# NeYesem Şişiyorumun Çaresi Bulundu mu?

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- Şişkinlik (bloating)-his- semptom-objektif ölçümlenebilir bir bulgu değil
- Şişme (abdominal distention) - objektif bir bulgu-ölçümü yapılabilen karın çevresinde artış

# Rome III Functional Gastrointestinal Disorders (FGID)

- A. Functional esophageal disorders
  - A1. Functional heartburn
  - A2. Functional chest pain of presumed esophageal origin
  - A3. Functional dysphagia
  - A4. Globus
- B. Functional gastroduodenal disorders
  - B1. Functional dyspepsia
    - B1a. Postprandial distress syndrome
    - B1b. Epigastric pain syndrome
  - B2. Belching disorders
    - B2a. Aerophagia
    - B2b. Unspecified excessive belching
  - B3. Nausea and vomiting disorders
    - B3a. Chronic idiopathic nausea
    - B3b. Functional vomiting
    - B3c. Cyclic vomiting syndrome
  - B4. Rumination syndrome in adults
- C. Functional bowel disorders
  - C1. Irritable bowel syndrome
  - C2. Functional bloating
  - C3. Functional constipation
  - C4. Functional diarrhea
  - C5. Unspecified functional bowel disorder
- D. Functional abdominal pain syndrome
- E. Functional gallbladder and Sphincter of Oddi (SO) disorders
  - E1. Functional gallbladder disorder
  - E2. Functional biliary SO disorder
  - E3. Functional pancreatic SO disorder
- F. Functional anorectal disorders
  - F1. Functional fecal incontinence
  - F2. Functional anorectal pain
    - F2a. Chronic proctalgia
      - F2a1. Levator ani syndrome
      - F2a2. Unspecified functional anorectal pain
    - F2b. Proctalgia fugax
  - F3. Functional defecation disorders
    - F3a. Dyssynergic defecation
    - F3b. Inadequate defecatory propulsion

# ROMA III SINIFLAMA-İBS

- Semptomlar tanıdan en az 6 ay önce başlamalı
- Tekrarlayan karın ağrısı veya rahatsızlık hissi, ayda en az üç gün, son üç ay içerisinde  ve aşağıdakilerden en az  ikisi ile ilişkili olmak
  - Dışkılama ile rahatlama
  - Şikayetlerin başlaması ile birlikte dışkı sıklığında değişiklik
  - Şikayetlerin başlaması ile birlikte dışkı şeklinde ve görüntüsünde değişiklik

# ROMA III SINIFLAMASI

- IBS- K (KONSTİPASYON)
  - >25%  kaka sert
  - <25%  kaka gevşek  ve sulu
- IBS-D (DİYARE)
  - >25%  kaka gevşek  ve sulu
  - <25%  kaka sert
- IBS- M (MİKS)
  - >25%  kaka gevşek  ve sulu
  - >25% kaka sert

# İBS - Şişkinlik

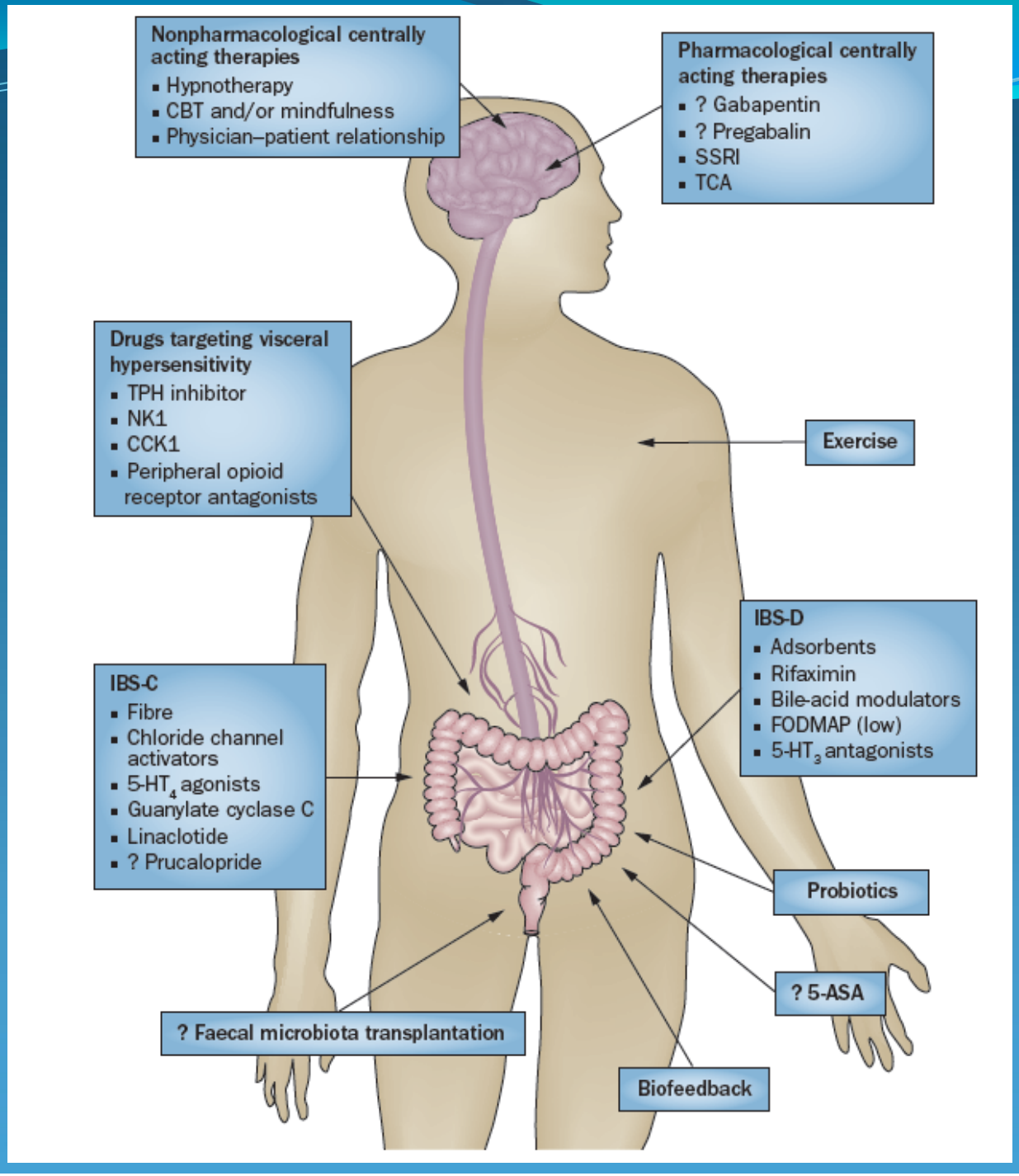
- İBS : %3 -20 prevelans
- en sık sindirim hastalığı
- ciddi sağlık ve ekonomik yükler
- İBS ; % 50- 90'nı şişkinlik
- Kadın/ erkek ; 2/1
- IBS-K  daha sıklıkla ve şiddetli
- İBS tüm zamanlarının %28'inde şişkinlikten ve %33'ünde karın ağrısı

