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The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Electronic Nicotine-Delivery Systems for Smoking Cessation

Reto Auer, M.D., Anna Schoeni, Ph.D., Jean-Paul Humair, M.D., M.P.H., Isabelle Jacot-Sadowski, M.D., Ivan Berlin, M.D., Ph.D., Mirah J. Stuber, M.D., Moa Lina Haller, M.D., Rodrigo Casagrande Tango, M.D., M.P.H., Anja Frei, Ph.D., Alexandra Strassmann, Ph.D., Philip Bruggmann, M.D., Florent Baty, Ph.D., Martin Brutsche, M.D., Ph.D., Kali Tal, Ph.D., Stéphanie Baggio, Ph.D., Julian Jakob, M.D., Nicolas Sambiagio, Ph.D., Nancy B. Hopf, Ph.D., Martin Feller, M.D., Nicolas Rodondi, M.D., and Aurélie Berthet, Ph.D.

Clinical Infectious Diseases

MAJOR ARTICLE

IDSA Infectious Diseases Society of America · hivma hiv medicine association · OXFORD

An Open-Label, Randomized Trial Comparing Fidaxomicin With Oral Vancomycin for the Treatment of *Clostridioides difficile* Infection in Hospitalized Patients Receiving Concomitant Antibiotics for Concurrent Infections

Krishna Rao,[1,2] Qianzi Zhao,[1,2] Justin Bell,[1,2] Jay Krishnan,[1] Oryan Henig,[1,2] Jolene Daniel,[1,2] Kara Sawaya,[3] Owen Albin,[1,2] John P. Mills,[1,2] Lindsay A. Petty,[1,2] Kevin Gregg,[1,2] Daniel Kaul,[1,2] Anurag N. Malani,[3] Jason Pogue,[4] and Keith S. Kaye[1,2]

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BACKGROUND

Electronic nicotine-delivery systems — also called e-cigarettes — are used by some tobacco smokers to assist with quitting. Evidence regarding the efficacy and safety of these systems is needed.

METHODS

In this open-label, controlled trial, we randomly assigned adults who were smoking at least five tobacco cigarettes per day and who wanted to set a quit date to an intervention group, which received free e-cigarettes and e-liquids, standard-of-care smoking-cessation counseling, and optional (not free) nicotine-replacement therapy, or to a control group, which received standard counseling and a voucher, which they could use for any purpose, including nicotine-replacement therapy. The primary outcome was biochemically validated, continuous abstinence from smoking at 6 months. Secondary outcomes included participant-reported abstinence from tobacco and from any nicotine (including smoking, e-cigarettes, and nicotine-replacement therapy) at 6 months, respiratory symptoms, and serious adverse events.

RESULTS

A total of 1246 participants underwent randomization; 622 participants were assigned to the intervention group, and 624 to the control group. The percentage of participants with validated continuous abstinence from tobacco smoking was 28.9% in the intervention group and 16.3% in the control group (relative risk, 1.77; 95% confidence interval, 1.43 to 2.20). The percentage of participants who abstained from smoking in the 7 days before the 6-month visit was 59.6% in the intervention group and 38.5% in the control group, but the percentage who abstained from any nicotine use was 20.1% in the intervention group and 33.7% in the control group. Serious adverse events occurred in 25 participants (4.0%) in the intervention group and in 31 (5.0%) in the control group; adverse events occurred in 272 participants (43.7%) and 229 participants (36.7%), respectively.

CONCLUSIONS

The addition of e-cigarettes to standard smoking-cessation counseling resulted in greater abstinence from tobacco use among smokers than smoking-cessation counseling alone. (Funded by the Swiss National Science Foundation and others; ESTxENDS ClinicalTrials.gov number, NCT03589989.)

Cigarrillos electrónicos
(sistemas electrónicos de administración de nicotina)

Ayuda potencial para abandono del hábito tabáquico
+/- uso prolongado

Métodos

- Ensayo abierto, aleatorizado y controlado en 5 centros de Suiza (Ud. Ensayos Clínicos de Berna)

- Julio 2018 hasta Junio 2021

- Reclutamiento: centro de atención sanitaria, prensa, transporte público y redes sociales

Inclusión: Fumadores ≥ 18 años, ≥ 5 cig/día durante ≥ 12 meses, cuyo propósito era abandono del hábito en los 3 meses posteriores a la inscripción.

