Bioestadística para no Estadísticos

LECTURA CRÍTICA

Grupo 7

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Esquema de la presentación

1. Resumen del artículo
2. Lectura crítica I: 4 ejemplos de cumplimiento de la CONSORT
3. Lectura crítica II: 4 ejemplos de no cumplimiento de la CONSORT
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ARTICULO:

"Effects on routine prophylactic supplementation with iron and folic acid on admission to hospital and mortality in preschool children in a high malaria transmission setting: community-based, randomised, placebo-controlled trial."

Sazawal *et al.* 2006 *Lancet* 367: 133-143

Antecedentes

- **Anaemia caused by iron deficiency is common in children younger than age 5 years in eastern Africa.**

- **Concern that universal supplementation of children with iron and folic acid in areas of high malaria transmission might be harmful.**

Métodos

- **Randomised, placebo-controlled trial of children aged 1–35 months and living in Pemba, Zanzibar.**
- **Randomization of children to daily oral supplementation with:**
  1. **Iron and folic acid (n=7950)**
  2. **Iron, folic acid, and zinc (n=8120)**
  3. **Placebo (n=8006)**
  4. **Zinc (n=758)**
- **Primary endpoints: all-cause mortality and admission to hospital.**
- **Analyses were by intention to treat.**

Resultados

- **The iron and folic acid-containing groups of the trial were stopped early on Aug 19, 2003, on the recommendation of the data and safety monitoring board. To this date, 24 076 children contributed a follow-up of 25 524 child-years.**

- **Those who received iron and folic acid with or without zinc were 12% (95% CI 2–23, p=0·02) more likely to die or need treatment in hospital for an adverse event and 11% (1–23%, p=0·03) more likely to be admitted tohospital; there were also 15% (7 to 41, p=0·19) more deaths in these groups.**

Conclusiones

- **Routine supplementation with iron and folic acid in preschool children in a population with high rates of malaria can result in an increased risk of severe illness and death.**

- **In the presence of an active programme to detect and treat malaria and other infections, iron-deficient and anaemic children can benefit from supplementation.**

- **However, supplementation of those who are not iron deficient might be harmful. As such, current guidelines for universal supplementation with iron and folic acid should be revised.**

Lectura crítica: Ejemplos del correcto cumplimiento de la lista CONSORT

Punto 1: Título / Resumen

Effects of routine prophylactic supplementation with iron and folic acid on admission to hospital and mortality in preschool children in a high malaria transmission setting: community-based, randomised, placebo-controlled trial

Sunil Sazawal, Robert E Black, Mahdi Ramsan, Hababu M Chwaya, Rebecca J Stoltzfus, Arup Dutta, Usha Dhingra, Ibrahim Kabole, Saikat Deb, Mashavi K Othman, Fatma M Kabole

Título:
Se indica que la asignación ha sido aleatorizada

Resumen

Background *Anaemia caused by iron deficiency is common in children younger than age 5 years in eastern Africa. However, there is concern that universal supplementation of children with iron and folic acid in areas of high malaria transmission might be harmful.*

Methods *We did a randomised, placebo-controlled trial, of children aged 1–35 months and living in Pemba, Zanzibar. We assigned children to daily oral supplementation with: iron (12·5 mg) and folic acid (50 g; n=7950), iron, folic acid, and zinc (n=8120), or placebo (n=8006); children aged 1–11 months received half the dose. Our primary endpoints were all-cause mortality and admission to hospital. Analyses were by intention to treat. This study is registered as an International Standard Randomised Controlled Trial, number ISRCTN59549825.*

Findings *The iron and folic acid-containing groups of the trial were stopped early on Aug 19, 2003, on the recommendation of the data and safety monitoring board. To this date, 24 076 children contributed a follow-up of 25 524 child-years. Those who received iron and folic acid with or without zinc were 12% (95% CI 2–23, p=0·02) more likely to die or need treatment in hospital for an adverse event and 11% (1–23%, p=0·03) more likely to be admitted to hospital; there were also 15% (7 to 41, p=0·19) more deaths in these groups.*

Interpretation *Routine supplementation with iron and folic acid in preschool children in a population with high rates of malaria can result in an increased risk of severe illness and death. In the presence of an active programme to detect and treat malaria and other infections, iron-deficient and anaemic children can benefit from supplementation. However, supplementation of those who are not iron deficient might be harmful. As such, current guidelines for universal supplementation with iron and folic acid should be revised.*

Resumen: Estructurado

Punto 3: Participantes

Criterios de Selección:

"we invited all children aged 1-35 months, likely to remain resident on the island, and not having severe malnutrition needing rehabilitation to participate" ..."We invited all new births in the study area to be enrolled at age 1 month."