# Şişkinlik- Hastalar

- En iyi hissettikleri zaman sabah (%69),
- akşamları en berbat zamandır (%73),
- gece kısmen düzelme oluyor (%80),
- yemek yemekle kötüleşme var (%82),
- stres ile kötüleşme oluyor (%34),
- defakasyon ve yellenme ile ilişkisiz (%82),
- haftada birkezden daha fazla (%86)
- kısa zamanda başlıyor (10 dakikadan daha kısa) (%61)

# Patofizyoloji

- Gaz fazlalığı
- Barsakta Gazın Sevk ve İdaresi
- Duysal Fonksiyon Bozukluk; viseral hipersensitivite
- Motor Bozuluk; motilite
- Ön Karın Duvarında Bozuk Musküler Aktivite
- Karbonhidarat İntolaransı : laktoz, fruktoz ve sorbitol
- Barsak Florası Değişiklikleri: SBBO


Nonpharmacological centrally acting therapies
▪ Hypnotherapy
▪ CBT and/or mindfulness
▪ Physician–patient relationship
Pharmacological centrally acting therapies
▪ ? Gabapentin
▪ ? Pregabalin
▪ SSRI
▪ TCA
Drugs targeting visceral hypersensitivity
▪ TPH inhibitor
▪ NK1
▪ CCK1
▪ Peripheral opioid receptor antagonists
Exercise
IBS-D
▪ Adsorbents
▪ Rifaximin
▪ Bile-acid modulators
▪ FODMAP (low)
▪ 5-HT3 antagonists
IBS-C
▪ Fibre
▪ Chloride channel activators
▪ 5-HT4 agonists
▪ Guanylate cyclase C
▪ Linaclotide
▪ ? Prucalopride
Probiotics
? 5-ASA
? Faecal microbiota transplantation
Biofeedback

# ALARM BELİRTİLERİ

- Yaş>50
- Niyetsiz kilo kaybı
- Ailede  GI kanser hikayesi
- Ateş/ titreme
- Endemik bölgelere seyahat hikayesi
- Noktürnal semptomlar
- Hematokeziya
- Artirit, deri lezyonlar, LAP, abdominal kitle

# ANTİBİYOTİKLER

- SBBO: laktüloz nefes testi?
- Rifaximin: emilmeyen, (yan etki ve resistans)
- Kronik kullanım
- Konstipe olmayan IBS hastalarında
- Yüksek doz: 2400 mg/gün
- Neomisin: laktüloz nefes testi düzelmesi (pimentel et.al)
- Doksosiklin, amox/clu, ciprofloksasin
- Süre?, tekrar?

