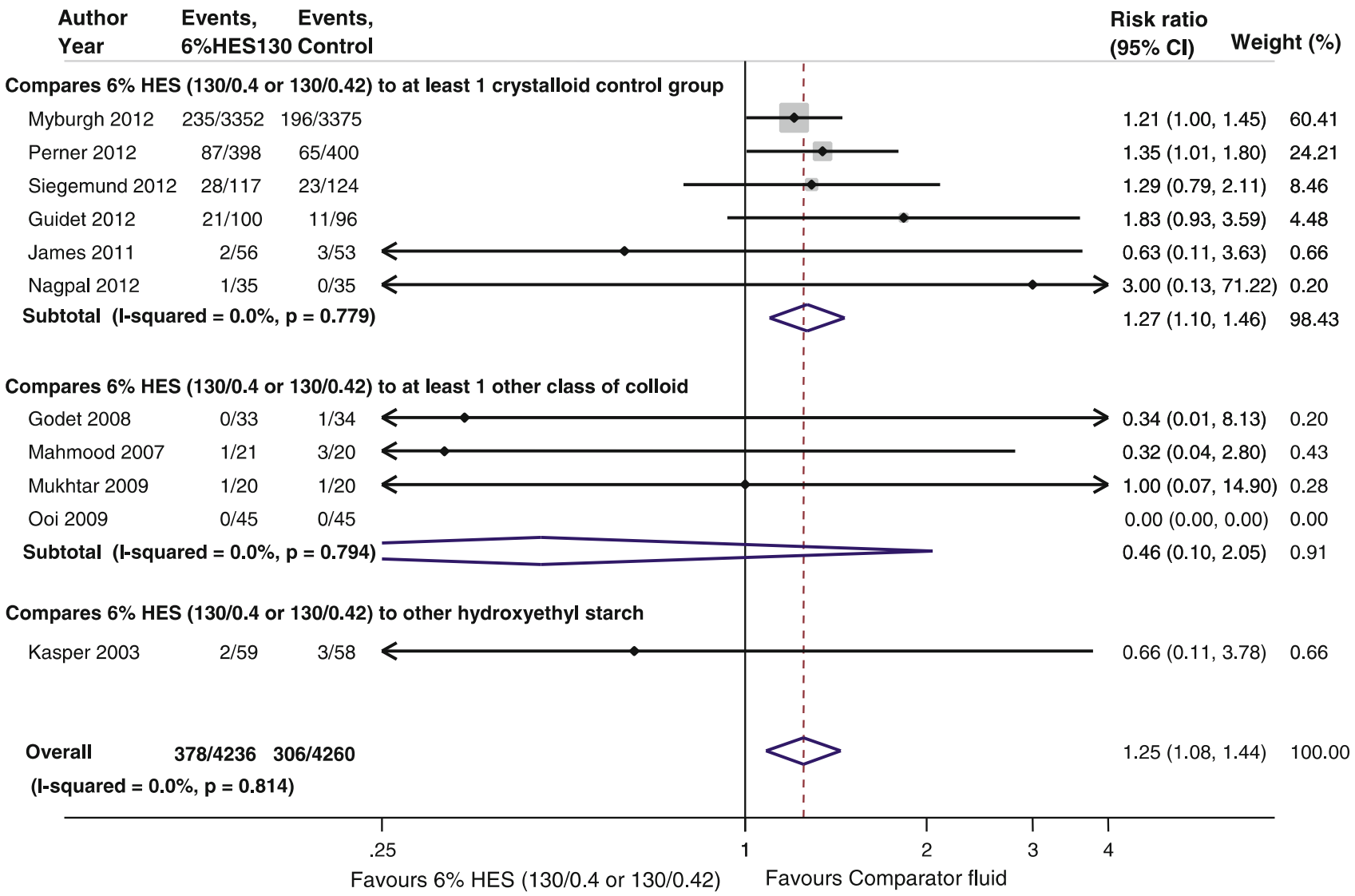


Fig. 3 Forest plot of pooled estimates for need for renal replacement therapy. 6 % HES 130 = 6 % hydroxyethyl starch with a molecular weight of 130 kD and a molar substitution ratio of approximately 0.4. CI = confidence interval. Studies reporting at least one event in each group are arranged in ascending year of publication. Weights are from random effects analysis

Intensive Care Med (2013) 39:811–822
DOI 10.1007/s00134-013-2863-6

SYSTEMATIC REVIEW

Amit Patel
Umeer Waheed
Stephen J. Brett

Randomised trials of 6 % tetrastarch (hydroxyethyl starch 130/0.4 or 0.42) for severe sepsis reporting mortality: systematic review and meta-analysis

Abstract *Purpose:* To assess the impact of 6 % tetrastarch [hydroxyethyl starch (HES) 130/0.4 and 130/0.42] in severe sepsis patients. The primary outcome measure was 90-day mortality. *Methods:* A structured literature search was undertaken to identify prospective randomised controlled trials (RCTs) in adult patients with severe sepsis receiving 6 % tetrastarch (of potato or waxy maize origin) as part of fluid resuscitation in comparison with other non-HES fluids after randomisation in the critical care setting. A systematic review and meta-analysis were performed. *Results:* Six RCTs were included ($n = 3{,}033$): three from 2012 ($n = 2{,}913$) had low risk of bias. Median tetrastarch exposure was 37.4 ml/kg (range 30–43 ml/kg). Ninety-day mortality was associated with tetrastarch exposure [relative risk (RR) 1.13; 95 % confidence interval (CI) 1.02–1.25; $p = 0.02$] compared with crystalloid. The number needed to harm (NNH) was 28.8 (95 % CI 14.6–942.5). Publication bias and statistical heterogeneity ($I^2 = 0$ %) were not present. Tetrastarch exposure was also associated with renal replacement therapy ($p = 0.01$; NNH 15.7) and allogeneic transfusion support ($p = 0.001$; NNH 9.9). No difference between groups was observed for 28-day mortality, for comparison with colloid as control, or for waxy maize-derived tetrastarch, but power was lacking. Overall mortality was associated with tetrastarch exposure (RR 1.13; 95 % CI 1.02–1.25; $p = 0.02$). *Conclusions:* In our analysis, 6 % tetrastarch as part of initial fluid resuscitation for severe sepsis was associated with harm and, as alternatives exist, in our view should be avoided.

Keywords 6 % tetrastarch · 6 % hydroxyethyl starch (HES) 130/0.4 or 0.42 · Severe sepsis · Mortality · Renal

Выводы: В нашем анализе, 6% ГЭК как часть стартовой инфузионной терапии для лечения тяжелого сепсиса был связан с осложнениями и, при наличии альтернативы, на наш взгляд, его следует избегать.

Intensive Care Med (2013) 39:1963–1971
DOI 10.1007/s00134-013-3090-x

ORIGINAL ARTICLE

Pro

Rasmus G. Müller
Nicolai Haase
Jørn Wetterslev
Anders Perner

Effects of hydroxyethyl starch in subgroups of patients with severe sepsis: exploratory post-hoc analyses of a randomised trial

Abstract *Purpose:* It has been speculated that certain subgroups of sepsis patients may benefit from treatment with hydroxyethyl starch (HES) 130/0.42, specifically in the earlier resuscitation of patients with more severely impaired circulation. *Methods:* This was a post-hoc, subgroup analysis of all 798 patients with severe sepsis randomised in the 6S trial according to time from ICU admission to randomisation, surgery and fluids given prior to randomisation and markers of shock at randomisation. Intervention effects estimated as risk ratios were analysed between the HES versus Ringer's acetate groups to detect subgroup heterogeneity of the effects on 90-day mortality. Multiple logistic regression was used to adjust for risk factors. *Results:* Most baseline characteristics were comparable between the HES and Ringer's acetate groups in the different subgroups. There was no heterogeneity in the intervention effect on 90-day mortality in the following subgroups: randomisation earlier than 4 h after ICU admission versus later (test of interaction $P = 0.85$), surgery versus no surgery ($P = 0.42$), colloids given versus not given ($P = 0.57$), <2 l of crystalloids given prior to randomisation vs. >2 l ($P = 0.88$) or plasma lactate >4 mmol/l versus <4 mmol/l ($P = 0.54$), hypotension versus no hypotension ($P = 0.32$) or use of vasopressor or inotropic agents at randomisation versus no use ($P = 0.10$). *Conclusions:* The increased 90-day mortality observed in patients with severe sepsis resuscitated with HES 130/0.42 did not appear to depend on time course, surgery or fluids given prior to randomisation or on markers of shock at randomisation. As the analyses were planned post hoc and their power is reduced, the results should be interpreted with caution.

Keywords Hydroxyethyl starch · Colloids · Resuscitation · Sepsis

Выводы:

У пациентов с тяжелым сепсисом 90-дневная летальность не связана с ГЭК 130/0.42; по-видимому, она зависит от времени начала лечения, хирургического вмешательства или начала инфузии…

Полученные результаты следует интерпретировать с осторожностью.