Localización y descripción del área geográfica del estudio:

"…trial on Pemba, the smaller of the two islands of the Zanzibar archipelago."

"The island has a population of about 350 000, most of whom are Afro-Shiraji muslims, and has a tropical climate. Malaria is holoendemic with year-round transmission that is highest in June–September.17 The intensity of malaria transmission is representative of coastal east Africa, where a yearly inoculation rate of 405 infective bites per person has been described.18 Plasmodium falciparum accounts for nearly all serious cases of clinical malaria. Governmental malaria-control activities at the time of the trial were based on diagnosis and treatment of suspected cases. A baseline census, including a birth history for women of reproductive age, indicated an infant mortality rate of 89 per 1000 livebirths"

Correcta definición de los participantes, ámbito y lugar donde se recogieron los datos.

Punto 8: Aleatorización

Tipo de aleatorización:

“ Randomisation was by household”

Método:

“We used a permuted block allocation sequence with a block length of 16 that was generated by WHO”

Punto 14: Reclutamiento

Fechas de reclutamiento

a) Estudio Principal:

"*Enrolment into the main study was undertaken one district at a time, starting in January, 2002, and finishing in May, 2002*"

b) Subestudio:

"*We started enrolment into the substudy and the first round of blood collection in March, and completed it in November, 2002*"

Interrupción del ensayo y tiempos de seguimiento:

"*On the recommendation of the data and safety monitoring board, we stopped treatment in the iron, folic acid, and zinc group and in the iron and folic acid group on Aug 19, 2003, converting the trial into one with two arms—zinc versus placebo.*" ... "*At the time of stopping the trial, mean duration of follow-up in the study was 383 days (SD 171). The total follow-up was 25 524 child-years (figure 1); follow-up for age 1–5 months, 6–11 months, and 12 months or older was 527, 2545, and 22 452 child-years, respectively*".

Lectura crítica:
Ejemplos del incorrecto cumplimiento de la lista CONSORT

Punto 2: Antecedentes

- Revisión bilbliográfica y estado actual del tema

Se hace una breve revisión de los estudios previos realizados

- Justificación del ensayo

Se plantea la necesidad de realizar ensayos específicamente diseñados para evaluar el efecto de la suplementación con Fe sobre la morbi-mortalidad en zonas endémicas de malaria.

No se justifica el diseño del estudio : ¿Cuál es el motivo por el que un grupo recibe Zinc? Hipótesis?

Punto 4: Intervenciones

- Descripción de las intervenciones

Escasa, poco detalle. Llama la atención la frase:

"*We gave no specific instructions as to when tablets should be taken*"

¿Cómo y cuando se administraron los suplementos de hierro, ácido fólico?

- Duración/Seguimiento de los participantes

No se indica el tiempo previsto de seguimiento.

Punto 11: Cegado (Enmascaramiento)

- Cegado del investigador y los participantes

"To ensure masking, we labelled the strips of supplements with 16 letter codes-four for each of the groups“

" the supplement code was not known to the investigators"