**Table 2.** Studies for Rifaximin Treatment in Irritable Bowel Syndrome Patients

| Author (yr) | Study design | Diagnostic criteria | IBS subtypes | Mean age / Female ratio (n) rifaximin vs. placebo | Drug dosage | Treatment duration (days) | RR for global symptoms (rifaximin, %) | RR for bloating |
|---|---|---|---|---|---|---|---|---|
| Sharara et al[45] (2006) | Double-blind, placebo-controlled, single center | 70 met Rome II | All (IBS-D 20.0%, IBS-C 38.3%, IBS-M 41.7%) | 42.2/52.4% (63) vs. 38.9/57.4% (61) | 400 mg b.i.d. | 10 | 41.3 | NA (bloating score; 24.4 → 20.8) ($P = 0.001$) |
| Pimentel et al[109] (2011) | Double-blind, placebo-controlled, multi-center (TARGET 1) | Rome II | Excluded IBS-C | 46.2/76.1% (309) vs. 45.5/70.7% (314) | 550 mg t.i.d. | 14 | 40.8 | 39.5% |
| Pimentel et al[109] (2011) | Double-blind, placebo-controlled, multi-center (TARGET 2) | Rome II | Excluded IBS-C | 45.9/72.1% (315) vs. 46.3/70.3% (320) | 550 mg t.i.d. | 14 | 40.6 | 41.0% |
| Peralta et al[111] (2009) | Observational analysis, single arm, single center | Rome II | All (IBS-D 35.2%, IBS-C 20.4%, IBS-M 44.4%) | NA (54) | 1,200 mg/day | 7 | NA | NA (symptom score; 2.3 → 0.8) ($P = 0.003$) |
| Yang et al[113] (2008) | Retrospective study, single center | Rome I | NA | NA (84) | 1,200 mg/day | NA (follow-up duration; median 11 months) | 69.0 (other antibiotics, 44.0) | NA |
| Pimentel et al[44] (2006) | Double-blind, randomized, placebo-controlled study, 2 centers | Rome I | All (%; NA) | 39.1/67.4% (43) vs. 38.2/65.9% (44) | 400 mg t.i.d. | 10 | 36.40 | NA |
| Jolley et al[112] (2011) | Retrospective study, single center | Rome III | All (IBS-D 28.0%, IBS-C 20.0%, IBS-M 15.0%, not reported in 37.0%; 1,200 mg/d group) (30.0%, 20.0%, 14.0% and 37.0% respectively; high dose group) | 58.0/77.2% (162) vs. 60.0/72.8% (81) (high dose group) | 1,200 mg/day vs. 2,400 mg/day (high dose group) | 10 | 49.0 vs. 47.0 (high dose group) | NA |

IBS, irritable bowel syndrome; RR, response rate; NA, not available; IBS-D, IBS with diarrhea; IBS-C, IBS with constipation; IBS-M, mixed IBS.

# PROBİYOTİKLER

- Çelişkili sonuçlar
- Küçük, iyi dizayn edilmemiş çalışmalar
- Bifidobacterium infantis şişkinliğe faydalı olabilir
- Doz önemli
- Çok suşlu preperatlar olumlu neticeler
- VSL 3 yetersiz yanıt

**Table 3.** Summary of Studies for Probiotics in Irritable Bowel Syndrome

| Author (yr) | Study design | Criteria | IBS subtypes | Sample size | Probiotic strains (daily dose) | Duration (weeks) | Results |
|---|---|---|---|---|---|---|---|
| Nobaek et al[41] (2000) | RCT | Rome I | All (IBS-C, IBS-D, IBS-M) | 60 | *L. plantarum* DSM 9843 (299V) ($5 \times 10^7$ CFU/mL) | 4 | Flatulence; improved in test group ($P < 0.05$)<br>Pain, bloating; no benefit over placebo |
| O'Mahony et al[114] (2005) | RCT | Rome II | All | 75 | *L. salivarius* UCC 4331 or *B. infantis* 35624 | 8 | Abdominal pain, bowel movement difficulty; significantly improved in *B. infantis* group (all $P < 0.05$)<br>Bloating; improved in *B. infantis* group ($P < 0.05$)<br>No benefit in *L. salivarius* group |
| Whorwell et al[115] (2006) | RCT | Rome II | All | 362 | *B. infantis* 35624 (3 groups; $1 \times 10^6$, $1 \times 10^8$ or $1 \times 10^{10}$ CFU/mL) | 4 | Abdominal pain, bloating, incomplete evacuation, straining, passage of gas; improved only in $1 \times 10^8$ group (all $P < 0.05$) |
| Kim et al[120] (2005) | RCT | Rome II | All | 48 | VSL#3 | 4-8 | Flatulence; improved in test group ($P < 0.01$)<br>Failed to show improvement in bloating |
| Niv et al[124] (2005) | RCT | Rome II | All | 54 | *L. reuteri* ATCC 55730 ($1 \times 10^8$ CFU/tablet, twice a day) | 26 | Abdominal pain, bloating, gases, visible abdominal swelling, GSS; improved, but no benefit over placebo |
| Guglielmetti et al[116] (2011) | RCT | Rome III | All | 122 | *B. bifidum* MIMBb75 ($1 \times 10^9$ CFU/capsule, once a day) | 4 | Pain, distension/bloating, GSS; significantly reduced in test group (all $P < 0.0001$) |
| Choi et al[121] (2011) | RCT | Rome II | IBS-D, IBS-M | 67 | *S. boulardii* ($2 \times 10^{11}$ cells/day) | 4 | Quality of life; significant improvement in test group ($P < 0.05$)<br>Bloating; no benefit over placebo |
| Kicha et al[122] (2012) | RCT | Rome III | IBS-D | 50 | A mixture of *L. acidophilus, L. plantarum, L. rhamnosus, B. breve, B. lactis, B. longum and S. thermophilus* ($1 \times 10^{10}$ CFU/day) | 8 | Adequate relief of overall IBS symptoms in test group ($P < 0.05$)<br>Bloating; no benefit over placebo |
| Ducrotté et al[117] (2012) | RCT | Rome III | All | 214 | *L. plantarum* DSM 9843 (299V) ($1 \times 10^8$ CFU/day) | 4 | Abdominal pain, bloating; improved in test group (all $P < 0.05$) |
| Yoon et al[118] (2013) | RCT | Rome III | All | 49 | A mixture of *B. longum, B. bifidum, B. lactis, L. acidophilus, L.rhamnosus* and *S. thermophilus* ($5 \times 10^9$ cells/capsule, twice daily) | 4 | GSS; significantly relieved in test group ($P = 0.03$)<br>Abdominal pain, bloating; improved, but no statistical significance over placebo |