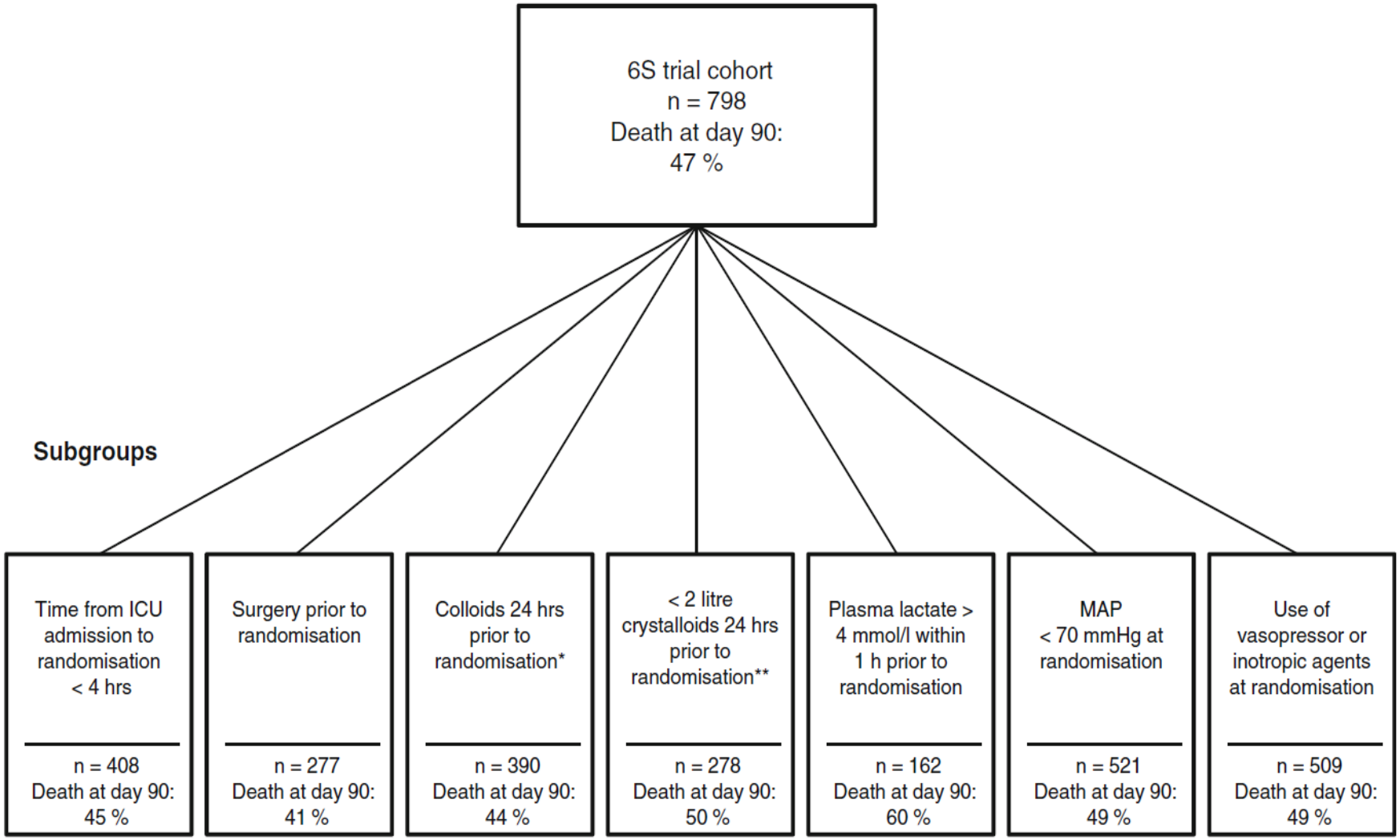
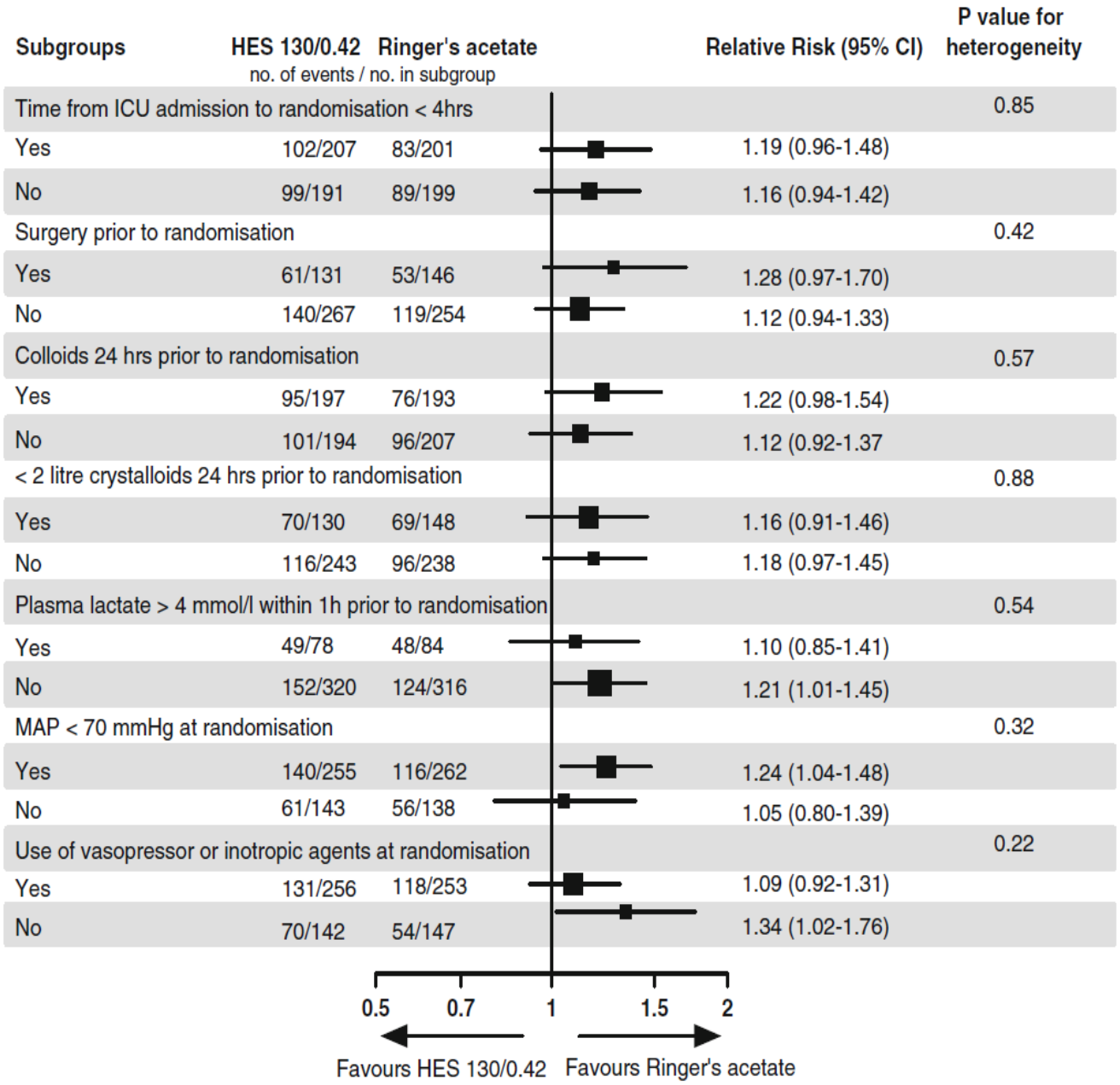


Fig. 1 Trial cohort and subgrouping with mortality at day 90 given as a percentage. *6S* Scandinavian Starch for Severe Sepsis/Septic Shock trial, *ICU* intensive care unit, *MAP* mean arterial pressure. In the colloid sub-group, data were missing for seven patients, all in the hydroxyethyl starch (HES) group, regarding colloids given during the 24 h immediately prior to randomisation (*single asterisk*). Data were also missing for 39 patients on the volume of crystalloids given during the 24 h immediately prior to randomisation (*double asterisk*). These patients were not analysed

Fig. 2 Relative risks of death at day 90 with 95 % confidence intervals (*CIs*) in subgroups of patients resuscitated with HES 130/0.42 vs. Ringer's acetate. In the colloid sub-group, data were missing for seven patients, all in the HES group. Data were also missing for 39 patients in the analysis of fluids given prior to randomisation. These patients were not analysed



Intensive Care Med
DOI 10.1007/s00134-014-3311-y

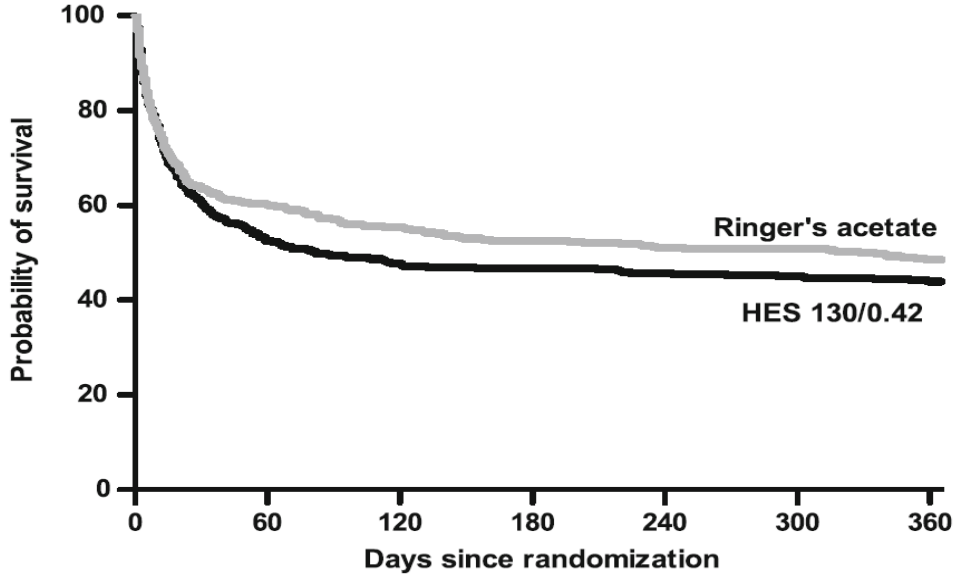
SEVEN-DAY PROFILE PUBLICATION

Anders Perner
Nicolai Haase
Per Winkel
Anne B. Guttormsen
Jyrki Tenhunen
Gudmundur Klemenzson
Rasmus G. Müller
Anders Åneman
Jørn Wetterslev

Long-term outcomes in patients with severe sepsis randomised to resuscitation with hydroxyethyl starch 130/0.42 or Ringer's acetate

Abstract *Purpose:* We assessed long-term mortality and hospitalisation in patients with severe sepsis resuscitated with hydroxyethyl starch (HES) or Ringer's acetate. *Methods:* This was an investigator-initiated, parallel-grouped, blinded randomised trial using computer-generated allocation sequence and centralised allocation data that included 804 patients with severe sepsis needing fluid resuscitation in 26 general intensive care units (ICUs) in Scandinavia. Patients were allocated to fluid resuscitation using either 6 % HES 130/0.42 or Ringer's acetate during ICU admission. We assessed mortality rates at 6 months, 1 year and at the time of longest follow-up and days alive and out of hospital at 1 year. *Results:* The vital status of all patients was obtained at a median of 22 (range 13–36) months after randomisation. Mortality rates in the HES versus Ringer's groups at 6 months were 53.3 (212/398 patients) versus 47.5 % (190/400) [relative risk 1.12; 95 % confidence interval (CI) 0.98–1.29; $P = 0.10$], respectively; at 1 year, 56.0 (223/398) versus 51.5 % (206/400) (1.09; 95 % CI 0.96–1.24; $P = 0.20$), respectively; at the time of longest follow-up, 59.8 (238/398) versus 56.3 % (225/400) (1.06; 95 % CI 0.94–1.20; $P = 0.31$), respectively. Percentage of days alive and out of hospital at 1 year in the HES versus Ringer's groups was 24 (0–87 days) versus 63 % (0–90) ($P = 0.07$). *Conclusions:* The long-term mortality rates did not differ in patients with severe sepsis assigned to HES 130/0.42 versus Ringer's acetate, but we could not reject a 24 % relative increased or a 4 % relative decreased mortality at 1 year with HES at the 95 % confidence level.

