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CRITICAL READING: TREATMENT OF VOMITING

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Abstract: This paper critically reviews a scientific article based on the following question: Is ondansetron the reference drug to address acute gastroenteritis in paediatric emergencies? The article by Freedman has been selected (Freedman et al., 2006). The results indicate a deficit in the methodology used when comparing ondansetron with placebo.

Keywords: Ondansetron, Emergency Treatment, Placebo.

LECTURA CRÍTICA: TRATAMIENTO DEL VÓMITO

Resumen: Se realiza la revisión de un artículo de revisión crítica partiendo de la siguiente pregunta: ¿Es el ondansetrón el fármaco de referencia para abordar la gastroenteritis aguda en las urgencias pediátricas? Se ha seleccionado el artículo de Freedman (Freedman et al., 2006). Los resultados aluden a un déficit en la metodología utilizada al comparar el ondansetrón con un placebo.

Palabras clave: Ondansetrón, Tratamiento de Urgencia, Placebo.

LEITURA CRÍTICA: TRATAMENTO DO VÓMITO

Resumo: É realizada a revisão de um artigo de revisão crítica tendo como base a seguinte pergunta: O ondansetron é o fármaco de referência para abordar a gastroenterite aguda nas urgências pediátricas? Foi selecionado o artigo de Freedman (Freedman et al., 2006). Os resultados indicam um déficit a nível da metodologia utilizada para comparar o ondansetron com um placebo.

Palavras-chave: Ondansetron, tratamento de urgência, placebo.

APPROACH TO THE PROBLEM

Although oral rehydration therapy is recommended for children with mild to moderate dehydration, it remains underused. Doctors in the emergency department are more likely to choose the intravenous route during oral rehydration when vomiting is a major symptom. In one survey, 36% of paediatricians reported that vomiting was a contraindication to oral rehydration. Therefore, a safe and effective method of controlling vomiting is likely to increase the utilisation rate and success of oral rehydration. This speeds up the approach in the emergency department and reduces the pressure in these units by discharging the child more quickly and safely.

One of the most popular medications due to its powerful antiemetic effect is ondansetron. However, several studies questioned its prescription in paediatric patients, due to its potential to generate heart arrhythmias and cause diarrhoea, among others, which becomes a relative contraindication in cases where diarrhoea is the predominant symptom, coupled with vomiting. This situation is very common in the approach to acute gastroenteritis in both paediatric and adult emergency departments.

In view of the foregoing, is ondansetron the reference drug to address acute gastroenteritis in paediatric emergencies? (Freedman, Adler, Seshadri, & Powell, 2006).

	Problem (P)	**Intervention (I)**	**Comparison (C)**	**Outcome (O)**
General approach	Treatment of vomiting in children	Administration of ondansetron	Placebo	Reduced presence and frequency of vomiting, improved oral intake, less need for intravenous fluid replacement.
Specific approach	Treatment of vomiting in children between 6 months and 10 years of age with acute gastroenteritis (in emergency departments)	Administration of oral ondansetron (orally dissolving tablets)	Placebo (same format)	

Source: (Freedman et al., 2006)

LET'S ANSWER THE QUESTION

Based on that question, we searched for evidence in reference sources and found the article by Freedman (Freedman et al., 2006), published in a very high-impact journal. This author has continued to publish studies in this line of research and has been included in several systematic reviews, including the systematic review of the AAP.

A quick reading of the article focusing on the abstract suggests some very promising conclusions that seem to suit our question: "In children with gastroenteritis and dehydration, a single dose of oral ondansetron reduces vomiting and facilitates oral rehydration and may thus be well suited for use in the emergency department." However, the methods section states: "We enrolled 215 children 6 months through 10

years of age who were treated in a pediatric emergency department for gastroenteritis and dehydration. After being randomly assigned to treatment with orally disintegrating ondansetron tablets or placebo…". Additionally, the results section indicates: "As compared with children who received placebo, children who received ondansetron were less likely to vomit (14 percent vs. 35 percent; relative risk, 0.40; 95 percent confidence interval, 0.26 to 0.61), vomited less often (mean number of episodes per child, 0.18 vs. 0.65; P<0.001), had greater oral intake (239 ml vs. 196 ml, P=0.001), and were less likely to be treated by intravenous rehydration (14 percent vs. 31 percent; relative risk, 0.46; 95 percent confidence interval, 0.26 to 0.79)."

There is therefore a clear difference in favour of this medication compared to placebo. Is this the answer we are looking for?

