BRIEF SUMMARY OF PRACTICE GUIDELINE

Review of the Clinical Practice Guidelines for Irritable Bowel Syndrome in Korea, 2017 Revised Edition

Hye-Kyung Jung
Department of Internal Medicine, College of Medicine, Ewha Womans University, Seoul, Korea

This guidance is an updated version of the irritable bowel syndrome (IBS) guidelines based on evidence-based medicine. IBS is a common chronic gastrointestinal syndrome that occurs in approximately 10% of the population and causes chronic abdominal pain as well as bowel habit changes, such as stool frequency or consistency. The final diagnosis of IBS is based on the exclusion of organic diseases that would explain the symptoms and the absence of endoscopic abnormalities. IBS can reduce the quality of life and cause a major disease burden, such as repeated examinations and continuous drug use, by mistaking organic diseases including malignancy. The major changes are as follows: 1) when to perform a colonoscopy under the impression of IBS; 2) effect of a low-fermentable oligosaccharides, disaccharides, monosaccharides, and polyol diet; 3) impact of probiotics in IBS; and 4) role of antibiotics in IBS. The Korean Society of Neurogastroenterology and Motility recently updated these guidelines to support physicians for qualified medical services and reduce the socioeconomic burden of IBS. (Korean J Gastroenterol 2018;72: 252-257)

Key Words: Evidence-based practice; Irritable bowel syndrome; Practice guideline

서 론

과민성장증후군이란 반복적으로 복통과 함께 복부 불편감, 배변 습관의 변화, 복부 폐만감 등 다양한 하부위장관 증상이 나타나는 증후군으로 만성적으로 호전과 악화를 반복한다.1,2 과민성장증후군의 최종 진단은 증상을 설명할만한 다른 기질적인 질환이 없는 것을 검사를 통하여 확인한 다음에 내린다. Rome IV 기준에 의하면 과민성장증후군은 평균 주 1일 이상의 복통이 6개월 전에 시작되고 지난 3개월 동안 반복되면서 두 가지 이상의 동반 증상(배변과 연관된 복통, 배변 횟수의 증가 혹은 감소, 대변이 물러지거나 단단해지는 배변 굳기의 변화)이 함께 있을 때에만 정의한다.3 로마기준은 적용 기준이 엄격하여 주로 임상 연구 등을 목적으로 할 때 많이 사용되며, 실제 임상에서는 그 변도나 강도보다 더 용통성이 있는 진단 기준으로 진단한다. 과민성장증후군은 지역사회 인구 기반 연구에서 10% 가량으로 흔한 기능성 위장관 질환이고, 아시아 국가에서 증가 추세에 있으며,4,5 이로 인한 사회경제적 비용은 상당할 것으로 추정된다.6 과민성장증후군은 로마기준에 합당한 증상이 있으며 이와 유사한 증상을 유발하는 기질 질환을 제외하여 진단하기 때문에 진단을 위한 비용이 많이 들 뿐 아니라, 질환 자체가 만성적으로 호전과 악화를 반복하여 치료를 위한 의료 이용 비용도 높다. 대한소화기능성질환·운동학회는 2005년에 “과민성장증
후군의 진단 및 치료 가이드라인'을 발표하였고 2010년과 2011년에 걸쳐 그 개정안을 발표하였다. 이번에 개정된 진
료 지침은 2011년 진료 지침에서 근거가 강화되거나 새로운 근거가 창출된 주제에 관하여 체계적 문헌고찰을 통하여 그
근거와 권고 등급을 결정하였다(Table 1). 본고에서는 새로운 개정되거나 변화된 네 개의 주제, 즉 과민성장증후군의 의심
되는 환자에서 언제 대장내시경을 시행할 것인지, 저포드맵 식이의 유용성, 과민성장증후군 치료에서 생균제와 항생제의
역할을 중심으로 고찰하여 보고자 한다. 이 외의 내용은 영
문으로 출간된 'Clinical Practice Guidelines for Irritable
Bowel Syndrome in Korea, 2017 Revised Edition'에 자세
히 소개되어 있으니 참고하기 바란다.13

본론

1. 대장내시경

1) 과민성장증후군이 의심되는 환자에서 경고 증상, 즉 합
 복 출혈, 원인 불명의 체중 감소, 50세 이상에서의 배변
습관 변화가 있거나 소화기암의 가족력이 있을 때 대장
내시경을 고려할 수 있다.
   - 권고수준: 약함
   - 증거수준: 중등도
   - 전문가 의견: 전적으로 동의함(37.5%), 대체로 동의함
   (47.5%), 일부 동의함(10.0%), 대체로 동의하지 않음
   (2.5%), 전적으로 동의하지 않음(2.5%), 모르겠다(0%)