Exclusión:
- Embarazadas o período de lactancia
- Uso previo (3m previos) de nicotonina u otro fármaco (varenciclina o bupropion)
- Uso previo (3m previos) de cigarrillos electrónicos

- Aprobado por el comité de ética de cada centro

Manejo por enfermería

Participantes: Elegían la fecha objetivo para abandono del tabaco

- Terapia cognitivo-conductual
- Entrevistas motivacionales
- Decisión compartida frente a uso de medicación para abandono (nicotina u otra farmacología)

- ***Grupo control***

  Visita inicial: vale 50 francos suizos (dólares) para cualquier propósito incluido terapia de reemplazo, parches de nicotina

- ***Grupo intervención***

  Asesoramiento estándar +/- uso nicotina

  2 kits de cigarrillos electrónicos y 5 baterías; con elección entre seis sabores y concentración de nicotina

Visitas: Inicial, fecha objetivo, sem 1, 2, 4 y 8 tras objetivo

*Visita clínica presencial a los **6 meses** tras la fecha estimada de abandono.*

- Variables demográficas
- Antecedente de tabaquismo y nivel del monóxido de carbono espirado
- Síntomas de abstinencia
- Síntomas respiratorios

Datos sobre hábito y/o eventos adversos.

Objetivos

OBJETIVO PRIMARIO:

Abstinencia del hábito tabáquico durante 6 meses tras la fecha objetivo de dejar de fumar

- Validación bioquímica con nivel de anabasina (<3ng/mL) en orina
- Nivel de monóxido de carbono exhalado < 9 ppm

OBJETIVO SECUNDARIO:

- Abstinencia sostenida del hábito tabáquico durante 6 meses sin validación bioquímica
- Abstinencia con permisión de 5 cig (validado BQ)
- Abstinencia con período extra de 2 sem (BQ)
- Abstinencia los 7 días previos a la visita de los 6 meses, (validado o no bioquímicamente)

- Biomarcador de consumo de tabaco activo (no en terapia de reemplazo de nicotina)
- Vida media de eliminación 16 h

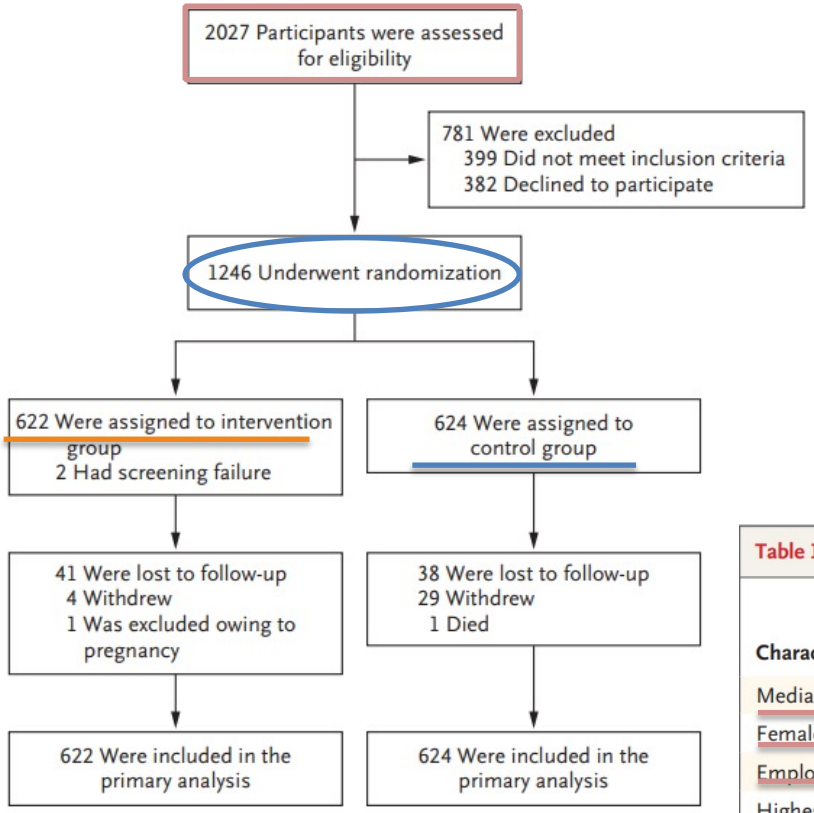


Figure 1. Enrollment, Assignment, and Follow-up.

Table 1. Characteristics of the Participants at Baseline.*

Characteristic	Control Group (N=624)	Intervention Group (N=622)	Total (N=1246)
Median age (IQR) — yr	39 (30–52)	37 (28–51)	38 (29–51)
Female gender identity — no. (%)	295 (47.3)	290 (46.6)	585 (47.0)
Employed — no. (%)	465 (74.5)	438 (70.4)	903 (72.5)
Highest educational level — no. (%)			
Obligatory school, some obligatory school, or no formal schooling†	45 (7.2)	50 (8.0)	95 (7.6)
Secondary education	277 (44.4)	291 (46.8)	568 (45.6)
Tertiary education	302 (48.4)	281 (45.2)	583 (46.8)
Median age at which smoking was started (IQR) — yr‡	16 (15–19)	16 (15–18)	16 (15–19)
Median no. of cigarettes per day (IQR)	15 (10–20)	15 (10–20)	15 (10–20)
At least one previous attempt to quit smoking — no. (%)‡	530 (84.9)	531 (85.4)	1061 (85.2)
Fagerström Test for Nicotine Dependence score‡§	4.4±2.3	4.3±2.3	4.3±2.3
Median expired CO level (IQR) — ppm¶	20 (12–29)	20 (13–29)	20 (12–29)

Table 2. Primary and Secondary Outcomes.