UNPRETENTIOUS CRITICAL READING

The "overall quality" of a clinical research study is a complex concept that includes three elements:

- The first element is clinical relevance, i.e. questions and, above all, research outcomes that are useful for clinical decision-making.
- The second element is "methodological quality" or the extent to which study design, realisation, and analysis minimise selection bias, measurement bias, and confusion bias, i.e., the extent to which the study is valid or, so to speak, the extent to which the results are credible.
- The third element is the applicability or transferability of the results to a specific patient (or to a specific group of patients), considering the other elements influencing the application of that evidence (the "representativeness" of the patients in that specific RCT, risk/benefit balance, availability, patient values, costs, etc.).

One of the key aspects that has been pointed out as "uncertain" in the reading is COMPARISON. This is very much the practical and ethical domain of the RCT. From the practising clinician's point of view, it only makes sense to compare new interventions with interventions with already proven effects, or at least with the usual treatments. This reproduces the real possible decision-making dilemma, i.e. new treatment versus usual treatment. Not using proven treatments in these comparisons would therefore be maleficent.

Comparative interventions reflect the point of friction between two different dialectic styles, i.e. that of clinical practice and that of clinical research. Comparative interventions are therefore a vital issue that determines the study design in a number of ways.

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Firstly, comparative interventions require an explicit knowledge of the state of the art of the treatments available for the health condition or clinical setting in question (preferably by means of a systematic review). Secondly, the existence of effective treatments limits the use of placebo as a research technique and makes it necessary to include effective treatments in comparisons.

And here is the question: Are there other well-known and frequently used antiemetic treatments for the proposed scenario?

Comparisons with placebo inevitably lead to a selection bias regarding the asymmetric comparison between an effective drug and a passive element (or an element from which no outcomes are expected). In addition, this type of comparison may lead to an overestimation of the drug's results in terms of the proposed objective, which is to be prescribed as an element that reduces the presence of an event (in this case, vomiting) in the chosen population and setting.

As a result, the correction of the model clashes with the relevance of the chosen comparison model.

The most widespread review tool for clinical trials (CONSORT) does not point to evident shortcomings in the article. See Table 1. .

Table 1. Sample checklist of information to include when reporting a randomised clinical trial

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item
Title and abstract		
	1a	Identification as a randomised trial in the title
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)
Introduction		
Background and objectives	2a	Scientific background and explanation of rationale
	2b	Specific objectives or hypotheses
Methods		
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons
Participants	4a	Eligibility criteria for participants
	4b	Settings and locations where the data were collected
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed
	6b	Any changes to trial outcomes after the trial commenced, with reasons
Sample size	7a	How sample size was determined
	7b	When applicable, explanation of any interim analyses and stopping guidelines
Randomisation:		
Sequence generation	8a	Method used to generate the random allocation sequence
	8b	Type of randomisation; details of any restriction (such as blocking and block size)
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions
Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how
	11b	If relevant, description of the similarity of interventions

Source: CONSORT 2010 http://www.consort-statement.org/

A FINAL THOUGHT

The Declaration of Helsinski specifies when placebo can be used in clinical research: "The benefits, risks, burdens and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. This does not exclude the use of placebo, or no treatment, in studies where no proven prophylactic, diagnostic or therapeutic method exists."

Ondansetron may be a first-line drug in the clinical setting in question (Higgins & Green, 2011), but it is no less true that the comparison method chosen is quite unfortunate.

Choosing these comparison models is not uncommon, even in prestigious and international studies. There is an example where a bizarre title shows how this practice is prevalent in scientific studies. Using a correct methodology is not enough to ensure quality (Tomasik et al., 2016).