IBS, irritable bowel syndrome; RCT, randomized controlled trial; IBS-C, IBS with constipation; IBS-D, IBS with diarrhea; IBS-M, mixed IBS; *L. plantarum*, *Lactobacillus plantarum*; *L. salivarius*; *Lactobacillus salivarius*; *B. infantis*; *Bifidobacterium infantis*; *L. reuteri*, *Lactobacillus reuteri*; *B. bifidum*; *Bifidobacterium bifidum*; *S. boulardii*, *Saccharomyces boulardii*; *L. acidophilus*, *Lactobacillus acidophilus*; *L. rhamnosus*, *Lactobacillus rhamnosus*; *B. lactis*, *Bifidobacterium lactis*; *B. longum*, *Bifidobacterium longum*, *S. thermophilus*, *Streptococcus thermophilus*; GSS, global symptom score.

# PROKİNETİKLER

- Çelişkili sonuçlar
- Cisapride (5- hidroksitriptamin 4) reseptör agonisti
- Levosulpride
- Acotiamide
- Tegaserod : 5 HT4 parsiyal agonisiti- 2007
- Neostigmin: potent prokinetik
- Domperidon: faydasız
- Piridostigmine: küçük çalışma, sınırda fayda

**Table 4.** Summary of Studies for Prokinetics in Irritable Bowel Syndome

| Author (yr) | Study design | Diagnosic Criteria | IBS subtypes | Sample size | Prokinetics used (daily dose) | Duration (wk) | Results |
|---|---|---|---|---|---|---|---|
| Schütze et al[124] (1997) | RCT | Rome I | IBS-C | 96 | Cisapride (5 mg t.i.d., titrated to 10 mg t.i.d. if no response after 4 wk) | 12 | Bloating, GSS; not superior to placebo<br>Difficulty of stool passage; significant improvement in test group ($P < 0.05$) |
| Müller-Lissner et al[125] (2001) | RCT | Rome I | All (IBS-D, IBS-C, IBS-M) | 881 | Tegaserod (2 mg or 6 mg b.i.d.) | 12 | Abdominal pain/discomfort; improved in both test groups ($P < 0.05$), more consistent efficacyover time in higher dose group<br>Bloating; favorable trend in reduction in both test groups |
| Novick et al[120] (2002) | RCT | Rome I | All | 1,519 (all female) | Tegaserod (6 mg b.i.d.) | 12 | Abdominal pain, bloating, stool consistency, GSS; improved in test group (all $P < 0.05$) |
| Kellow et al[121] (2003) | RCT | Rome II | Excluded IBS-D | 520 | Tegaserod (6 mg b.i.d.) | 12 | GSS; improved in test group ($P < 0.0001$)<br>Abdominal pain, bloating, hard stools; improved in test group (all $P < 0.05$) |
| Tack et al[122] (2005) | RCT | Rome II | IBS-C | 2,660 (all female) | Tegaserod (6 mg b.i.d.) | 4 | Abdominal pain, bloating, constipation; improved in test group (all $P < 0.0001$) |
| Chey et al[169] (2008) | RCT | Rome II | IBS-C, IBS-M | 661 (all female) | Tegaserod (6 mg b.i.d.) | 4 | Overall symptom; relieved in test group ($P < 0.001$)<br>Bloating; no benefit over placebo |
| George et al[170] (2008) | RCT | Rome II | IBS-C | 510 | Renzapride (1 mg, 2 mg or 4 mg o.d.) | 12 | Stool frequency, stool consistency; improved in 2 mg and 4 mg o.d. groups (all $P < 0.05$)<br>Bloating; reduction in 1mg o.d. group ($P = 0.01$) |

RCT, randomized controlled trial; GSS, global symptom score; IBS, irritable bowel syndrome; IBS-D, IBS with diarrhea; IBS-C, IBS with constipation; IBS-M, mixed IBS.