Outcome	Control Group N = 624	Intervention Group N = 622	Difference, Intervention vs. Control (95% CI)*	Crude Relative Risk (95% CI)†	Adjusted Relative Risk (95% CI)‡
	number (percent)			*percentage points*	
Primary outcome: continuous abstinence from smoking at 6 months§ *Validación bioquímica*	102 (16.3)	180 (28.9)	12.6 (8.0–17.2)	1.77 (1.43–2.20)	1.71 (1.39–2.12)
Secondary outcomes¶					
Continuous abstinence, without biochemical validation	146 (23.4)	237 (38.1)	14.7 (9.6–19.8)	1.63 (1.37–1.94)	1.57 (1.32–1.85)
Sustained abstinence allowing a 2-week grace period, with biochemical validation	110 (17.6)	191 (30.7)	13.1 (8.4–17.8)	1.74 (1.42–2.14)	1.70 (1.39–2.08)
Sustained abstinence allowing up to 5 cigarettes, with biochemical validation	109 (17.5)	219 (35.2)	17.7 (12.9–22.5)	2.02 (1.65–2.46)	1.96 (1.61–2.38)
Abstinence within previous 7 days, with biochemical validation	133 (21.3)	245 (39.4)	18.1 (13.1–23.1)	1.85 (1.54–2.21)	1.74 (1.47–2.07)
Abstinence within previous 7 days, without biochemical validation	200 (32.1)	332 (53.4)	21.3 (16.0–26.7)	1.67 (1.45–1.91)	1.56 (1.37–1.77)

90,8% → datos sobre el tabaquismo y los eventos adversos graves *a los 6 meses*

63,9% obtenidos presencialmente

23,4% obtenidos telefónicamente, correo electrónico o correo postal

2,8% obtenidos de familiares

0,2% obtenidos del médico general

0,5% obtenidos de fuentes desconocidas.

Adherencia a la terapia **en la 1 sem de la fecha prevista** de abandono del hábito

90% participantes en **grupo de intervención**

- 95,9% utilizó cigarrillos electrónicos
- 6,8% terapia de reemplazo de nicotina
- 0,5% terapia farmacológica
  (bupropion, varenciclina)

86% en el **grupo de control**

- 3,9% utilizó cigarrillos electrónicos
- 63,6% terapia de reemplazo de nicotina
- 4,1% terapia farmacológica

Table 3. Participant-Reported Use of Tobacco Cigarettes, E-cigarettes, and Nicotine-Replacement Therapy at 6 Months.*

84,8%

Participant-Reported Use	Control Group N=504	Intervention Group N=552	Difference, Intervention vs. Control	
	number (percent)		*percentage points*	
No tobacco cigarettes: "tobacco abstainers"	194 (38.5)	329 (59.6)	21.1	No cig de tabaco, independientemente cig electrónicos
No tobacco cigarettes, no e-cigarettes: "tobacco and e-cigarette abstainers"	179 (35.5)	62 (11.2)	−24.3	
With nicotine-replacement therapy	14 (2.8)	1 (0.2)	−2.6	
With smoking-cessation medication	1 (0.2)	0	−0.2	
E-cigarettes and no tobacco cigarettes: "exclusive e-cigarette users"	15 (3.0)	267 (48.4)	45.5	
E-cigarettes without nicotine	5 (1.0)	50 (9.1)	8.1	
E-cigarettes with nicotine	10 (2.0)	217 (39.3)	37.3	
E-cigarettes and nicotine-replacement therapy	0	1 (0.2)	0.2	
E-cigarettes and smoking-cessation medication	0	0	0	
No nicotine: "nicotine abstainers"†	170 (33.7)	111 (20.1)	−13.6	No cig tabaco, cig electrónicos con nicotina o terapia de reemplazo de nicotina
Tobacco cigarettes	310 (61.5)	223 (40.4)	−21.1	
Tobacco cigarettes and no e-cigarettes: "exclusive smokers"	294 (58.3)	122 (22.1)	−36.2	Uso cig tabaco pero no cig electrónicos
Tobacco cigarettes and nicotine-replacement therapy	18 (3.6)	4 (0.7)	−2.9	
Tobacco cigarettes and smoking-cessation medication	2 (0.4)	0	−0.4	
E-cigarettes and tobacco cigarettes: "dual users"	16 (3.2)	101 (18.3)	15.1	Uso cig. tabaco y electrónicos
Without nicotine in e-cigarettes	5 (1.0)	10 (1.8)	0.8	
With nicotine in e-cigarettes	11 (2.2)	91 (16.5)	14.3	
With nicotine-replacement therapy	1 (0.2)	4 (0.7)	0.5	
With smoking-cessation medication	0	0	0	