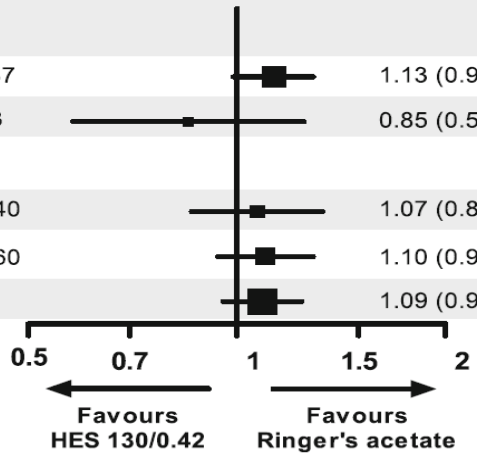
A Time to death



No. at risk				
HES 130/0.42	398	190	182	175
Ringer's Acetate	400	221	204	194

B Relative risk of death at 1 year

Subgroup	HES 130/0.42	Ringer's acetate	Relative risk (95%-CI)	P value for heterogeneity
	no of events / no in subgroup			
Shock at the time of randomisation				0.15
Yes	197/336	175/337	1.13 (0.99-1.29)	
No	26/62	31/63	0.85 (0.58-1.25)	
Acute kidney injury at the time of randomisation				0.83
Yes	78/142	72/140	1.07 (0.86-1.33)	
No	145/256	134/260	1.10 (0.94-1.29)	
All patients			1.09 (0.96-1.24)	



Hydroxyethyl Starch or Saline for Fluid Resuscitation in Intensive Care

N Engl J Med 2012;367:1901-11.
DOI: 10.1056/NEJMoa1209759

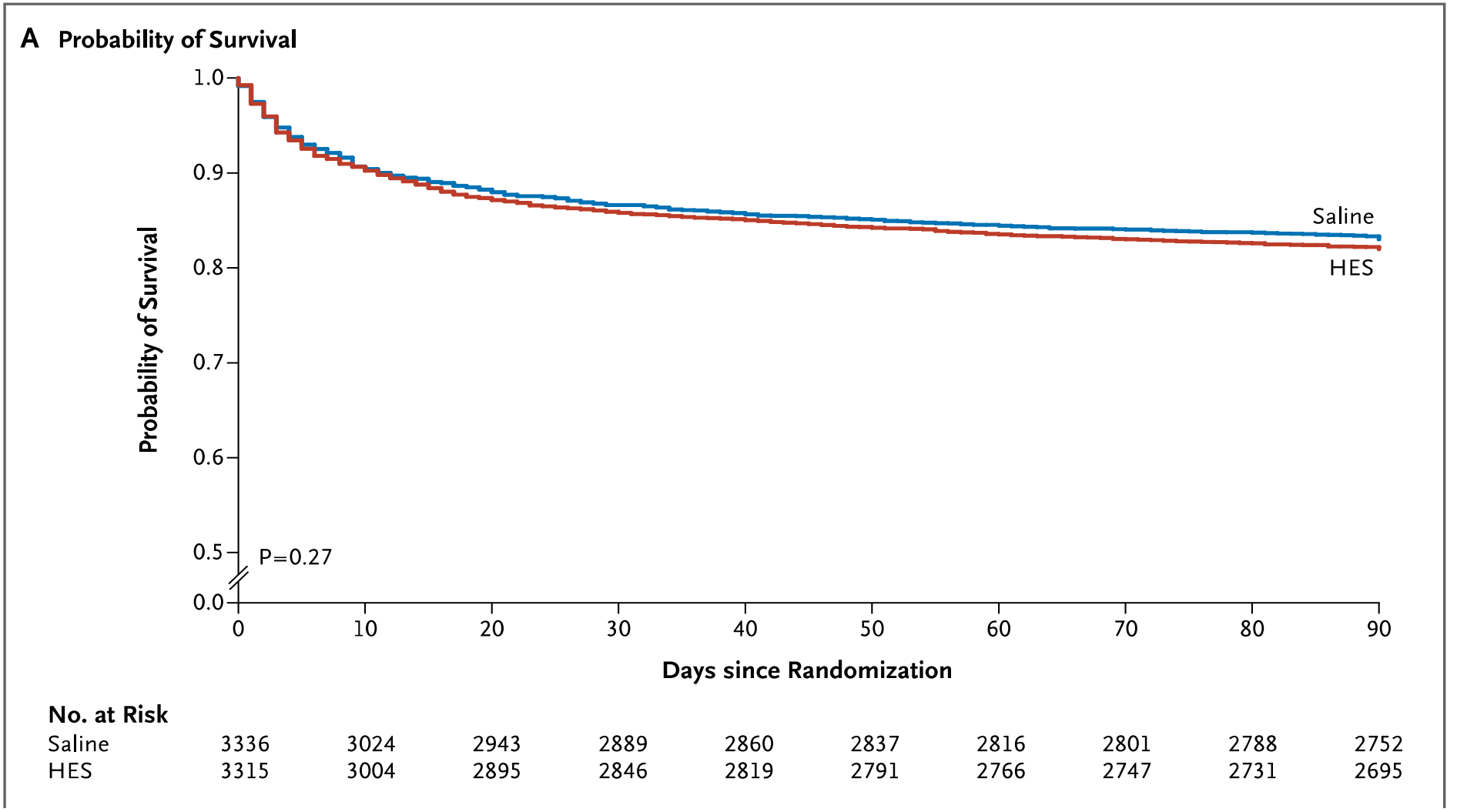
John A. Myburgh, M.D., Ph.D., Simon Finfer, M.D., Rinaldo Bellomo, M.D., Laurent Billot, M.Sc., Alan Cass, M.D., Ph.D., David Gattas, M.D., Parisa Glass, Ph.D., Jeffrey Lipman, M.D., Bette Liu, Ph.D., Colin McArthur, M.D., Shay McGuinness, M.D., Dorrilyn Rajbhandari, R.N., Colman B. Taylor, M.N.D., and Steven A.R. Webb, M.D., Ph.D., for the CHEST Investigators and the Australian and New Zealand Intensive Care Society Clinical Trials Group*

METHODS

We randomly assigned 7000 patients who had been admitted to an intensive care unit (ICU) in a 1:1 ratio to receive either 6% HES with a molecular weight of 130 kD and a molar substitution ratio of 0.4 (130/0.4, Voluven) in 0.9% sodium chloride or 0.9% sodium chloride (saline) for all fluid resuscitation until ICU discharge, death, or 90 days after randomization. The primary outcome was death within 90 days. Secondary outcomes included acute kidney injury and failure and treatment with renal-replacement therapy.

RESULTS

A total of 597 of 3315 patients (18.0%) in the HES group and 566 of 3336 (17.0%) in the saline group died (relative risk in the HES group, 1.06; 95% confidence interval [CI], 0.96 to 1.18; P=0.26). There was no significant difference in mortality in six predefined subgroups. Renal-replacement therapy was used in 235 of 3352 patients (7.0%) in the HES group and 196 of 3375 (5.8%) in the saline group (relative risk, 1.21; 95% CI, 1.00 to 1.45; P=0.04). In the HES and saline groups, renal injury occurred in 34.6% and 38.0% of patients, respectively (P=0.005), and renal failure occurred in 10.4% and 9.2% of patients, respectively (P=0.12). HES was associated with significantly more adverse events (5.3% vs. 2.8%, P<0.001).



CONCLUSIONS

In patients in the ICU, there was no significant difference in 90-day mortality between patients resuscitated with 6% HES (130/0.4) or saline. However, more patients who received resuscitation with HES were treated with renal-replacement therapy. (Funded by the National Health and Medical Research Council of Australia and others; CHEST ClinicalTrials.gov number, NCT00935168.)

Effects of Fluid Resuscitation With Colloids vs Crystalloids on Mortality in Critically Ill Patients Presenting With Hypovolemic Shock

The CRISTAL Randomized Trial

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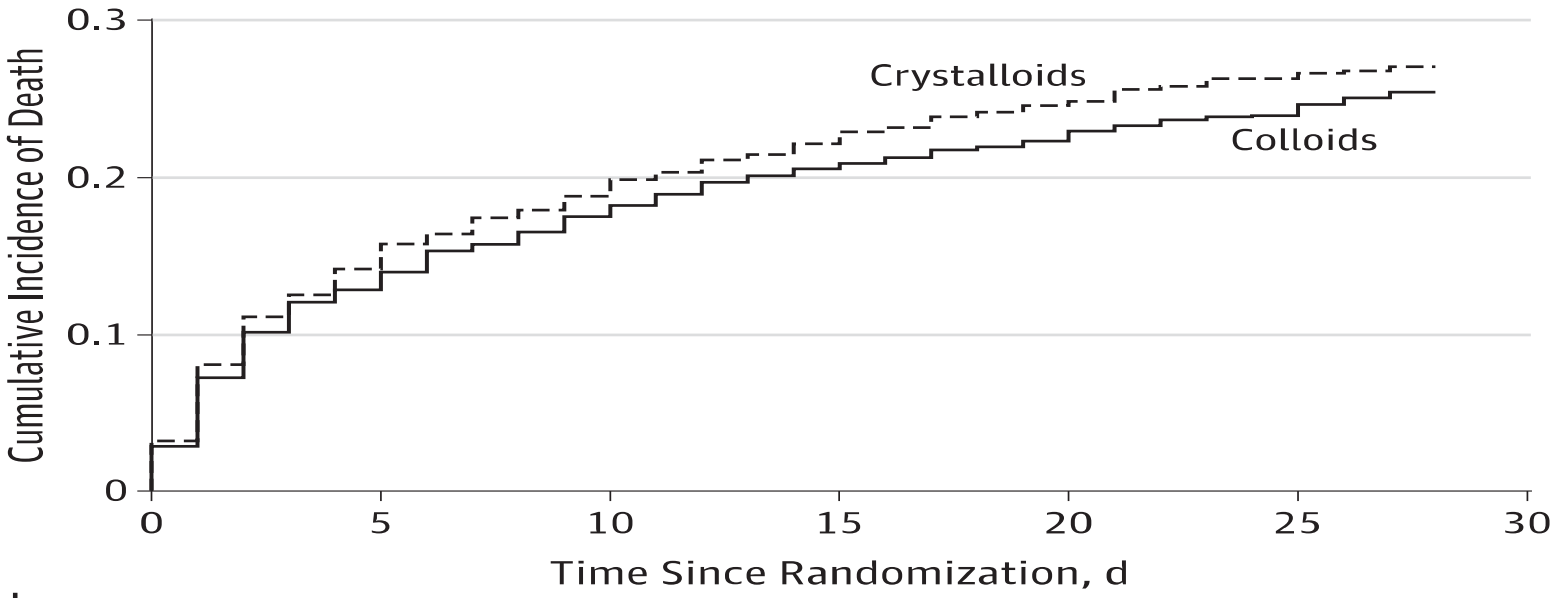
MAIN OUTCOMES AND MEASURES The primary outcome was death within 28 days. Secondary outcomes included 90-day mortality; and days alive and not receiving renal replacement therapy, mechanical ventilation, or vasopressor therapy.

