Avaliação Crítica da Literatura Médica

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Avaliação Crítica

Estudos sobre Tratamento

Formulação da Pergunta

Tratamento

Questões terapêuticas
Qual o melhor intervenção?
Qual a melhor dosagem?
Qual a melhor via de administração?
Qual a duração da intervenção?
Qual a segurança?

Tipo de estudo primário
Ensaios clínicos randomizados

Paciente do sexo masculino, 40 anos com hepatite B crônica, HBsAg e HBeAg positivos por mais de 6 meses

- Qual o melhor tratamento para esse paciente?
- O tratamento influencia na história natural da hepatite B Crônica?
- O tratamento com um medicamento é melhor do que a combinação de anti-virais?
- Quais variáveis são preditoras de boa resposta?

Identificação e Seleção dos Estudos

Estratégia com maior especificidade e menor sensibilidade

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randomized controlled trial[Publication Type]
OR controlled clinical trial[Publication Type]
OR randomized controlled trials[MeSH Terms]
OR random allocation[MeSH Terms]
OR double blind method[MeSH Terms]
OR single blind method[MeSH Terms]
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Roteiro para Avaliação da Qualidade Metodológica

Estudos sobre testes diagnósticos

Users guides to the medical literature. How to use an article about a therapy or prevention.
JAMA 1994;271(1):59-63.
JAMA 1993;270(21):2598-601.
http://www.cche.net/principles/content_all.asp

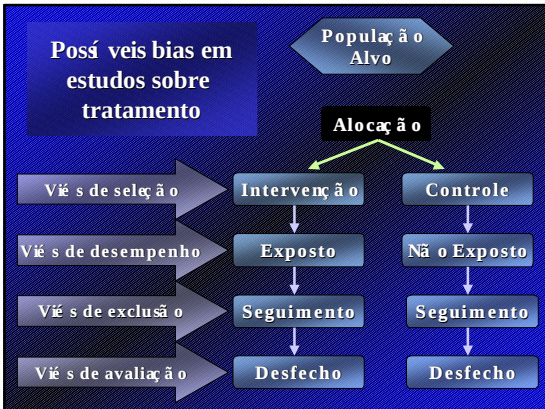
:

Schulz KF, Chalmers I, Hayes RJ, Altman DG. Empirical evidence of bias. Dimensions of methodological quality associated with estimates of treatment effects in controlled trials.
JAMA. 1995 Feb 1;273(5):408-12.

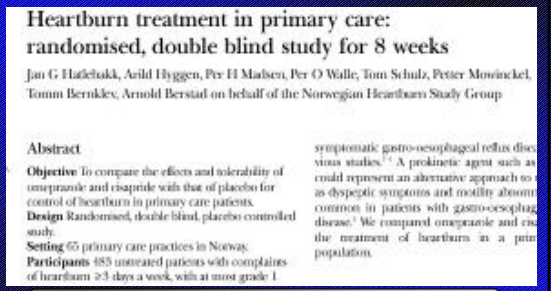
Roteiro para Avaliação da Qualidade Metodológica

- **Validade do estudo**
- **Importância para a prática clínica**
- **Aplicabilidade ao meu paciente**

Possíveis bias em estudos sobre tratamento



Avaliando um estudo



Heartburn treatment in primary care: randomised, double blind study for 8 weeks

Jan G Hatlebakk, Arild Hyggen, Per H Madsen, Per O Walle, Tom Schulz, Petter Mowinckel, Tomm Bernklev, Arnold Berstad on behalf of the Norwegian Heartburn Study Group

Abstract

Objective To compare the effects and tolerability of omeprazole and cisapride with that of placebo for control of heartburn in primary care patients.
Design Randomised, double blind, placebo controlled study.
Setting 65 primary care practices in Norway.
Participants 485 untreated patients with complaints of heartburn ≥3 days a week, with at most grade 1

symptomatic gastro-oesophageal reflux dise
vious studies.[1-4] A prokinetic agent such as
could represent an alternative approach to
as dyspeptic symptoms and motility abnorm
common in patients with gastro-oesophag
disease.[5] We compared omeprazole and cis
the treatment of heartburn in a prim
population.

BMJ 1999; 319: 550-553

Os resultados são válidos?

- **A seleção dos pacientes foi aleatória?**
- **A geração da seqüência da alocação foi apropriada?**
- **Sigilo da alocação foi apropriado?**

Estudo aleatório

Geração apropriada

Assignment
Randomisation was done in blocks of eight for each network. The randomisation list was computer generated and all packing of study drugs was done in one pharmaceutical laboratory to ensure that patients and investigators were blinded to study assignment.