# ANTİSPAZMOTİKLER

- IBS tx sık kullanılanlar
- Motilite ve düz kas spazmı
- Şişkinlik için bazılarında fayda gösterilmiş
- Otilinium için data sağlam
- Daha büyük, iyi dizayn edilmiş çalışmalar gerekli

**Table 5.** Summary of Studies for Spasmolytics in Irritable Bowel Syndrome

| Author (yr) | Study design | Diagnostic criteria | IBS subtypes | Sample size | Spasmolytics used (daily dose) | Duration (weeks) | Results |
|---|---|---|---|---|---|---|---|
| Battaglia et al[141] (1998) | RCT | Drossman's criteria for IBS | NA | 325 | Otilonium bromide (40 mg t.i.d.) | 15 | Abdominal pain, distension; significant reduction (all $P < 0.05$) |
| Dobrilla et al[171] (1990) | RCT | Clinical diagnosis and investigations | NA | 70 | Cimetropium (50 mg t.i.d.) | 12 | Severity and frequency of abdominal pain; significantly decreased ($P = 0.0005$ and 0.001, respectively)<br>Abdominal distension; decreased, but not statistically significant ($P = 0.055$) |
| Glende et al[143] (2002) | RCT | Rome I | All (IBS-D, IBS-C, IBS-M) | 378 | Otilonium bromide (40 mg t.i.d) | 15 | Abdominal pain, distension; improved in test group (all $P < 0.05$) |
| Mitchel et al[172] (2002) | RCT | Rome II | All | 107 | Alverine (150 mg t.i.d.) | 12 | Abdominal pain, bloating, general well-being; failed to show benefit over placebo |
| Clave et al[140] (2011) | RCT | Rome II | All | 356 | Otilonium bromide (40 mg t.i.d.) | 15 | Abdominal pain ($P = 0.03$), bloating ($P = 0.02$), global efficacy ($P = 0.047$); significant benefit over placebo |
| Chang et al[173] (2011) | RCT | Rome II | All | 117 | Otilonium bromide (40 mg t.i.d.)<br>Ornebeverine (100 mg t.i.d.) | 8 | Abdominal pain, flatulence, bloating, global assessment; relieved in both treatment group (all $P < 0.05$) |

NA, not available; RCT, randomized controlled trial; IBS, irritable bowel syndrome; IBS-D, IBS with diarrhea; IBS-C, IBS with constipation; IBS-M, mixed IBS.

# DİYET TEDAVİLERİ

- Yüksek derecede fermente edilebilen, kısa zincirli karbonhidrattan fakir  diyet (FODMAB)
- Fruktoz intolaransı
- Faydalı olabilir

**Table 6.** Summary of Studies for Dietary Interventions in Irritable Bowel Syndrome

| Author (yr) | Study design | Subjects included | Sample size | Dietary interventions | Results |
|---|---|---|---|---|---|
| Choi et al[147] (2008) | Prospective study, single arm, single center | IBS (Rome II) | 26 | Fructose-restricted diet (mean follow-up of 13 mo) | Abdominal pain, belching, fullness, bloating; significant relief (all $P < 0.02$) |
| Shepherd et al[148] (2008) | RCT | IBS (Rome II) | 25 | Low FODMAP diet before trial (median 24 mo)<br>Fructan, fructose, fructan-fructose mix, or glucose drinks (for 2 wk) | Abdominal pain, bloating; significantly increased in fructan, fructose, and mix group compared with glucose group (all $P < 0.01$) |
| Ong et al[89] (2010) | Single-blind, crossover intervention trial | IBS (Rome III) vs. healthy subjects | 15 vs. 15 | Low (9 g/day) or high (50 g/day) in FODMAPs for 2 days | Abdominal pain, bloating, excessive flatus; increased with HFD in IBS patients (all $P < 0.01$) |
| de Roest et al[151] (2013) | Prospective study, single arm | IBS | 90 | low FODMAP diet (mean follow-up of 15.7 mo) | Abdominal pain, bloating, flatulence, diarrhea; significantly improved compared to baseline (all $P < 0.001$) |

RCT, randomized controlled study; IBS, irritable bowel syndrome; FODMAPs, fermentable oligo-, di-, and mono-saccharides and polyols HFD, high FODMAP diet.

# GAZ AZALTICI İLAÇLAR

- Köpükleşmeyi engelleyen (antifoaming) ajanlar
- Simeticone: silocon türevi
- FGID etkili ; Bernstein et al.
- Aktif köür- simeticone: RCT etkili

**Table 7.** Summary of Studies for Gas-reducing Substances in Functional Gastrointestinal Disorder

| Author (yr) | Study design | Subjects included | Sample size | Drugs used (daily dose) | Duration | Results |
|---|---|---|---|---|---|---|
| Bernstein et al[153] (1974) | RCT | FGID | 41 | Simethicone (50 mg, number of tablets unclear) | 10 days | Fullness, bloating, distension; significant improvement in test group (all $P < 0.005$) |
| Holtmann et al[154] (2002) | RCT | FD | 185 | Simethicone (105 mg t.i.d.) or cisapride (10 mg t.i.d.) | 8 wk | Overall symptom, fullness, pain; improved in both test groups<br>Bloating; no benefit |
| Lecuyer et al[155] (2009) | RCT | Patients with fullness, bloating, nausea or slow digestion | 132 | Simethicone and activated charcoal (Carbosylane®) | 3 mo | Overall complaints; no improvement over placebo<br>Fullness, bloating; significant improvement in test group (all $P < 0.05$) |
| Wittmann et al[174] (2010) | RCT | IBS (Rome III) | 412 | Alverine citrate/Simethicone (60 mg/300 mg t.i.d.) | 4 wk | Abdominal pain, discomfort; superior efficacy in test group ($P = 0.047$)<br>Bloating; no evidence |

RCT,randomized controlled study; FGID, functional gastrointestinal disorder; FD, functional dyspepsia; IBS, irritable bowel syndrome.