RESULTS Within 28 days, there were 359 deaths (25.4%) in colloids group vs 390 deaths (27.0%) in crystalloids group (relative risk [RR], 0.96 [95% CI, 0.88 to 1.04]; *P* = .26). Within 90 days, there were 434 deaths (30.7%) in colloids group vs 493 deaths (34.2%) in crystalloids group (RR, 0.92 [95% CI, 0.86 to 0.99]; *P* = .03). Renal replacement therapy was used in 156 (11.0%) in colloids group vs 181 (12.5%) in crystalloids group (RR, 0.93 [95% CI, 0.83 to 1.03]; *P* = .19). There were more days alive without mechanical ventilation in the colloids group vs the crystalloids group by 7 days (mean: 2.1 vs 1.8 days, respectively; mean difference, 0.30 [95% CI, 0.09 to 0.48] days; *P* = .01) and by 28 days (mean: 14.6 vs 13.5 days; mean difference, 1.10 [95% CI, 0.14 to 2.06] days; *P* = .01) and alive without vasopressor therapy by 7 days (mean: 5.0 vs 4.7 days; mean difference, 0.30 [95% CI, −0.03 to 0.50] days; *P* = .04) and by 28 days (mean: 16.2 vs 15.2 days; mean difference, 1.04 [95% CI, −0.04 to 2.10] days; *P* = .03).

Figure 2. Cumulative Incidence of Death Within First 28 Days After Randomization



No. at risk

Colloids	1414	1233	1167	1124	1099	1076
Crystalloids	1443	1239	1172	1124	1089	1064

CONCLUSIONS AND RELEVANCE Among ICU patients with hypovolemia, the use of colloids vs crystalloids did not result in a significant difference in 28-day mortality. Although 90-day mortality was lower among patients receiving colloids, this finding should be considered exploratory and requires further study before reaching conclusions about efficacy.

Guidet et al. Critical Care 2012, 16:R94
http://ccforum.com/content/16/3/R94

CRITICAL CARE

RESEARCH Open Access

Assessment of hemodynamic efficacy and safety of 6% hydroxyethylstarch 130/0.4 vs. 0.9% NaCl fluid replacement in patients with severe sepsis: The CRYSTMAS study

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Abstract

Introduction: Inadequate initial treatment and delayed hemodynamic stabilization (HDS) may be associated with increased risk of death in severe sepsis patients.

Methods: In order to compare the hemodynamic efficacy and safety of 6% HES 130/0.4 and NaCl 0.9% for HDS in patients with severe sepsis, we designed a prospective, multicenter, active-controlled, double-blind, randomized study in intensive care units.

Results: 174 out of 196 patients reached HDS (88 and 86 patients for HES and NaCl, respectively). Significantly less HES was used to reach HDS vs. NaCl (1,379 ±886 ml in the HES group and 1,709 ±1,164 ml in the NaCl group (mean difference = -331± 1,033, 95% CI -640 to -21, P = 0.0185). Time to reach HDS was 11.8 10.1 hours vs. 14.3 ±11.1 hours for HES and NaCl, respectively. Total quantity of study drug infused over four consecutive days, ICU and hospital LOS, and area under the curve of SOFA score were comparable. Acute renal failure occurred in 24 (24.5%) and 19 (20%) patients for HES and NaCl, respectively (P = 0.454). There was no difference between AKIN and RIFLE criteria among groups and no difference in mortality, coagulation, or pruritus up to 90 days after treatment initiation.

Conclusion: Significantly less volume was required to achieve HDS for HES vs. NaCl in the initial phase of fluid resuscitation in severe sepsis patients without any difference for adverse events in both groups.

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DOI 10.1007/s00134-015-3741-1

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Guiding fluid resuscitation in critically ill patients: how to evaluate the available tools?

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Table 1 A selection of the major trials in severe sepsis (references 1–20, see ESM) and ARDS (references 21–30, see ESM) published in the past 15 years, with severity scores and mortality

Trial/year of publication	Aim of study/intervention being assessed (controls treated with "standard of care" at the time)	No. of patients included	28-day mortality		APACHE II/III, SAPS II, and SOFA scores
			Study patients (%)	Controls (%)	
Major trials in patients with severe sepsis and septic shock, with or without ARDS					
KyberSept 2001[1]	Antithrombin III (AT III) vs. controls	2314	38.9	38.7	SAPS II 49/49
PROWESS 2001[2]	Protein C (activated) (aPC) vs. controls	1690	24.7	30.8	APACHE II 25.0/24.6[a]
OPTIMIST 2003[3]	Tissue factor pathway inhibitor vs. controls	1754	34.2	33.9	APACHE II 25.0/25.0[a]
Intensive insulin 2006[4]	Intensive insulin vs. standard in medical patients	1200	37.3	40.0	APACHE II 23/23[a]
CATS trial 2007[5]	Epinephrine alone vs. norepinephrine plus dobutamine for septic shock	330	40	34	SAPS II 54/52, SOFA 11/11[a]
VASST trial[6]	Vasopressin vs. Norepinephrin	778	35.4	39.3	APACHE II 27.1/27.0[a]
CORTICUS 2008[7]	Hydrocortisone vs. controls	499	34.3	31.5	SAPS II 49.5/48.6, SOFA 10.6/10.6[a]
SepNet 2008[8]	10 %HES 200/0.5 and intensive insulin vs. controls	537	25.7	25.1	APACHE II 20.3/20.2
Edusepsis trial[9]	Effect of a national education program on mortality	2319	31.1	36.4	APACHE II 21.3/21.0
NICE SUGAR 2009[10]	Intensive insulin therapy vs. controls	6104	27.5	24.9	APACHE II 21.1/21/1
6S Trial 2012[11]	Starch (6 % HES 130/0.42) vs. or Ringer's acetate	798	39.0	36.0	SAPS II 50/51, SOFA 7//7
SepNet 2012[12]	Empiric meropenem vs. meropenem plus moxifloxacin	600	23.9	21.9	APACHE II 21.3/21.9, SOFA 9.7/9.4 (8.3/7.9)
IVOIRE 2013[13]	High volume CVVH vs. standard CVVH in ARF	137	37.9	40.8	SAPS score 68/64, SOFA score 12/12
SEPSISPAM 2014[14]	High vs. low blood pressure	776	36.6	34.0	SAPS score 56.1/57.2, SOFA score 10.7/10.8[a]
ALBIOS 2014[15]	Albumin vs. crystalloids	1818	31.8	32.0	SAPS scores 48/48 (predicted mortality 45 %), SOFA 8/8

Основные рекомендации

Intensive Care Med (2012) 38:368–383
DOI 10.1007/s00134-012-2472-9

SPECIAL ARTICLE

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Consensus statement of the ESICM task force on colloid volume therapy in critically ill patients

Summary and Conclusions

We recommend not to use HES with molecular weight $\geq$200 kDa and/or degree of substitution >0.4 in patients with severe sepsis or risk of acute kidney injury and suggest not to use 6% HES 130/0.4 or gelatin in these populations outside the context of clinical trials. We recommend not to use colloids in patients with head injury and not to administer gelatins and HES in organ donors. We suggest not to use hyperoncotic solutions for fluid resuscitation. We conclude and recommend that any new colloid should be introduced into clinical practice only after its patient-important safety parameters are established.

I. Мы рекомендуем не использовать ГЭК с молекулярной массой более 200 кДа и / или степени замещения более 0,4 у пациентов с тяжелым сепсисом (класс 1B) и рекомендуем не использовать ГЭК у других пациентов с повышенным риском развития ОПН (класс 1C).
II. Мы полагаем, что ГЭК 130/0.4 целесообразно использовать при тяжелом сепсисе и у других пациентов в ОАР с повышенным риском ОПН или кровотечения только при клинических испытаниях, а не в обычной клинической практике (степень 2C).
III. Мы полагаем, что альбумин может быть включен в программу ИТТ тяжелого сепсиса (класс 2B).
IV. Мы рекомендуем использовать альбумин у больных с ЧМТ (класс 1C). Мы рекомендуем не использовать синтетические коллоиды у больных с ЧМТ или при внутричерепном кровоизлиянии (степень 1C).
V. Мы предлагаем не использовать желатин у пациентов в ОРИТ, у которых имеется высокий риск для возникновения ОПН или кровотечения вне контекста клинических испытаний (степень 2C).
VI. Мы рекомендуем не использовать ГЭК или желатин при трансплантации донорских органов вне контекста клинических испытаний (класс 1C).