***SEGURIDAD** a lo largo del estudio*

- Grupo control: 1 fallecimiento

	Grupo de intervención	Grupo control	Significación estadística
Eventos adversos	272 **(43,7%)** → 425 eventos	229 (36,7%) → 336 eventos	RR, 1,19; IC del 95%, 1,04 a 1,37; p no ajustado **= 0,01**
Eventos adversos graves	25 (4%)	31 (5%)	RR, 0,81; IC del 95%, 0,48 a 1,35; p no ajustado = 0,49
Enfermedad por SARS CoV2	18	8	
Utilización de antibioterapia	54 (8,7%) → 61 episodios de uso ATB	43 (6,9%) → 56 episodios	RR, 0,81; 1,26; IC 95%, 0,86 a 1,85

SÍNTOMATOLOGÍA RESPIRATORIA a los 6 meses

Datos del 81% de grupo intervención y 66% grupo control

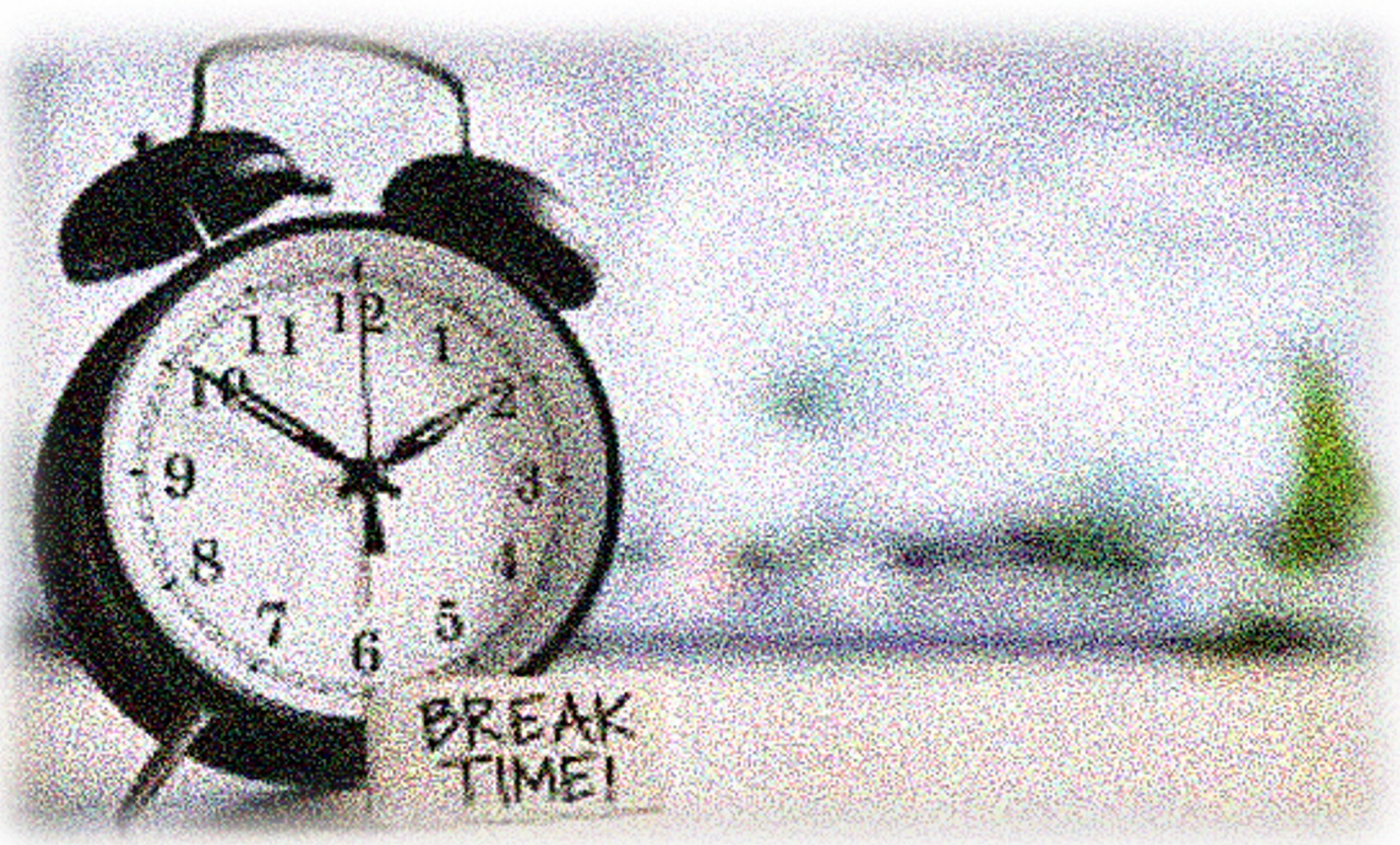
	Grupo de intervención	Grupo control
Tos	59%	66%
Expectoración	38%	49%
Sin opresión torácica	73%	72%