Sigilo de alocação apropriado?

Masking
Study drugs were double blinded using a double dummy technique. Drugs were dispensed and collected by the network pharmacy. Randomisation lists for emergency use were kept at the pharmacies, at the research coordination office, and at the research laboratory of the sponsor, but the code was not broken until the database had been formally closed.

Randomização controlada pela farmácia

Os resultados são válidos?
Guia Primário

Todos os pacientes incluídos no estudo foram levdados em conta na conclusão?

Seguimento completo.

Análise "intenção de" para tratar.

Análise por "intenção para tratar?"

Statistics
We performed an "all patients treated" analysis, including all randomised patients who took at least one dose of study drug. A χ^2 test was used for comparison of the main efficacy variables and adverse events. Concomitant gastrointestinal symptoms and use of antacids were compared using the Kruskal-Wallis non-parametric test.

Seguimento foi completo?

Forty seven patients were prematurely withdrawn (see website). Thirty four patients with adequate control of heartburn at the 4 week visit reported not to have adequate control of heartburn at the 8 week visit—placebo 11 (33%), cisapride 12 (35%), and omeprazole 11 (12%)—significantly less often in the omeprazole group ($P<0.001$). Median antacid

Os resultados são válidos?
Guia Secundário

Pacientes, médicos e investigadores estavam "cegos" para o tratamento?

Masking
Study drugs were double blinded using a double dummy technique. Drugs were dispensed and collected by the network pharmacy. Randomisation lists for emergency use were kept at the pharmacies, at the research coordination office, and at the research laboratory of the sponsor, but the code was not broken until the database had been formally closed.

Os grupos eram similares no no iń cio do estudo?

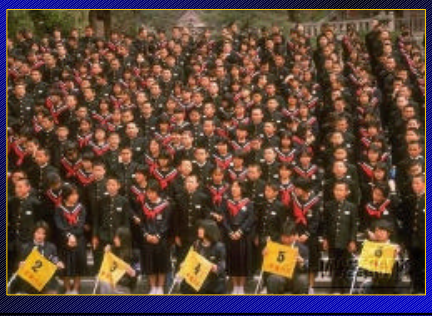


Table 1 Personal and endoscopic details of patients treated in each study arm. Values are percentages unless stated otherwise

Variable	Placebo (n=156)	Cisapride (n=163)	Omeprazole (n=161)
Male	50	50	57
Median age (years)	49.6	47.2	48.0
Median weight (kg)	76	78	77
Helicobacter pylori	39	37	32
Hiatal hernia	33	39	39
Berstad classification of reflux oesophagitis:			
No oesophagitis	52	43	52
Grade 1	48	57	48
Los Angeles classification of reflux oesophagitis:			
No oesophagitis	50	42	49
Grade A	24	33	26
Grade B	26	26	26
Severity of heartburn 7 days before randomisation:			
Mild	21	22	20
Moderate	64	72	68
Severe	15	6	12
Mean No of days with heartburn before randomisation	5.5	5.4	5.7
Patients with heartburn all 7 days before randomisation	47	45	54

Aparte a intervenç ã o experimental, os grupos foram tratados igualmente?

Interventions

Patients received either one capsule of omeprazole 20 mg (Astra Hässle, Mölndal, Sweden) and two tablets of placebo before breakfast and supper (omeprazole group), one capsule of placebo before breakfast and two tablets of cisapride 10 mg (Janssen Pharmaceutica, Beerse, Belgium) before breakfast and supper (cisapride group), or placebo for both (placebo group). Calcium carbonate antacid tablets (Titralac Nycomed, Oslo, Norway) with a buffering capacity of 7 mmol per tablet were provided for use only when heartburn occurred.

Quais são os resultados

Qual o efeito do tratamento?

Adequate control of heartburn was achieved after 4 weeks in 71% of patients taking omeprazole, 22% taking cisapride, and 18% taking placebo; a statistically significant difference in favour of omeprazole (*v* cisapride and placebo, $P < 0.0001$; cisapride *v* placebo, non-significant). Table 2 shows the results after 2 and 8 weeks. Results were similar after 4 weeks in patients with or without reflux oesophagitis (omeprazole 72% *v* 71%; cisapride 20% *v* 23%; placebo 10% *v* 24%). Patients taking omeprazole who were positive for *H pylori* achieved adequate control of heartburn more often than patients who were negative for *H pylori* (86%

Qual o efeito do tratamento?