VII. Мы рекомендуем, чтобы любой новый коллоид должн быть введен в клиническую практику только после оценки его безопасности для пациента (степень 1С).
VIII. Мы предлагаем не использовать гиперонкотические препараты для инфузионной терапии вне контекста клинических испытаний (степень 2С). IX. Мы рекомендуем провести переоценку существующих доз для ГЭК и для желатина (класс 1В).
X. Признавая вероятность того, что, **несмотря на рекомендацию или предложение об обратном, врачи будут продолжать использовать ГЭК**, мы обсуждали возможность выпуска заявлением, описывающим кумулятивные пороговые дозы. Учитывая различия мнений между членами рабочей группы, мы провели голосование на предпочтения и результаты таковы: шесть из восьми членов комиссии предпочли не выдавать такое заявление (используя в качестве обоснования, что мы не знаем, если такая «безопасный» доза); два из них - 10 мл / кг в ГЭК с молекулярной массой С200 кДа и / или степени замещения более 0,4; и 10 мл / кг и 15 мл / кг ГЭК 130/0.4).
Два из восьми - суммарная дозах 0 до 30 мл / кг.

Intensive Care Med (2013) 39:998–1001
DOI 10.1007/s00134-013-2890-3

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Lauralyn McIntyre

New insights into fluid resuscitation

Table 1 Summary table of systematic reviews and meta-analyses published in 2013 comparing hydroxyethyl starch preparations (HES) versus other resuscitation fluids in randomized controlled trials that reported mortality and use of renal replacement therapy (RRT) as outcome measures

Systematic review	HES preparation	Comparator	Patient population	Mortality RR (95 % CI)	RRT RR (95 % CI)
Gattas [6]	6 % HES (130/0.4–0.42)	Isotonic saline Hypertonic saline Lactated Ringer's Acetated Ringer's Albumin 4 %, 5 %, 20 % Gelatin 4 % Polygeline 3.4 % Dextran 70 HES (200/0.5) HES (670/0.75)	Acutely ill patients in intensive care, perioperative and operative setting	1.08 (1.00–1.17)	1.25 (1.08–1.44)
Haase [7]	6 % HES (130/0.4–0.42)	Isotonic saline Lactated Ringer's Acetated Ringer's Albumin 20 %	Sepsis/septic shock	1.04 (0.89–1.22)	1.36 (1.08–1.72)
Zarychanski [5]	6–10 % HES (130/0.4–0.42) 6–10 % HES (200/0.43–0.66)	Isotonic saline Hypertonic saline Lactated Ringer's Acetated Ringer's Albumin 4 %, 5 %, 20 % Gelatin 3 %, 4 % Plasma	Critically ill patients in emergency or intensive care setting	1.06 (1.00–1.13)	1.32 (1.15–1.50)
Patel [4]	6 % HES (130/0.4–0.42)	Isotonic saline Acetated Ringer's Albumin 20 %	Severe sepsis	1.13 (1.02–1.25)	1.42 (1.09–1.85)

RR relative risk, *95 % CI* 95 % confidence interval

So, what does this mean for clinicians in 2013? That increased caution about use of colloids, particularly with HES, in critically ill patients is evident. However, crystalloids as alternative resuscitation fluids do not automatically confer increased safety to our patients.

Resuscitation with normal saline is associated with chloride excess that has been associated with adverse metabolic effects and potential nephrotoxicity [13].

To date, no high-quality RCT has been conducted comparing the effects of saline, the most commonly used crystalloid globally, versus "balanced" salt solutions. This is a further fundamental research question that needs to be addressed.

As the optimal type of resuscitation fluid remains uncertain, more attention needs to be given to the dose and volumes administered.

Fluids accumulate over time. This is associated with development of interstitial oedema and applies to both colloids and crystalloids. There is an increasing body of observational evidence suggesting that excess use of intravenous fluids is associated with adverse outcomes [14]. Accumulation of HES within the reticulo-endothelial system is implicated in adverse events and toxicity.

Tetrastarches continue to be widely used in surgical patients undergoing general anaesthesia. In the light of data in critically ill patients, there is an imperative to evaluate their safety and efficacy in large RCTs powered for patient-centred outcomes relevant to perioperative patients.

Итак, что же это означает для клиницистов в 2013 году? Что **увеличивается осторожность при использовании коллоидов коллоидов, в частности, с ГЭК больных в критическом состоянии.**

Однако сводная таблица систематических обзоров и мета-анализов РКИ, опубликованных в 2013 году показывает отсутствие разницы в летальности и необходимости ЗПТ при использовании ГЭК другими инфузионными средами.

Кристаллоиды как альтернативные жидкости для инфузионной терапии не могут быть признаны автоматически безопасными.

Применение физиологического раствора связана с избытком хлорида, что связано с неблагоприятными метаболические эффекты и потенциальной нефротоксичностью .

На сегодняшний день нет качественных РКИ по сравнению эффектов физиологического раствора против" сбалансированных" солевых растворов

Жидкости накапливаются с течением времени. Это связано с развитием интерстициального отека и относится как к коллоидам и кристаллоидам.

Существует возрастающее число обсервационное доказательств того, что избыточное использование внутривенных инфузий связано с неблагоприятными исходами.

Intensive Care Med (2014) 40:256–259
DOI 10.1007/s00134-013-3167-6

Hydroxyethyl starch: putting patient safety first

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Konrad Reinhart
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Second EMA–PRAC review position

Following an appeal by companies that manufacture HES, the EMA–PRAC convened a second meeting using different advisors. The recommendations from this are that (1) HES may continue to be used in severe haemorrhage at the discretion of the treating physician and (2) its continued use in the perioperative environment must be subject to further research including monitoring of renal function for 90 days [9]. These recommendations received majority approval by the EMA's Coordination Group for Mutual Recognition and Decentralised Procedures—Human (CMDh) [10] and will be sent to the European Commission for ratification.

Вторая позиция EMA-PRAC

После апелляции компаний, которые производят ГЭК, EMA-PRAC созвало второе совещание с экспертами.
Рекомендации :
(1) ГЭК могут по-прежнему использоваться при массивном кровотечении по усмотрению лечащего врача и
(2) Продолжение использования ГЭК в периоперационном периоде должна подлежать дальнейшему исследованию, включая мониторинг функции почек в течение 90 дней [9].

Intensive Care Med (2015) 41:1611–1619
DOI 10.1007/s00134-015-3878-y

ORIGINAL

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Resuscitation fluid use in Australian and New Zealand Intensive Care Units between 2007 and 2013

Conclusion: Fluid resuscitation practice in Australia and New Zeal- and adult ICUs has changed over the 6-year study period. Crystalloid use increased primarily due to an increase in the use of buffered salt solutions while overall the use of colloid has decreased.

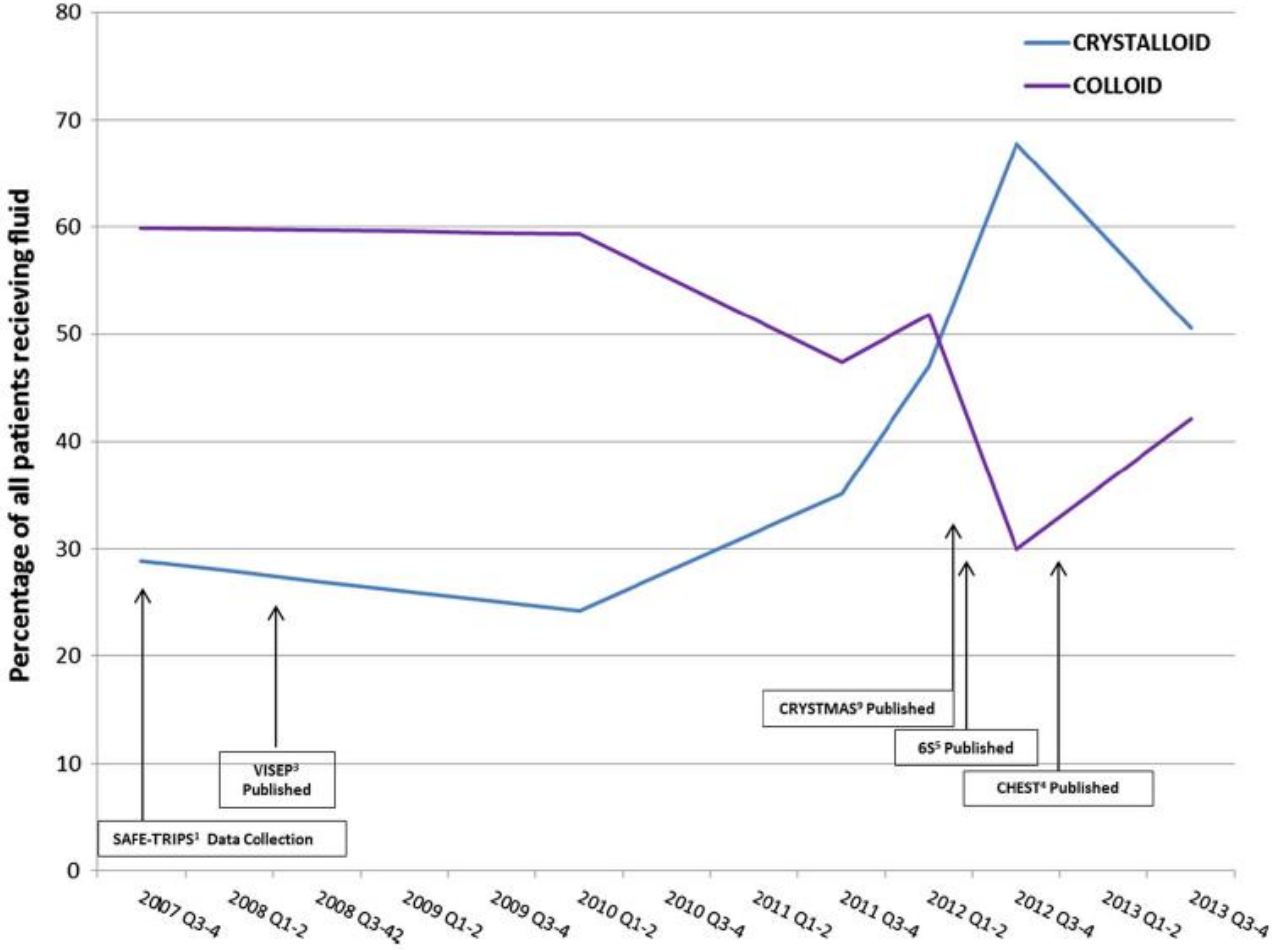

Fig. 1 Time trend of crystalloid and colloid administered between 2007 and 2013 in relation to key published research