Discusión y conclusiones

- Superioridad de cigarrillos electrónicos vs terapia estándar para abstinencia del hábito tabáquico.
- Superioridad de cigarrillos electrónicos vs terapia de reemplazo nicotina, pero continuaron fumando e-cigarrilos.
- Más eventos adversos (nivel tóxico bajo de cig electrónicos) aunque no graves
- *Abstinencia en el grupo de intervención pero uso de cigarrillos electrónicos con nicotina alto.*

Limitaciones

- Los participantes conocía su asignación al grupo
- Cigarrillos electrónicos y líquidos gratuitos al grupo intervención y no terapia de sustitución de nicotina gratuita en el grupo control.
- Seguimiento hasta 6 meses. Faltaría seguimiento a largo plazo.
- Faltan datos de validación bioquímica
- Realizado en población de Suiza. No extrapolable a resto de población.


BREAK
TIME!

Clinical Infectious Diseases

MAJOR ARTICLE

An Open-Label, Randomized Trial Comparing Fidaxomicin With Oral Vancomycin for the Treatment of *Clostridioides difficile* Infection in Hospitalized Patients Receiving Concomitant Antibiotics for Concurrent Infections

Krishna Rao,[1,2] Qianzi Zhao,[1,2] Justin Bell,[1,2] Jay Krishnan,[1] Oryan Henig,[1,2] Jolene Daniel,[1,2] Kara Sawaya,[3] Owen Albin,[1,2] John P. Mills,[1,2] Lindsay A. Petty,[1,2] Kevin Gregg,[1,2] Daniel Kaul,[1,2] Anurag N. Malani,[3] Jason Pogue,[4] and Keith S. Kaye[1,2]

[1]Department of Internal Medicine, University of Michigan Medical School, University of Michigan, Ann Arbor, Michigan, USA; [2]Division of Infectious Diseases, University of Michigan Medical School, University of Michigan, Ann Arbor, Michigan, USA; [3]Division of Infectious Diseases, Trinity Health Michigan, Ann Arbor, Michigan, USA; and [4]Department of Clinical Pharmacy at the University of Michigan College of Pharmacy, University of Michigan, Ann Arbor, Michigan, USA

Background. Recurrent *Clostridioides difficile* infection (rCDI) occurs frequently, and concomitant antibiotic (CA) during the initial episode for treatment of non-CDI is a major risk factor. We sought to address the comparative efficacy of fidaxomicin versus vancomycin in the setting of CA during the initial CDI episode.

Methods. We conducted a randomized, controlled, open-label trial at 2 hospitals in Ann Arbor, Michigan. We consecutively consented and enrolled hospitalized patients ≥18 years old with diarrhea, a positive test for *C. difficile*, and ≥1 qualifying CA. Complicated CDI, CDI treatment for >24 hours prior to enrollment, and planned long-term (>12 weeks) CA use were notable exclusions. Clinical cure was defined as resolution of diarrhea for 2 consecutive days maintained until 2 days after therapy, and rCDI as recurrent diarrhea with positive testing ≤30 days after initial treatment. Patients were randomized to fidaxomicin or vancomycin.

Results. Baseline characteristics were similar in the 2 groups of 144 patients. Rates of clinical cure (73% vs 62.9%, $P = .195$) and rCDI (3.3% vs 4.0%; $P > .99$) were similar for fidaxomicin and vancomycin in the intention-to-treat and per-protocol cohorts, respectively. Only 4 patients developed rCDI.

Conclusions. In this study of patients with CDI receiving CA, a numerically higher proportion were cured with fidaxomicin versus vancomycin, but this result did not reach statistical significance. Overall recurrence was lower than anticipated in both arms compared with previous studies that did not extend duration of CDI treatment during CA.

Clinical Trials Registration. www.clinicaltrials.gov (NCT02692651).

Keywords. *Clostridioides difficile* infection; randomized controlled trial; antibiotics; gut microbiome; recurrent infection.

La infección por *C. Difficile* (ICD) presenta una morbi-mortalidad importante.

EEUU 400.000 infecciones totales; > 200.000 hospitalizaciones anuales.