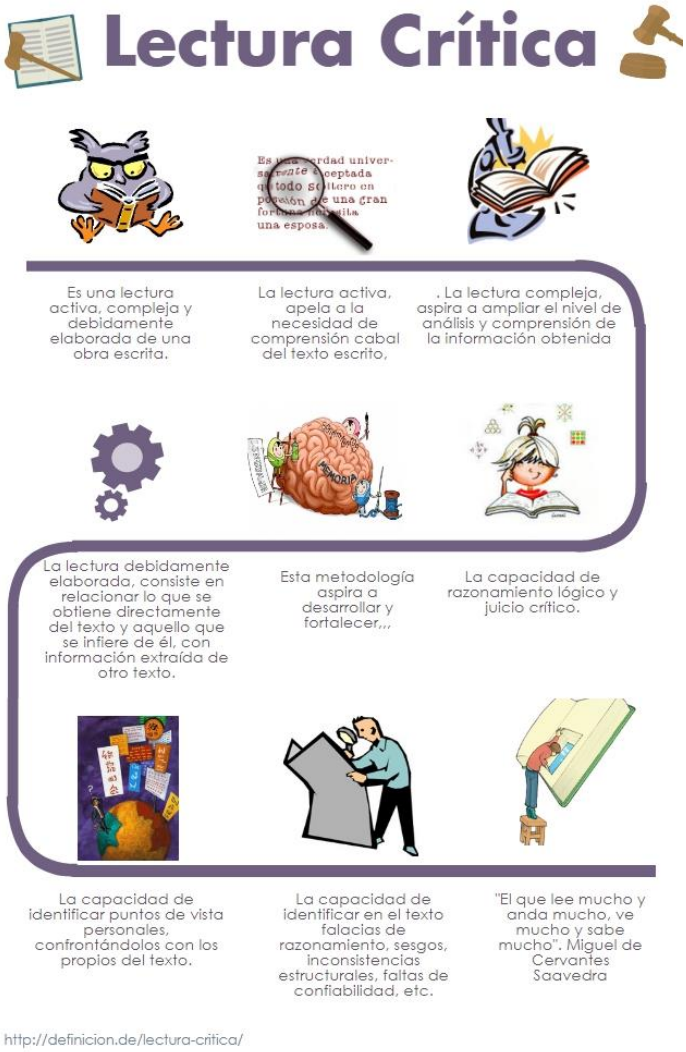

Table 2. Critical reading Translation.

Spanish	English
Lectura crítica	Critical reading
Es una lectura activa, compleja y debidamente elaborada de una obra escrita.	Critical reading is the active, complex, and properly conducted reading of a written work.
La lectura activa apela a la necesidad de comprensión cabal del texto escrito.	Active reading addresses the need for a thorough understanding of a written text.
La lectura compleja aspira a ampliar el nivel de análisis y comprensión de la información obtenida.	Complex reading aims to broaden the level of analysis and understanding of the information obtained.
La lectura debidamente elaborada consiste en relacionar lo que se obtiene directamente del texto y aquello que se infiere de él, con información extraída de otro texto.	A well-conducted reading consists of connecting that which is obtained directly from the text and that which is inferred from it, with information extracted from another text.
Esta metodología aspira a desarrollar y fortalecer…	This method aims to develop and strengthen...
La capacidad de razonamiento lógico y juicio crítico.	The capacity for logical reasoning and critical judgement.
La capacidad de identificar puntos de vista personales, confrontándolos con los propios del texto.	The ability to identify personal points of view and compare them with those in the text.
La capacidad de identificar en el texto falacias de razonamiento, sesgos, inconsistencias estructurales, faltas de confiabilidad, etc.	The ability to identify in the text logical fallacies, biases, structural inconsistencies, lack of reliability, etc.
"El que lee mucho y anda mucho, ve mucho y sabe mucho". Miguel de Cervantes Saavedra	"He who reads a lot and walks a lot, sees a lot and knows a lot." Miguel de Cervantes Saavedra.

J Renin Angiotensin Aldosterone Syst. 2004 Jun;5(2):59-63.

A putative placebo comparison of the SCOPE and LIFE trials.

Meredith PA[1], Murray LS, McMurray JJ; SCOPE trial; LIFE trial.

It is also worth noting that, at the end of the selected article, in the section on conflicts of interest and acknowledgements, it is indicated that the study had been supported, among other institutions, by GlaxoSmithKline, the company that developed the molecule under the commercial name of Zofran®.

Thus, the use of ondansetron for these clinical features in question would require a review comparing the efficacy of ondansetron with other drugs, as there are numerous

alternatives that have yielded positive results and are safe and widely used (Meredith, Murray, & McMurray, 2004).

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REFERENCES

Freedman, S. B., Adler, M., Seshadri, R., & Powell, E. C. (2006). Oral Ondansetron for Gastroenteritis in a Pediatric Emergency Department. *New England Journal of Medicine*, *354*(16), 1698–1705. https://doi.org/10.1056/NEJMoa055119

Higgins, J. P. T., & Green, S. (2011). Manual Cochrane de revisiones sistemáticas de intervenciones. In *Centro Cochrane Iberoamericano*. https://training.cochrane.org/es/manual-cochrane-de-revisiones-sistemáticas-de-intervenciones.

Meredith, P. A., Murray, L. S., & McMurray, J. J. (2004). A putative placebo comparison of the SCOPE and LIFE trials. *Journal of the Renin-Angiotensin-Aldosterone System*, *5*(2), 59–63. https://doi.org/10.3317/jraas.2004.011

Tomasik, E., Ziółkowska, E., Kołodziej, M., & Szajewska, H. (2016, September). Systematic review with meta-analysis: ondansetron for vomiting in children with acute gastroenteritis. *Alimentary Pharmacology and Therapeutics*, Vol. 44, pp. 438–446. https://doi.org/10.1111/apt.13728

RINSAD

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