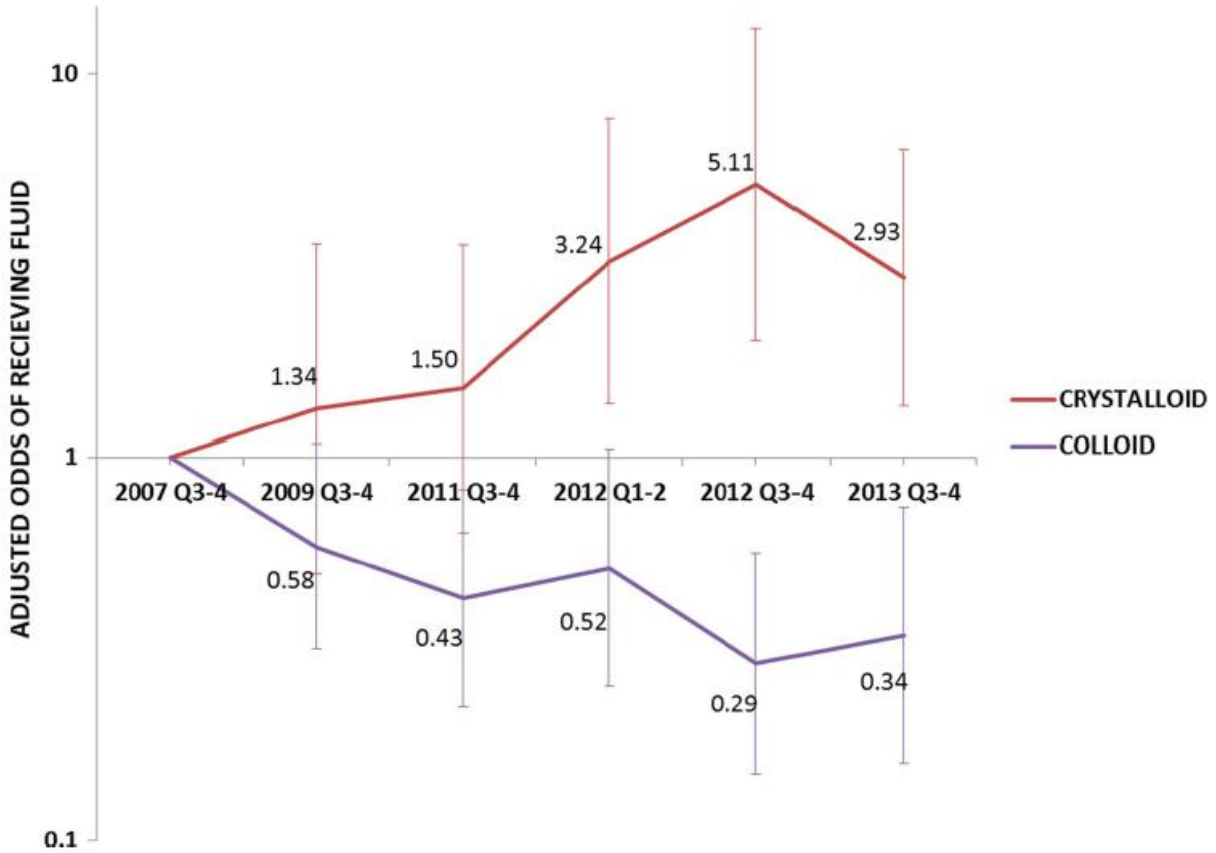

Fig. 2 Adjusted odds of patients receiving a crystalloid or colloid for fluid resuscitation

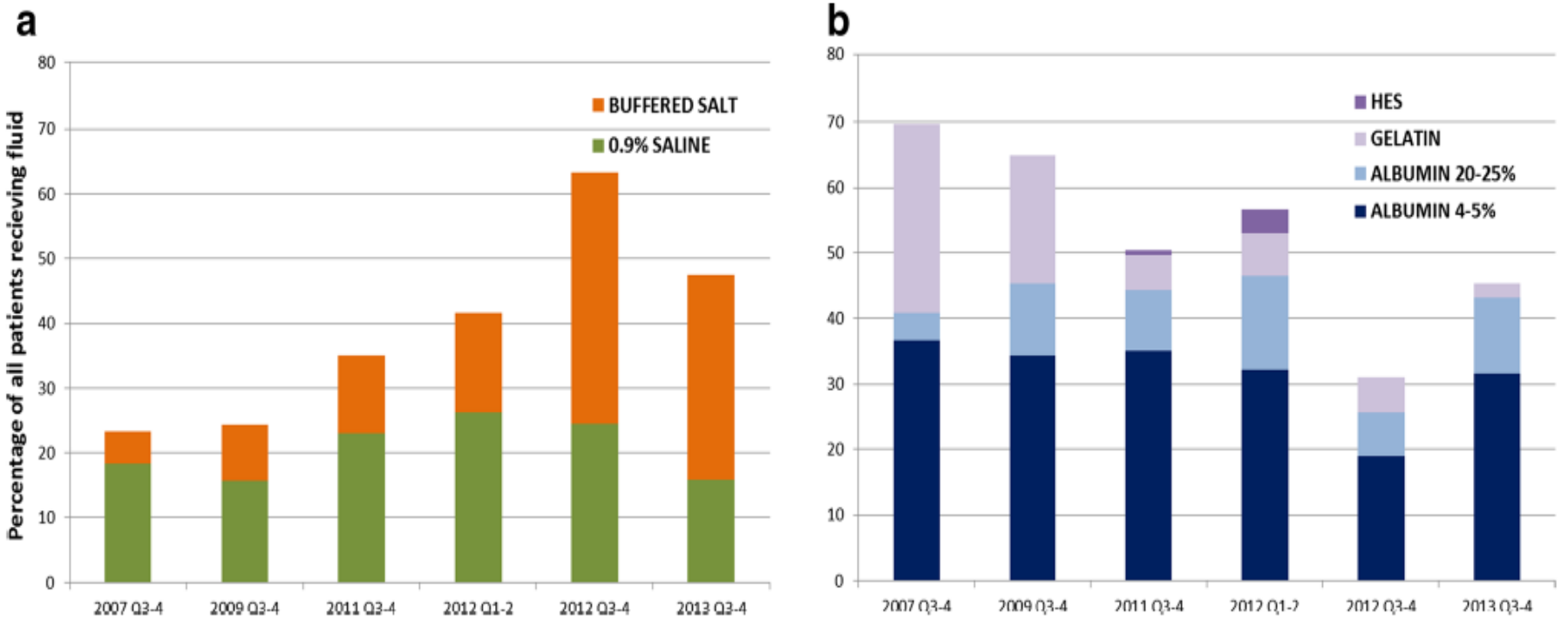

Fig. 3 Proportion of all patients receiving selected types of crystalloid (**a**) and colloid (**b**) solutions between 2007 and 2013. Only selected fluids are reported and percentages do not match Fig. 1 as patients can have more than one type of fluid administered

Li et al. BMC Anesthesiology
DOI 10.1186/s12871-015-0053-5

BMC Anesthesiology

RESEARCH ARTICLE Open Access

Ringer's lactate, but not hydroxyethyl starch, prolongs the food intolerance time after major abdominal surgery; an open-labelled clinical trial

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Кристаллоиды - не так все просто!

Abstract

Background: The infusion of large amounts of Ringer's lactate prolongs the functional gastrointestinal recovery time and increases the number of complications after open abdominal surgery. We performed an open-labelled clinical trial to determine whether hydroxyethyl starch or Ringer's lactate exerts these adverse effects when the surgery is performed by laparoscopy.

Methods: Eighty-eight patients scheduled for major abdominal cancer surgery (83% by laparoscopy) received a first-line fluid treatment with 9 ml/kg of either 6% hydroxyethyl starch 130/0.4 (Voluven) or Ringer's lactate, just after induction of anaesthesia; this was followed by a second-line infusion with 12 ml/kg of either starch or Ringer's lactate over 1 hour. Further therapy was managed at the discretion of the attending anaesthetist. Outcome data consisted of postoperative gastrointestinal recovery time, complications and length of hospital stay.

Results: The order of the infusions had no impact on the outcome. Both the administration of ≥ 2 L of Ringer's lactate and the development of a surgical complication were associated with a longer time period of paralytic ileus and food intolerance (two-way ANOVA, $P < 0.02$), but only surgical complications prolonged the length of hospital stay ($P < 0.001$). The independent effect of Ringer's lactate and complications of food intolerance time amounted to 2 days each. The infusion of ≥ 1 L of hydroxyethyl starch did not adversely affect gastrointestinal recovery.

Conclusions: Ringer's lactate, but not hydroxyethyl starch, prolonged the gastrointestinal recovery time in patients undergoing laparoscopic cancer surgery. Surgical complications prolonged the hospital stay.

Table 2 Comparison of operations with and without postoperative complications

	No complications	Complications	ANOVA
N	66	22	
Age (years)	58 (12)	64 (9)	$P < 0.05$
Body weight (kg)	60 (9)	59 (6)	NS
Males (per cent)	71	59	
Anaesthesia time (min)	250 (68)	295 (72)	$P < 0.01$
Operating time (min)	190 (65)	235 (78)	$P < 0.01$
Blood loss (ml)	175 (107)	229 (131)	
Urine output (ml)	426 (225)	614 (359)	$P < 0.02$
Starch (ml)	860 (328)	1000 (267)	NS
Ringer's lactate (ml)	1655 (681)	1590 (453)	NS
Erythrocytes (N; ml)	6; 432 (264)	6; 466 (272)	
Plasma (N; ml)	3; 335 (228)	2; 213 (205)	
Time in PACU (min)	76 (35)	66 (27)	NS
Paralytic ileus (days)	3.1 (1.1)	3.8 (1.3)	$P < 0.01$
Food intolerance (days)	4.6 (2.2)	6.2 (3.2)	$P < 0.03$
Length of hospital stay (days)	12.7 (3.4)	15.6 (3.9)	$P < 0.002$

Data are the mean (SD) or the actual number (N) of patients. NS = not statistically significant.