- La ICD recurrente es del 21,6%; después de 1 episodio (60.000 pacientes)
- El uso de antibioterapia concomitante por infección intercurrente supone un factor de riesgo importante y aumenta a su vez riesgo de fracaso terapéutico

Efficacy of Fidaxomicin Versus Vancomycin as Therapy for *Clostridium difficile* Infection in Individuals Taking Concomitant Antibiotics for Other Concurrent Infections

Kathleen M. Mullane,[1] Mark A. Miller,[2] Karl Weiss,[3] Arnold Lentnek,[4] Yoav Golan,[5] Pamela S. Sears,[6] Youe-Kong Shue,[6]

Clinical Trial > Lancet Infect Dis. 2012 Apr;12(4):281-9. doi: 10.1016/S1473-3099(11)70374-7. Epub 2012 Feb 8.

Fidaxomicin versus vancomycin for infection with Clostridium difficile in Europe, Canada, and the USA: a double-blind, non-inferiority, randomised controlled trial

Oliver A Cornely [1], Derrick W Crook, Roberto Esposito, André Poirier, Michael S Somero, Karl Weiss, Pamela Sears, Sherwood Gorbach; OPT-80-004 Clinical Study Group

Dos ensayos clínicos controlados aleatorizados → tasa de curación inferior a 8,2 % en los que reciben antibioterapia y una mediana de tiempo superior hasta curación (97 horas frente a 54 h en ausencia de antibioterapia concomitante)

Fidaxomicina superior a vancomicina oral, tasa de curación del 90% frente al 79,4% (diferencia del 10,6 %; IC del 95 %, 0,23-20,3 %; *P* = 0,04)

Métodos

- Ensayo aleatorizado, abierto y controlado en fase IV en Sistema de Salud Universidad de Michigan; hospital académico, Hospital Trinity Health Ann Arbor y un hospital universitario comunitario.
- Mayo 2017 y Mayo 2021
- Aprobado por el comité ético

Objetivos

- **OBJETIVO PRIMARIO**: Determinar la eficacia de la fidaxomicina frente a la vancomicina en adultos hospitalizados con ICD que también requieren un ciclo prolongado de antibioterapia.

- *OBJETIVO SECUNDARIO*: Impacto del tratamiento (fidaxomicina frente a vancomicina) sobre la recurrencia, duración de estancia hospitalaria, tasas de colectomía y la mortalidad a los 30 días.

Criterios inclusión:

- > 18 años con > 3 heces no formadas c/24h con prueba positiva frente *C. Difficile*
- > 1 antibiótico, de riesgo alto/medio, durante ≥ 5 días

Definición de antibioterapia de medio/alto riesgo: P/T, Cefepima, Ampicilina-Sulfabactam

Criterios exclusión

- Enfermedad grave complicada que compromete tratamiento vo
- Alérgicos a vancomicina o fidaxomicina
- Pacientes que se prevé que reciban metronidazol
- Pacientes que recibieron metronidazol o vancomicina durante > 24h dentro de las 72 h antes del ingreso
- Pacientes con laxantes en las 48h posteriores al resultado posteriores de la prueba
- Portadores de colostomía o ileostomía
- Pacientes que reciben o se prevé que estén con antibioterapia de riesgo medio o alto >12 semanas
- Pacientes con un episodio previo reciente de ICD (en las últimas 2 semanas)

Mayo 2017 y Mayo 2021 *(pandemia SARS CoV2)*

Se aleatorizaron en base a 2 criterios:

- Ingreso en UCI en el momento de la inscripción
- Episodio de ICD (estratificados en primer episodio/primera recurrencia o >1 recurrencia).