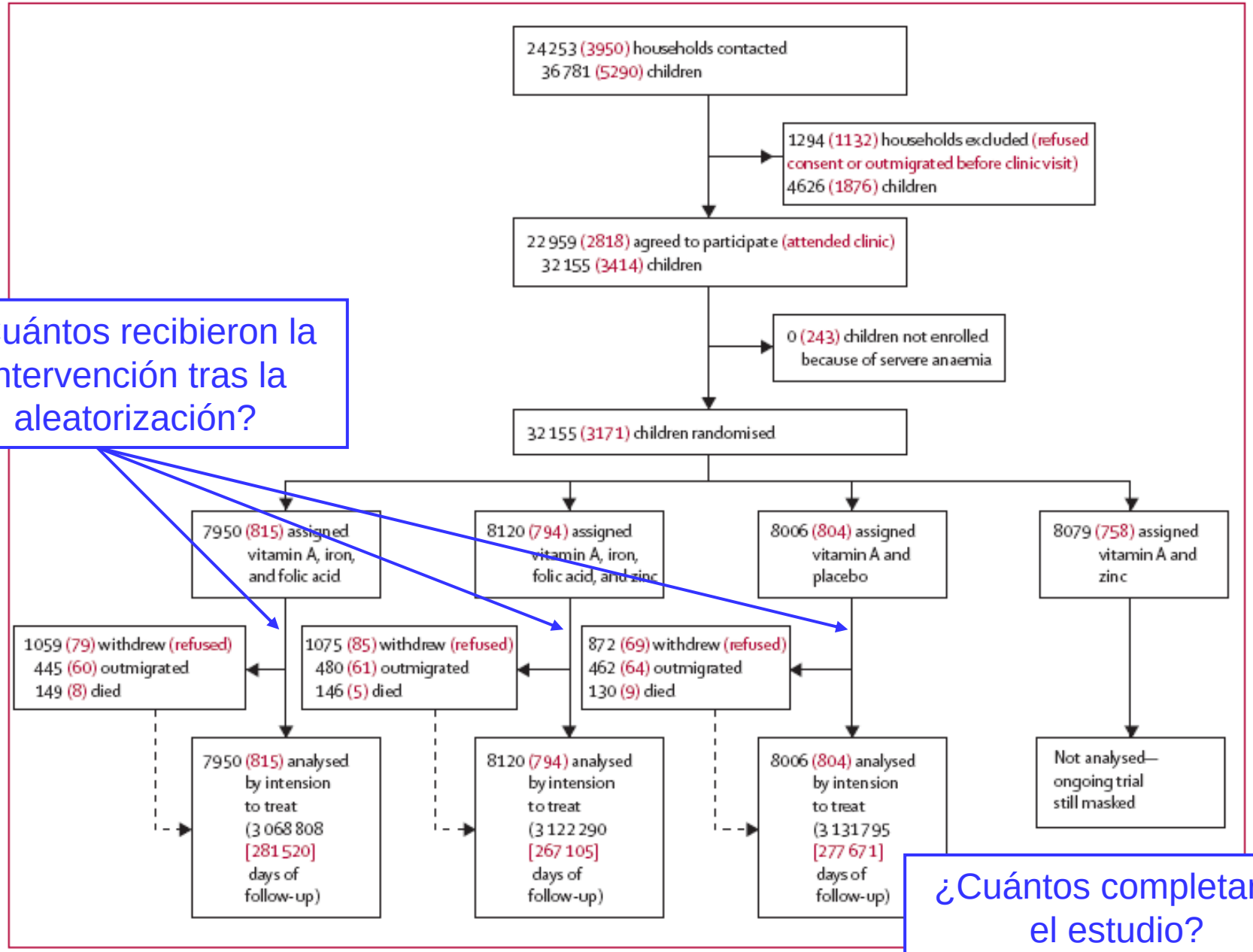
- ¿Y el resto del personal clave del estudio?

No se indica si los administradores de la intervención, los evaluadores y estadísticos estaban también cegados.

¿El enmascaramiento se realizó con éxito?

Punto 13: Flujo de participantes

¿Cuántos recibieron la intervención tras la aleatorización?



¿Cuántos completaron el estudio?

Figure 1: Trial profile
Text in red refers to substudy.

Lista CONSORT

CONSORT	Mejorable	OK	Comentarios
1. Titulo / Resumen		V	
2. Antecedentes	X		No se justifica del todo el diseño del estudio
3. Participantes		V	
4. Intervenciones	X		No quedan excesivamente claras las instrucciones impartidas, ni las pautas de toma de la suplementación.
5. Objetivos	X		Aunque están explicitados podrían describirse de manera más detallada.
6. Resultados		V	
7. Tamaño Muestral		V	
8. Aleatorización		V	
9. Asignación Oculta		V	
10. Implementación	X		El artículo no explica quien incluyó a los participantes ni quien les asignó un grupo de intervención.
11. Enmascaramiento	X		Sólo se tiene constancia del cegamiento de investigadores y participantes.

CONSORT	Mejorable	OK	Comentarios
12. Métodos Estadísticos	X		No se especifican los métodos de análisis que se preveían usar antes de la interrupción del ensayo.
13. Flujo de Participantes	X	V	Faltan algunos datos deseables en este tipo de diagrama, como el número participantes que recibieron la intervención.
14. Reclutamiento		V	
15. Datos Basales		V	
16. Números Analizados		V	Análisis por ITT
17. Resultados y Estimación	X		Los resultados reflejan los del análisis preliminar. No se mencionan los análisis/resultados previstos antes de administrar la intervención.
18. Análisis Complementarios		V	
19. Eventos Adversos		V	
20. Interpretación		V	
21. Generalización		V	
22. Evidencia Global		V	

Valoración Global del artículo

- Situación especial: estudio interrumpido por consejo del DSMB.

- En general el artículo sigue la lista CONSORT

- Falta información importante sobre las hipótesis del estudio que expliquen el diseño del ensayo (antecedentes).

- Descripción de las intervenciones escasa

- Análisis realizados y presentados no s ejustifican por el diseño del estudio

Gracias por vuestra atención.