# SIVI SEKRESYON ARTIRICILAR

- Lubiprostone
- Linaclotide.....FDA onaylı
- Barsak lümenine  sıvı sekresyonunu artırır ve barsak transit zamanını hızlandırır
- Konstipasyonda etkili,
- Şişkinlikte de etkili

**Table 8.** Summary of Studies for Stimulants of Fluid Secretion in Functional Gastrointestinal Disorder

| Author (yr) | Study design | Subjects included | Sample size | Drug used (daily dose) | Duration (wk) | Results |
|---|---|---|---|---|---|---|
| Johanson et al[156] (2007) | RCT | Chronic constipation | 129 | Lubiprostone (24 μg/day, 48 μg/day, or 72 μg/day) | 3 | Bloating; significant relief in all test groups ($P = 0.035$)<br>SBM frequency; improved in a dose-dependent manner |
| Drossman et al[157] (2009) | RCT | IBS-C (by Rome II) | 1,171 | Lubiprostone (8 μg twice daily) | 12 | Overall response rate; higher in test group ($P = 0.001$)<br>Abdominal pain, bloating, constipation severity; significant relief only in responders |
| Lembo et al[159] (2011) | RCT | Chronic constipation | 1,276 | Linaclotide (145 μg or 290 μg once daily) | 12 | CSBM; improved in both trials (all $P < 0.001$)<br>Abdominal discomfort, bloating, constipation severity; improved in both trials (all $P < 0.05$) |
| Quigley et al[158] (2013) | RCT | IBS-C | 1,608 | Linaclotide (290 μg once daily) | 12 or 26 | Abdominal discomfort, bloating, stool consistency; significant improvements in both trials (all $P < 0.0001$) |

RCT, randomized controlled trial; SBM, spontaneous bowel movement; IBS-C, IBS with constipation; CSBM, complete SBM.

# ANTİDEPRESANLAR

- SSRI
- TCA… viseral analjesik etkiler
- Fluoxetine: şişkinlikte etkisiz bulunmuş
- Parıxetine: İBS'de etkili fakat şişkinlikte yetersiz
- Citalopram: etkili olabilir
- Çelişkili sonuçlar var
- Daha büyük ve iyi dizayn edilmiş çalışmalara ihtiyaç var

**Table 9.** Summary of Studies for Antidepressants in Functional Gastointestinal Disorder

| Author (yr) | Study design | Subjects included | Sample size | Antidepressant used (daily dose) | Duration | Results |
|---|---|---|---|---|---|---|
| Kuiken et al[160] (2003) | RCT | IBS | 40 | Fluoxetine (20 mg/day) | 6 wk | Threshold for abdominal pain, bloating; no significant changes |
| Tabas et al[161] (2004) | RCT | IBS, not responding to high fiber diet | 81 | Paroxetine (10 mg/day) | 12 wk | Overall well-being; significantly improved ($P = 0.01$)<br>Abdominal pain, bloating; no benefit over placebo |
| Vahedi et al[175] (2005) | RCT | IBS-C (Rome II) | 44 | Fluoxetine (20 mg/day) | 12 wk | Abdominal discomfort, stool consistency, bloating; significant relief in test group (all $P < 0.05$) |
| Tack et al[162] (2006) | RCT | IBS (Rome II) | 23 | Citalopram (20 mg/day for 3 wk, then 40 mg/d for 3 wk) | 6 wk | Abdominal pain, bloating, overall well-being; significant relief in test group (all $P < 0.05$) |
| Vahedi et al[176] (2008) | RCT | IBS-D (Rome II) | 54 | Amitriptyline (10 mg/day) | 2 mo | Abdominal pain, loose stools, diarrhea; significant improvement in test group (all $P < 0.05$)<br>Flatulence; no benefit over placebo<br>Bloating; not evaluated |

RCT, randomized controlled study; IBS, irritable bowel syndrome; IBS-C, IBS with constipation; IBS-D, IBS with diarrhea.

# OPİOİD AGANİST İLAÇLAR

- IBS'de opioidlerle ilgili az çalışma
- Fedotozine: kappa reseptör agonisti: kolonik distansiyon ve viseral hissi azaltır
- Yemek sonrası dolgunluk ve şikinliği azaltıyor
- Asimadoline:kappa opioid agonist: IBS-D'de şişkinlikte mükemmel başarı
- Naloxane: küçük çalışma, başarılı (IBS-D ve IBS-M'de)