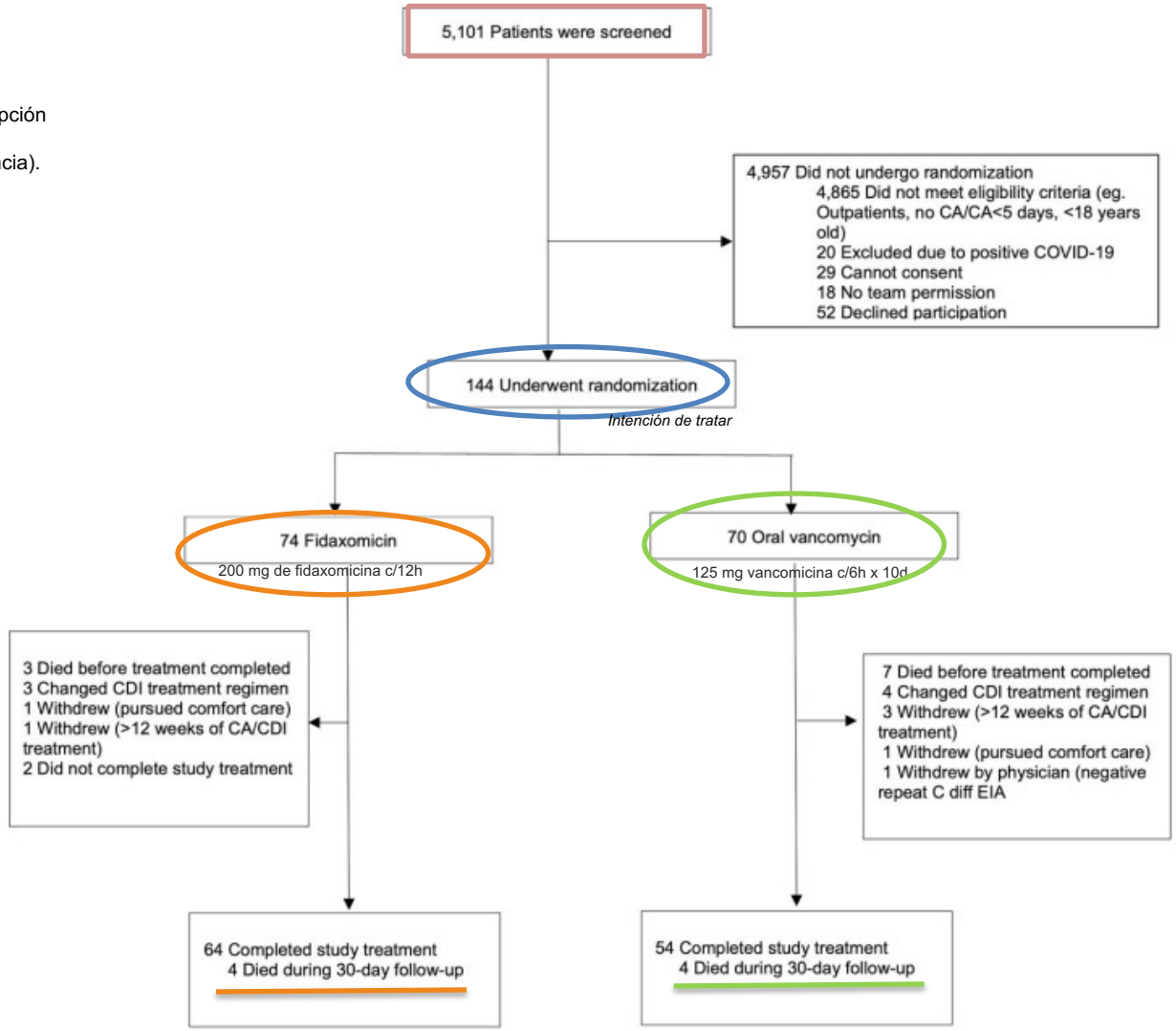


Table 1. Patient Characteristics

Patient Characteristics	Fidaxomicin (n = 74)	Oral Vancomycin (n = 70)	Overall (N = 144)
Age			
<65 y	51 (68.9%)	40 (57.1%)	91 (63.2%)
65–74 y	15 (20.3%)	20 (28.6%)	35 (24.3%)
>74 y	8 (10.8%)	10 (14.3%)	18 (12.5%)
Gender			
Male	34 (45.9%)	35 (50.0%)	69 (47.9%)
Female	40 (54.1%)	35 (50.0%)	75 (52.1%)
Race			
White	61	61	122
Black	10	5	15
Asian	2	3	5
Unknown/not reported	1	1	2
BMI (kg/m^2)			
Mean (SD)	26.7 (6.77)	28.2 (7.36)	27.4 (7.08)
Median [min, max]	25.1 [15.5, 48.2]	27.0 [15.2, 51.3]	26.2 [15.2, 51.3]
ICU			
Yes	12 (16.2%)	11 (15.7%)	23 (16.0%)
History of CDI			
Yes	16 (21.6%)	8 (11.4%)	24 (16.7%)
History of cancer			
Yes	34 (45.9%)	38 (54.3%)	72 (50.0%)
History of stem cell transplant			
Yes	4 (5.4%)	10 (14.3%)	14 (9.7%)
History of IBD			
Yes	3 (4.1%)	2 (2.9%)	5 (3.5%)
PPI			
Yes	29 (39.2%)	30 (42.9%)	59 (41.0%)
WBC at enrollment (10^3 cells/microliter)			
Mean (SD)	9.46 (7.37)	7.93 (6.90)	8.70 (7.15)
Median [min, max]	7.65 [0.100, 33.5]	8.05 [0.100, 36.3]	7.85 [0.100, 36.3]
Missing	12 (16.2%)	8 (11.4%)	20 (13.9%)
Creatinine at enrollment (mg/dL)			
Mean (SD)	1.11 (0.703)	1.36 (1.04)	1.23 (0.890)
Median [min, max]	0.885 [0.260, 3.27]	1.02 [0.420, 5.36]	0.920 [0.260, 5.36]
Missing	8 (10.8%)	6 (8.6%)	14 (9.7%)
Duration of CDI therapy, d	15 ± 12.2	17.2 ± 17	16.1 ± 14.7
Duration of CAs, d	16.5 (13.1)	20.6 (19.7)	18.4 (16.6)