Table 3 Operations with infusion of either < 2 L or ≥ 2 L of Ringer's lactate

	Ringer's lactate <2 L	Ringer's lactate ≥2 L	ANOVA
N	55	33	
Age (years)	58 (12)	63 (10)	$P < 0.05$
Body weight (kg)	60 (8)	59 (7)	NS
Males (per cent)	67	70	
Anaesthesia time (min)	258 (74)	268 (68)	NS
Operating time (min)	196 (76)	211 (63)	NS
Blood loss (ml)	167 (93)	221 (138)	$P < 0.05$
Urine output (ml)	444 (258)	502 (286)	NS
Starch (ml)	1009 (225)	705 (361)	$P < 0.001$
Ringer's lactate (ml)	1236 (358)	2310 (348)	$P < 0.001$
Erythrocytes (N; ml)	4; 183 (416)	6; 416 (40)	
Plasma (N; ml)	6; 367 (175)	7; 518 (308)	
Time in PACU (min)	66 (30)	86 (37)	$P < 0.01$
Paralytic ileus (days)	3.1 (1.2)	3.7 (1.1)	$P < 0.023$
Food intolerance (days)	4.4 (2.1)	6.1 (3.0)	$P < 0.004$
Complications per operation	0.27	0.21	NS
Infectious complications (N)	7	4	
Bleeding complications (N)	3	3	
Length of hospital stay (days)	13.3 (3.7)	13.7 (3.9)	NS

Data are the mean (SD) or N = the number of patients. NS = not statistically significant.

complications had a prolonged period of paralytic ileus

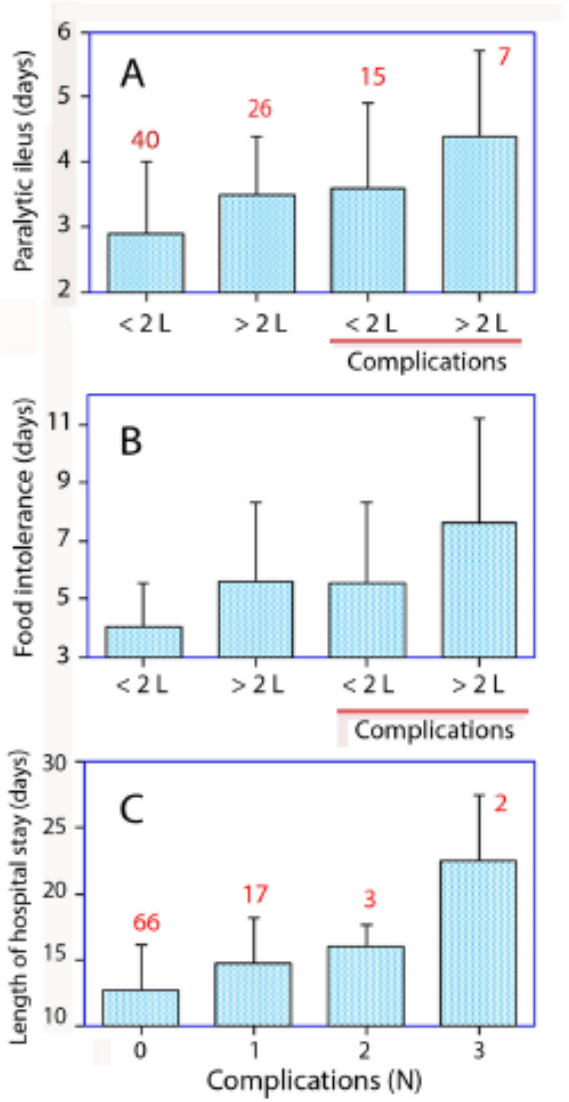


Figure 1 Duration of paralytic ileus **(A)** and food intolerance **(B)** depending on infusion of either < 2 L or ≥ 2 L of Ringer's lactate during surgery and whether postoperative complications developed. **(C)** The length of hospital stay increased with the number of complications (ANOVA $P < 0.002$). Data are the mean, and the error bars are the standard deviation. The number of patients in each group is indicated in red.

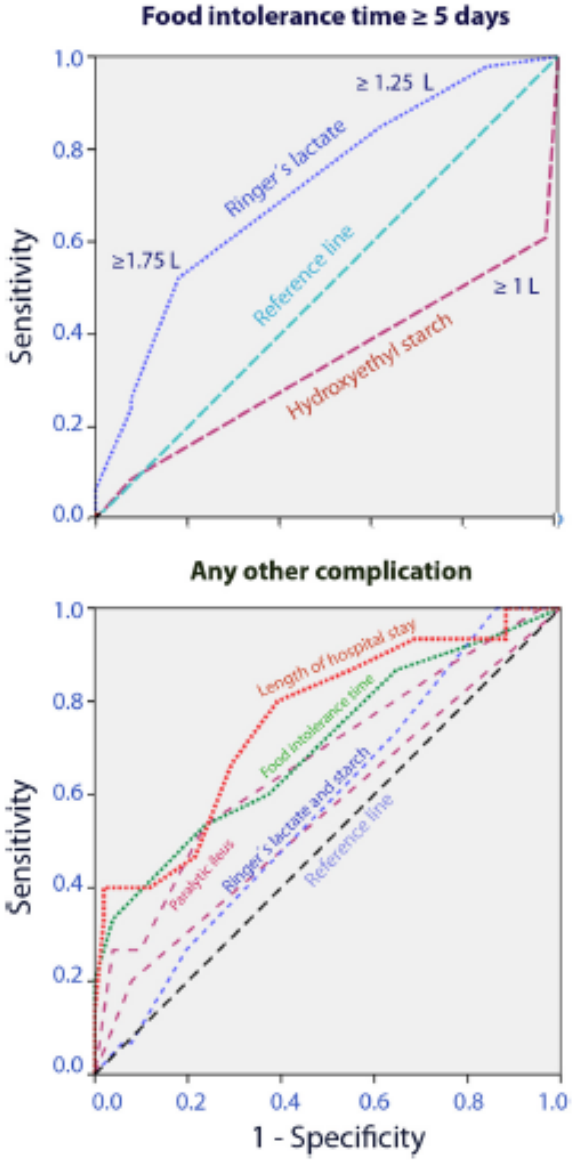


Figure 2 ROC curves illustrating the fluid volume needed **(A)** to predict prolongation of the postoperative period of food intolerance to ≥ 5 days and **(B)** to predict the occurrence of any other complication. Closeness to the reference line implies lack of relationship.

Ограничения по применению препаратов ГЭК в Российской Федерации – это реальность

МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РОССИЙСКОЙ ФЕДЕРАЦИИ

Рахмановский пер., 3, г. Москва, ГСП-4, 127994
тел.: 628-44-53, факс: 628-50-58

На № 06.08.2013 от № 20-2-2079227-О

Заявителям регистрации и производителям лекарственных препаратов Гидроксиэтилкрахмала (ГЭК)

В связи с письмом ФГБУ «Научный центр экспертизы средств медицинского применения» №8151 от 31.07.2013 Департамент государственного регулирования обращения лекарственных средств сообщает о необходимости внесения изменений в инструкции по применению зарегистрированных в Российской Федерации лекарственных препаратов для медицинского применения (ограничения по применению), содержащих в качестве действующего вещества гидроксиэтилкрахмал (ГЭК).

Учитывая вышеизложенное, в настоящее время считаем целесообразным внести в инструкции по применению лекарственных препаратов ГЭК ограничения по применению, а именно:

- не применять у тяжело больных пациентов, в том числе при сепсисе или находящихся в палатах интенсивной терапии;
- не применять у пациентов с нарушениями функции почек;
- отменять при первых признаках поражения почек;
- указать на необходимость мониторинга функции почек на протяжении 90 дней после вливания лекарственного препарата;
- не применять при открытых операциях на сердце;
- отменять при первых признаках коагулопатии.

Вместе с тем итоговое регуляторное решение Минздрава России целесообразно принять с учетом окончательного решения относительно продолжения применения лекарственных препаратов ГЭК в ЕС.

Первый заместитель
генерального директора

В.А.Меркулов

Ограничения по применению препаратов ГЭК в соответствии с письмом МЗ РФ

Учитывая вышеизложенное, в настоящее время считаем целесообразным внести в инструкции по применению лекарственных препаратов ГЭК ограничения по применению, а именно:

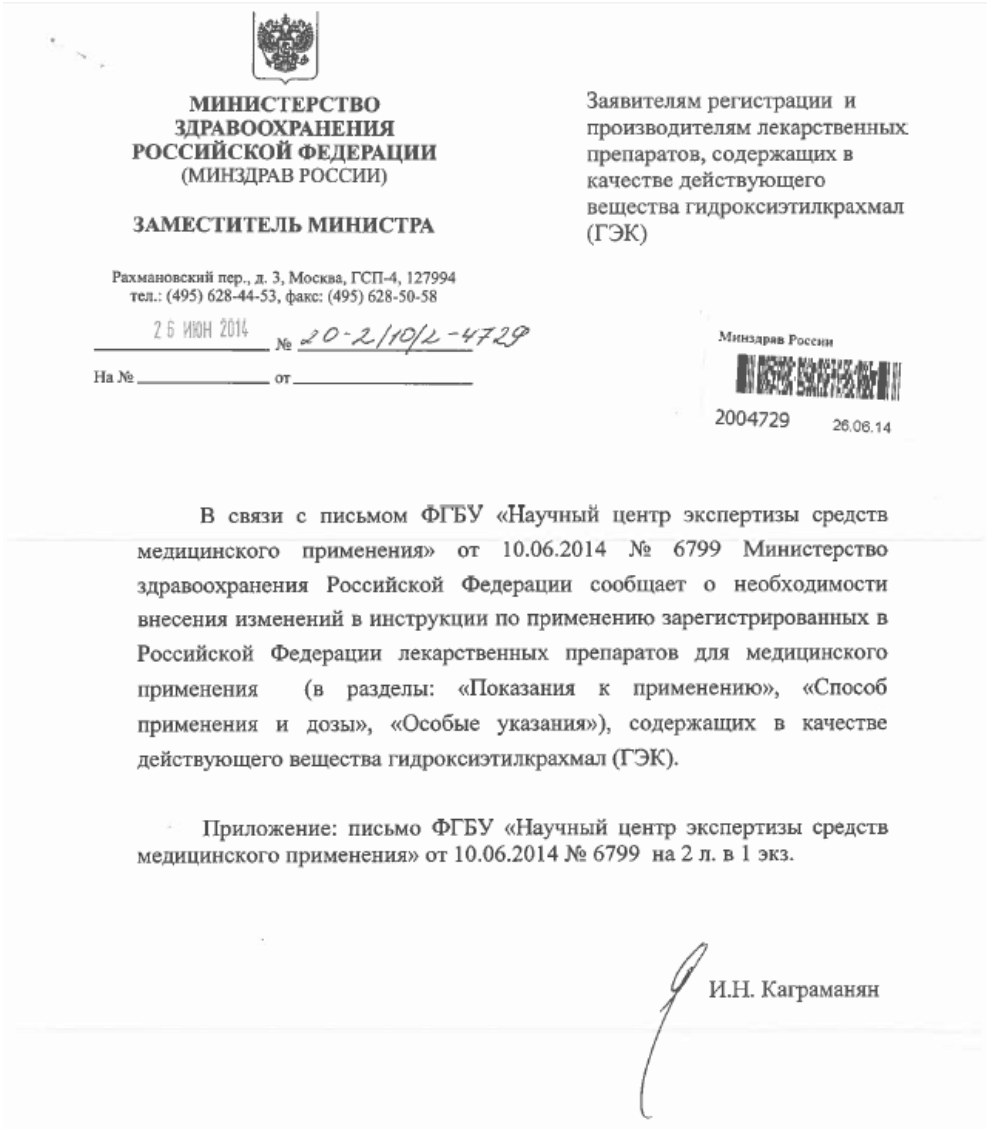
- не применять у тяжело больных пациентов, в том числе при сепсисе или находящихся в палатах интенсивной терапии;
- не применять у пациентов с нарушениями функции почек;
- отменять при первых признаках поражения почек;
- указать на необходимость мониторинга функции почек на протяжении 90 дней после вливания лекарственного препарата;
- не применять при открытых операциях на сердце;
- отменять при первых признаках коагулопатии.