**Table 10.** Summary of Studies for Opioid Agents in Functional Gastrointestinal Disorder

| Author (yr) | Study design | Subjects included | Sample size | Drug used (daily dose) | Duration (wk) | Results |
|---|---|---|---|---|---|---|
| Fraitag et al[164] (1994) | RCT | NUD | 146 | Fedotozine (10, 30 or 70 mg t.i.d.) | 6 | Postprandial fullness, bloating, abdominal pain and nausea; significant relief in 30 mg and 70 mg groups |
| Read et al[177] (1997) | RCT | FD | 271 | Fedotozine (30 mg t.i.d.) | 6 | Epigastric pain, postprandial fullness, nausea; significant improvement in test group<br>Bloating; not evaluated |
| Hawkes et al[166] (2002) | RCT | IBS-C, IBS-M (Rome II) | 28 | Naloxone (10 mg b.i.d.) | 8 | Abdominal pain, bloating, straining, urgency to defecate; improved, but no significant differences over placebo |
| Mangel et al[165] (2008) | RCT | IBS (Rome II) | 596 | Asimadoline (0.15, 0.5 or 1.0 mg b.i.d.) | 12 | Abdominal pain, bloating; improved only in IBS-D with both 0.5 mg and 1.0 mg dose |
| Szarka et al[178] (2007) | RCT | IBS (Rome II) | 100 | Asimadoline (on demand/up to 1.0 mg q.i.d.) | 4 | Abdominal pain/discomfort, frequency of bowel movements; not improved<br>Bloating; not evaluated |

RCT, randomized controlled trial; NUD, nonulcer dyspepsia; FD, functional dyspepsia; IBS-C, IBS with constipation; IBS-M, mixed IBS; IBS-D, IBS with diarrhea.

# TAMAMLAYICI-ALTERNATİF TIP HERBAL TEDAVİ

- Geleneksel tedaviler, Çin, Hint, Orta Doğu: Aktar
- Kısmi fayda
- Doz?
- Süre?
- Tekrarlanabilirlik?

Table 3. Single Herbal Medicines for IBS

| Reference | Sample size | Sample characteristics | Study design | Dose of active | Duration | Outcome |
|---|---|---|---|---|---|---|
| **Enteric-coated peppermint oil capsules** | | | | | | |
| Capello et al (2007) | 57 | All IBS forms, IBS determined by Rome II criteria | R,D,P | 225 mg peppermint oil per cap; 2 caps bid | 4 weeks rx; 4 weeks follow-up | Significant reduction in IBS symptoms after 4 weeks in peppermint oil group vs. placebo group |
| Merat et al (2010) | 90 | All IBS forms, IBS determined by Rome II criteria | R,D,P | 187 mg peppermint oil tid, 30 min before meals | 8 weeks | Significant reduction in abdominal pain and severity in peppermint oil group vs. placebo, significant increase in QOL in peppermint oil group vs. placebo |
| **Turmeric extract (standardized)** | | | | | | |
| Bundy et al (2004) | 207 | All IBS forms, IBS determined by Rome II criteria | R, non-D, non-P | 2 doses, 72 mg (1 tablet) or 144 mg (2 tablets) daily | 8 weeks | Significant improvement in IBS QOL at end of trial compared to baseline for both treatment groups |
| **Artichoke leaf extract** | | | | | | |
| Walker et al (2001) | 279 | All IBS forms, meeting at least 3 out of 5 Rome II criteria | R, non-D, non-P | 320 mg artichoke leaf extract per cap; 2 caps tid w/ meals | 6 weeks | Significant reduction of IBS-related symptoms evaluated on a Likert scale at end of study compared to baseline |
| Bundy et al (2004) | 208 | All IBS forms, meeting at least 3 out of 5 Rome II criteria | R, non-D, non-P | 320 mg (1 capsule) or 640 mg (2 capsules) of 1:5 artichoke leaf extract daily | 8 weeks | Significant reduction in NDI QOL score at end of trial compared to baseline |