Table 2. Concurrent Infection

Concurrent Infection[a]	Fidaxomicin, n (%)	Oral Vancomycin, n (%)	Total, N (%)
Total subjects	74	70	144
Bloodstream infection	6 (8)	14 (20)	20 (14)
UTI	21 (28)	8 (11)	29 (20)
SSTI	3 (4)	9 (13)	12 (8)
SSI	2 (3)	0 (0)	2 (2)
Respiratory tract infection	1 (1)	4 (6)	5 (3)
Abdominal infection	21 (28)	11 (16)	32 (22)
Bone infection	1 (1)	3 (4)	4 (3)
Meningitis/encephalitis	0 (0)	1 (1)	1 (1)
Pneumonia	10 (14)	11 (16)	21 (15)
Bypass graft infection	2 (3)	0 (0)	2 (2)
Diverticulitis of large intestine with abscess	1 (1)	0 (0)	1 (1)
Extensive spinal infection	0 (0)	1 (1)	1 (1)
Extraventricular drain prophylaxis	11 (15)	0 (0)	1 (1)
Helicobacter pylori infection	1 (1)	0 (0)	1 (1)
Vascular catheter-associated infection	0 (0)	1 (1)	1 (1)
Neutropenic fever	6 (8)	9 (13)	15 (10)
Pelvic abscess	1 (1)	1 (1)	2 (2)
Pericarditis	0 (0)	1 (1)	1 (1)
Perioperative, concern for fistula	0 (0)	1 (1)	1 (1)
Prophylaxis	1 (1)	2 (3)	3 (2)

Abbreviations: SSI, surgical site infection; SSTI, skin and skin structure infection; UTI, urinary tract infection.

[a]Some subjects had >1 indication for concomitant antibiotics.

Table 3. Patient Outcomes

Patient Outcomes	Fidaxomicin (n = 74)	Oral Vancomycin (n = 70)	Total (N = 144)	P[a]
Cure at EOT	54 (73.0%)	44 (62.9%)	98 (68.1%)	.195
Cure at EOT (per protocol)	54 (84.4%)	44 (81.5%)	98 (83%)	.864
LOS (median ± IQR), d	5 ± 9	6 ± 13	6 ± 11	.089
Recurrence during follow-up (per protocol)	2 (3.3%)	2 (4%)	4 (3.3%)	>.99
Sustained clinical cure (per protocol)[b]	52 (86.7%)	42 (84%)	94 (85.5%)	.693
Excluded from per-protocol analysis	14	20	34	…
Colectomy	0	0	0	…
Death during follow-up	4 (6.3%)	4 (7.4%)	8 (6.8%)	>.99
Withdrew, protocol deviation, or death before follow-up	10	16	36	…

Data are presented as n (%) unless otherwise indicated.

Abbreviations: EOT, end of treatment; IQR, interquartile range; LOS, length of stay.

[a]*P* value calculated with chi-square tests, *t* tests, or Wilcoxon rank-sum tests for categorical data, means, and medians, respectively.

[b]Clinical cure + no recurrence during follow-up.

Intención de tratar

Protocolo

No significación estadística

Discusión

- **No hubo diferencias significativas en las tasas de curación clínica con fidaxomicina vs vancomicina**

  → *Ventaja numérica* en la curación con fidaxomicina del 10% por intención de tratar
  → NNT 10 pacientes (objetivo en prediseño estudio 15%)

- Recidiva comprobada microbiológicamente fue muy baja, *posiblemente porque el tratamiento con C. difficile se extendió* para superponerse con los ciclos de AC.

- El riesgo de recurrencia general muy bajo en este estudio (3,3%) en comparación con lo observado típicamente en los pacientes hospitalizados.

- Este estudio no confirma los análisis de subgrupos de Cornely et al; posiblemente por diferencias en el tamaño muestral sin poder descartar que existan diferencias en los ribotipos.

Conclusión

→ Este estudio no pudo demostrar una diferencia significativa entre la vancomicina y la fidaxomicina para la curación clínica de la ICD.

Limitaciones

- Una sola región y en solo 2 centros médicos
- N inferior a la deseada (144 vs > 200)
- Evaluación subjetiva del resultado: diarrea
- Riesgo de recurrencia bajo → dificulta estudios de RR de recurrencia frente a diferentes terapias

Fortaleza

- Diseño prospectivo y aleatorizado

Junta de Castilla y León
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