Вместе с тем итоговое регуляторное решение Минздрава России целесообразно принять с учетом окончательного решения относительно продолжения применения лекарственных препаратов ГЭК в ЕС.

Первый заместитель
генерального директора

В.А.Меркулов

Письмо МЗ РФ о внесении дополнительных изменений в инструкции по применению ГЭК



МИНИСТЕРСТВО ЗДРАВООХРАНЕНИЯ РОССИЙСКОЙ ФЕДЕРАЦИИ
(МИНЗДРАВ РОССИИ)

ЗАМЕСТИТЕЛЬ МИНИСТРА

Рахмановский пер., д. 3, Москва, ГСП-4, 127994
тел.: (495) 628-44-53, факс: (495) 628-50-58

26 ИЮН 2014 № 20-2/10/2-4729

На № _____ от _____

Заявителям регистрации и производителям лекарственных препаратов, содержащих в качестве действующего вещества гидроксиэтилкрахмал (ГЭК)

Минздрав России
2004729 26.06.14

В связи с письмом ФГБУ «Научный центр экспертизы средств медицинского применения» от 10.06.2014 № 6799 Министерство здравоохранения Российской Федерации сообщает о необходимости внесения изменений в инструкции по применению зарегистрированных в Российской Федерации лекарственных препаратов для медицинского применения (в разделы: «Показания к применению», «Способ применения и дозы», «Особые указания»), содержащих в качестве действующего вещества гидроксиэтилкрахмал (ГЭК).

Приложение: письмо ФГБУ «Научный центр экспертизы средств медицинского применения» от 10.06.2014 № 6799 на 2 л. в 1 экз.

И.Н. Каграманян

Дополнительная информация, обязательная для внесения в инструкции по применению препаратов ГЭК в Российской Федерации

Согласно актуальной информации об опыте клинического применения препаратов, содержащих в качестве активного вещества гидроксиэтилкрахмала (ГЭК), и в связи с появлением новых сведений по безопасности и эффективности их применения, отраженных в действующих инструкциях препаратов ГЭК, зарегистрированных в Европейском союзе [1,2,3,4 и др.], необходимо пересмотреть и исправить показания к применению всех препаратов на основе ГЭК (независимо от концентрации, молекулярной массы и степени замещения) и оставить только следующее: «Лечение гиповолемии при острой кровопотере, если применение растворов кристаллоидов является недостаточным». Это требует также исправления раздела «Способ применения и дозы» и исключения из других разделов сведений о возможности (условиях) применения препарата по другим показаниям.

Ввиду тяжести нежелательных реакций, обусловленных применением гидроксиэтилкрахмала, в разделе «Особые указания» необходимо указывать следующую фразу: «Адекватные долгосрочные данные о применении препаратов гидроксиэтилкрахмала у пациентов, подвергшихся хирургическому вмешательству или получивших травму, отсутствуют. Ожидаемую пользу лечения следует тщательно соотносить с неопределенной долгосрочной безопасностью. Следует рассмотреть возможность применения других доступных терапевтических мер».

Intensive Care Med (2015) 41:1529–1537
DOI 10.1007/s00134-015-3850-x

SEVEN-DAY PROFILE PUBLICATION

Maurizio Cecconi
Christoph Hofer
Jean-Louis Teboul
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Cesar Aldecoa
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Jean-Yves Lefrant
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on behalf of the FENICE Investigators
and the ESICM Trial Group

Fluid challenges in intensive care: the FENICE study

A global inception cohort study

in intensive care units. There are clear benefits and harms from fluid therapy. Limited data on the indication, type, amount and rate of an FC in critically ill patients exist in the literature. The primary aim was to evaluate how physicians conduct FCs in terms of type, volume, and rate of given fluid; the secondary aim was to evaluate variables used to trigger an FC and to compare the proportion of patients receiving further fluid administration based on the response to the FC. *Methods:* This was an observational study conducted in ICUs around the world. Each participating unit entered a maximum of 20 patients with one FC. *Results:* 2213 patients were enrolled and analyzed in the study. The median [interquartile range] amount of fluid given during an FC was 500 ml (500–1000). The median time was 24 min (40–60 min), and the median rate of FC was 1000 [500–1333] ml/h. The main indication for FC was hypotension in 1211 (59 %, CI 57–61 %). In 43 % (CI 41–45 %) of the cases no hemodynamic variable was used. Static markers of preload were used in 785 of 2213 cases (36 %, CI 34–37 %). Dynamic indices of preload responsiveness were used in 483 of 2213 cases (22 %, CI 20–24 %). No safety variable for the FC was used in 72 % (CI 70–74 %) of the cases. There was no statistically significant difference in the proportion of patients who received further fluids after the FC between those with a positive, with an uncertain or with a negatively judged response. *Conclusions:* The current practice and evaluation of FC in critically ill patients are highly variable. Prediction of fluid responsiveness is not used routinely, safety limits are rarely used, and information from previous failed FCs is not always taken into account.

Table 2 Fluid challenge ($N = 2213$) characteristics

Volume (ml), median [IQR]	500 [500–999]		
Rate (ml/h), median [IQR]	1000 [500–1333]		
Type of fluids	*n*	% Of category	% All fluids
Crystalloids	1713		74.3 [72.5–76.1]
NaCl 0.9 %	786	45.9 [43.5–48.3]	34.1 [32.1–36.1]
Balanced	916	53.5 [51.1–55.9]	39.8 [37.8–41.8]
G5 % DW	4	0.2 [0.0–0.4]	0.2 [0.0–0.4]
G5 % NaCl 0.45 %	7	0.4 [0.1–0.7]	0.3 [0.1–0.5]
Colloids	591		25.6 [23.8–27.4]
HES	249	42.1 [38.1–46.1]	10.8 [9.5–12.1]
Albumin 4–5 %	101	17.1 [14.1–20.1]	4.3 [3.5–5.2]
Gelatin	203	34.3 [30.5–38.1]	8.8 [7.6–10.0]
Dextran	13	2.2 [1.0–3.4]	0.5 [0.2–0.8]
Albumin 20 %	25	4.2 [2.6–5.8]	1.1 [0.7–1.5]

NaCl saline, *balanced* crystalloids with chloride concentration lower than saline (i.e., Plasma Lyte, Hartman's), *G5 %* glucose 5 %, *DW* dextrose in water, *HES* hydroxyethyl starch

Table 3 Indications and variables used to predict fluid responsiveness ($N = 2213$)

Indication			*n* (%)
Hypotension			1211 (58.7 [56.7–60.8])
Weaning vasopressor			146 (7.1 [6.0–8.2])
Cardiac output			62 (3.0) [2.3–3.7]
Oliguria			372 (18.0 [16.4–19.6])
Skin mottling			36 (1.7 [1.2–2.2])
Lactate			128 (6.2 [5.2–7.2])
$SvO_2/ScvO_2$			10 (0.5 [0.2–0.8])
SVV/PPV			37 (1.8 [1.3–2.4])
CVP/PAOP			60 (2.9 [2.2–3.6])
Hemodynamic variable used to predict fluid responsiveness	*n*	% Of category	% All
No variable used	945		42.7 [40.6–44.8]
Any variable used	1268		57.3 [55.2–59.4]
Static	785		35.5 [33.5–37.5]
CVP	572	89.9 [87.8–92.0]	25.8 [24.0–27.6]
PAOP	31	4.9 [3.4–6.4]	1.4 [0.9–1.9]
GEDVI	33	5.2 [3.6–6.8]	1.5 [1.0–2.0]
Other	149	23.4 [20.4–26.4]	6.7 [5.7–7.8]
Dynamic	483		21.9 [20.2–23.6]
PPV	88	18.2 [14.8–21.6]	4.0 [3.2–4.8]
SVV	88	18.2 [14.8–21.6]	4.0 [3.2–4.8]
PPV + SVV	24	5.0 [3.1–6.9]	1.1 [0.7–1.5]
PLR	238	49.3 [44.8–53.8]	10.7 [9.4–12.0]
Echo variables	45	9.3 [6.7–11.9]	2.0 [1.4–2.6]

SvO_2 mixed venous oxygen saturation, *$ScvO_2$* central venous oxygen saturation, *SVV* stroke volume variation, *PPV* pulse pressure variation, *CVP* central venous pressure, *PAOP* pulmonary artery occlusion pressure, *GEDVI* global end diastolic volume, *PLR* passive leg raising, *Echo* echocardiography

Резюме – показания для ГЭК

- В процессе оперативных вмешательств
- Острая массивная кровопотеря
- Тяжелый сепсис без риска возникновения ОПН
- При критических состояниях, требующих инфузионной терапии, без риска кровотечения
- Использовать современные ГЭК и избегать высоких доз (более 15 мл/кг)

regional clinical hospital since 1942

Крас ГМУ

Благодарю за внимание!!!

Вопросы?