R: Randomized, D: Double-blind, P: Placebo-controlled
NDI=Nepean Dyspepsia Index

# BEKLENEN TEDAVİLER

**Table 3** | Selected emerging and possible future pharmacological and nonpharmacological treatments for IBS

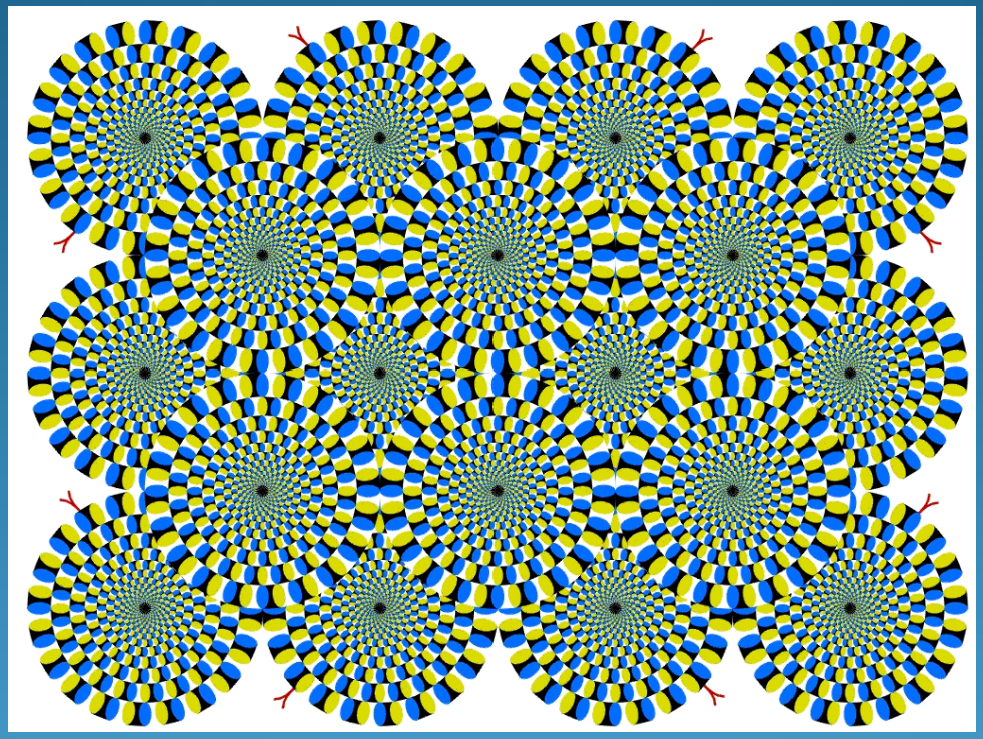
| Drug class | Example of drug name | Comments |
|---|---|---|
| ***Drugs targeting visceral hypersensitivity*** | | |
| Serotonin synthesis inhibitors | LX-1031 | Positive phase II trial data including favourable adverse event profile[101] |
| Neurokinin 1 receptor antagonist | AV608 | Further research on this molecule suspended due to safety concerns;[104] other neurokinin 1 receptor molecules might be useful |
| Cholecystokinin 1 antagonists | Dexloxiglumide | Limited human data emerging[106] |
| Peripheral opioid receptor antagonists | Asimadoline and JN-38488502 | Promising findings from animal data not replicated in human studies thus far[109] |
| ***Drugs targeting motility*** | | |
| 5-$HT_4$ agonists | Velusetrag, prucalopride, naronapride | Prucalopride effective in chronic constipation; data from trials in patients with IBS awaited |
| Corticotrophin releasing factor antagonists | Pexacerfont | Did not alter colonic transit in a large phase IIa study[122] |
| ***Bile-acid modulators*** | | |
| Bile-acid binder | Colesevelam | Case reports of efficacy and limited trial data[113] |
| Bile-acid-transporter inhibitor | A3309 | Promising data from patients with chronic constipation[130] |
| Bile acid | Chenodeoxycholate | Healthy volunteer data demonstrating accelerated colonic transit[111] |
| ***Drugs targeting inflammation*** | | |
| 5-aminosalicylic acid | Mesalazine | No data from well-designed trials in patients with IBS |
| Mast cell stabilizers | Ketoifen<br>Sodium cromoglycate | Promising data from small uncontrolled trials[116] |
| ***Centrally acting drugs*** | | |
| Benzodiazepine receptor modulators | Dextofisopam | Improved stool consistency in a small trial, but concerns about higher rates of abdominal pain than with placebo[118] |
| Antiepileptic | Pregabalin and gabapentin | Physiological effect on rectal sensory threshold,[120] but no clinical trials so far |
| ***Nonpharmacological treatments targeting the microbiota or motility*** | | |
| Faecal microbiota transplantation | Not applicable | Limited data from nonrandomized trials only[115] |
| Biofeedback | Not applicable | Promising data from uncontrolled trial including patients with constipation-predominant IBS[61] |

Table 8. Summary of Studies on Herbal Combinations for IBS

| Reference | Sample size | Sample characteristics | Study design | Dose | Duration | Outcome |
|---|---|---|---|---|---|---|
| **Iberogast®** | | | | | | |
| Madisch et al (2004) | 203 | All IBS forms, IBS determined by Rome II criteria | R,D,P | STW 5, STW 5-II, or bitter candytuft extract, 20 drops tid | 4 weeks | Significant reduction of IBS symptoms and abdominal pain in Iberogast and research solution compared to placebo |
| **Padma Lax®** | | | | | | |
| Sallon et al (2002) | 61 | IBS-C, IBS determined by Rome I criteria | R,D,P | 482 mg Padma Lax (n=34) or placebo (n=27), bid (once daily in subjects w/ loose stool) | 12 weeks | Significant reduction in symptom severity scores and abdominal pain in Padma Lax compared to placebo |
| **Traditional Chinese Herbal Medicine** | | | | | | |
| Bensoussan et al (1998) | 116 | All IBS forms, determined by Rome criteria (not specified) | R,D,P | Standard TCM mixture of 33 herbs (n=43), individualized formula (n=38), or placebo (n=35), 5 capsules tid | 16 weeks | Significant reduction in bowel symptom scores and increase in QOL for individual preparation and standard TCM compared to placebo |
| Wang et al (2008) | 24 | All IBS forms, evaluation not specified | R,non-D,P | 24 g Shugan Jianpi granules tid, 24 g Shugan Jianpi granules plus 15 g Smecta® tid, or cognitive therapy and lactein treatment as standard care | 2 weeks | Significant reduction in serotonin positive cells in both Shugan Jianpi groups compared to standard care |
| Leung et al (2006) | 119 | IBS-D, IBS determined by Rome II criteria | R,D,P | See Table 7 for daily dose of each herb (n=60) or placebo (n=59) | 8 weeks | No significant improvement in SF-36 or global symptoms compared to placebo |

R: Randomized, D: Double-blind, P: Placebo-controlled

# NeYesem Şişiyorumun Çaresi Bulundu mu?



# TEŞEKKÜRLER.....