Table 3 Proportion of patients achieving adequate control of heartburn, mean number of days per week with heartburn after 2, 4, and 8 weeks of treatment, and median number of antacid tablets consumed

Variable	Placebo (n=159)	Cisapride (n=163)	Omeprazole (n=161)	P value†
Patients (%) achieving adequate control of heartburn*				
2 weeks	15	21	59	<0.0001
4 weeks	18	22	71	
8 weeks	30	40	76	
Mean No of days per week with heartburn				
Baseline	5.5	5.4	5.7	<0.001
2 weeks	4.3	3.6	1.8	
4 weeks	3.9	3.4	1.2	
8 weeks	3.5	3.0	1.0	
Median No of antacid tablets consumed				
Weeks 1-2	13	9	2	<0.0001
Weeks 3-4	10	8	0	
Weeks 5-8	17	12	0	

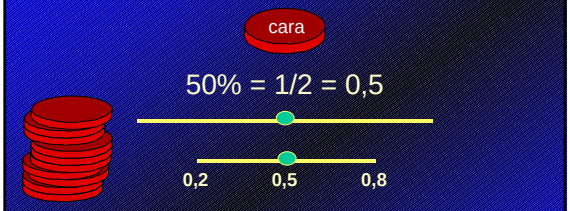
*No more than mild heartburn for ≤1 day per week.
†Omeprazole *v* cisapride or placebo.

Quais são os resultados

Qual a precisã o do efeito do tratamento?

Os autores apresentam o intervalo de confiança?

Probabilidade



n = 50 — IC 95% 0,35 a 0,65

n = 100 — IC 95% 0,40 a 0,60

n = 1000 — IC 95% 0,48 a 0,52

Os resultados vão auxiliar no tratamento do meu paciente?

Os resultados podem ser aplicados no tratamento dos meus pacientes?

Os resultados vão auxiliar no tratamento do meu paciente

Foram considerados todos os desfechos clinicamente importantes?

Foram considerados todos os desfechos clinicamente importantes?

Outcome measures

The primary efficacy variable was adequate control of heartburn, defined as ≤1 day with no more than mild heartburn in the 7 days before the 4 week visit. Heartburn was defined as burning substernal discomfort with no radiating component and described with common words. Secondary efficacy variables were antacid consumption, severity and number of days with heartburn in the 7 days before each visit, as well as severity of regurgitation, belching, dysphagia, abdominal pain or discomfort, epigastric pain or discomfort, bloating, nausea, and vomiting. Each symptom was graded as either 1 (mild; awareness of symptom but easily tolerated), 2 (moderate; interference with normal activities), or 3 (severe; inability to perform normal activities). Adverse events were defined as unintended unfavourable symptoms or deterioration of existing illness, as well as deterioration in clinical tests, whether considered treatment related or not.

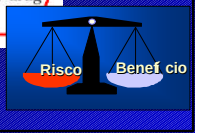
Os resultados vão auxiliar no tratamento do meu paciente

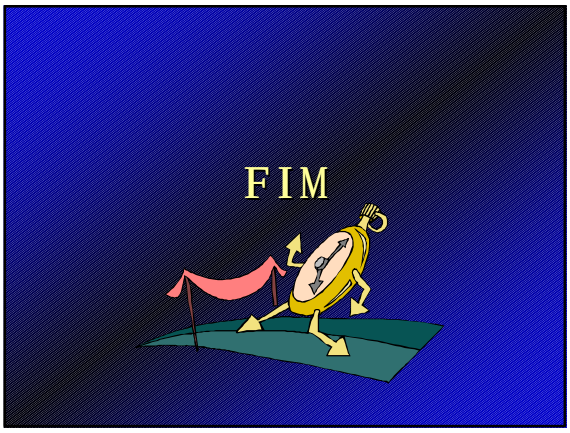
Os benefícios observados pelo tratamento superam possíveis malefícios e custos?

Os benefícios observados pelo tratamento superam possíveis malefícios e custos?

Adverse events

Adverse events were reported in significantly more patients receiving cisapride than either omeprazole (P = 0.024) or placebo (P = 0.004) after 4 weeks. The gastrointestinal and central nervous systems were most commonly affected. Five serious adverse events were reported (placebo, 1 adverse event; cisapride, 3; and omeprazole, 1), but the causal relation with study drug was scored as unlikely by the investigators.

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