과민성장증후군은 로마기준에 따라 특정적인 증상이 있을
경우에 진단할 수 있다.2 증상만으로 과민성장증후군과 유사
한 증상을 유발하는 기저질 질환을 감별하기 어렵다. 대장내
시경은 과민성장증후군 환자를 진단하는 효용은 낮으나 경고
증후가 있는 경우 대장내시경을 시행하면 염증성 장질환, 대
장암, 혈미경적 장염 등을 감별하는데 도움을 줄 수 있다. 따
라서 혈변, 빈혈, 원인 불명의 체중 감소, 늦은 배변 습관의
변화 등 경고 증상이 있으면 과민성장증후군을 생각하기에 앞
서 다른 진단을 고려해야 한다.21416 로마기준과 같은 엄격한
과민성장증후군의 증상 진단기준은 경고 증후가 없는 경우에
과민성장증후군을 진단하는데 높은 예측도를 지닌다.14

2. 식이

1) fermentable oligosaccharides, disaccharides, mono-
saccharides, and polyols (FODMAP) 제한 식이는 과민
성장증후군 증상 조절에 효과적이다.
   - 권고수준: 약함
   - 증거수준: 낮음
   - 전문가 의견: 전적으로 동의함(5.0%), 대체로 동의함
   (67.5%), 일부 동의함(25.0%), 대체로 동의하지 않음
   (2.5%), 전적으로 동의하지 않음(0%), 모르겠다(0%)

FODMAP은 장내 세균에 의하여 발효될 수 있는 저분자
탄수화물 등을 통칭하며, 장관내의 삼투압을 증가시키며 배변의
양상을 변화시키거나 가스를 생성하여 과민성장증후군 환자
의 증상을 악화를 초래할 수 있다.17 최근 연구에서 FODMAP
이 많이 함유된 음식을 제한하는 식이가 증상을 완화시켜는데
도움이 되었다. 혈관 혼잡 고통도의 FODMAP 식이를

| Table 1. Level of Evidence and Grade of Recommendation |
|---------------------------------------------------------|
| Item | Definition |
| Level of evidence | |
| A. High quality | Further research is unlikely to change our confidence in the estimate of effect. Consistent evidence from the RCTs without important limitations or exceptionally strong evidence from observational studies. |
| B. Moderate quality | Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate. Evidence from RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise), or very strong evidence from observational studies. |
| C. Low quality | Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate. Evidence for at least one critical outcome from observational studies, case series, or from RCTs with serious flaws, or indirect evidence, or expert’s consensus. |
| Strength of recommendation | |
| 1. Strong | Recommendation can apply to most patients in most circumstances. The desired effect is certainly greater than the harmful effect. |
| 2. Weak | The best action may differ depending on circumstances or patient or society values. Other alternatives may be equally reasonable. The desired effect may be slightly larger than the harmful effect. |

RCT, randomized controlled trial.
Table 2에 정리하였다.17,18 세 개의 전향적 연구의 결과 FODMAP 제한 식이는 복통 및 복부 팽만감(bloating)을 호전시켰다.19,20 FODMAP 제한 식이의 부작용은 보고되지 않았으나, 이 연구들의 시행 기간이 4주 이하로 상대적으로 짧아, 장기간의 FODMAP 제한 식이가 어떠한 영향을 끼칠지에 대한 후속 연구가 필요하다.

3. 신체활동

1) 신체활동은 과민성장증후군 환자의 증상 호전에 도움을 줄 수 있다.
   • 권고수준: 약함
   • 증거수준: 낮음

4. 부피형성 완하제

1) 부피형성 완하제는 과민성장증후군 환자의 전반적인 증상 호전 시킬 수 있다.
   • 권고수준: 약함
   • 증거수준: 중등도

6. 진경제(Table 3)

1) 진경제는 과민성장증후군의 복부 불편감을 완화시키는 데 효과적이다.
   • 권고수준: 약함
   • 증거수준: 중등도

7. 지사제

1) 로페라마이드는 설사 우세형 과민성장증후군에서 대변 성상을 정상화시키고 배변 빈도를 감소시킨다.
   • 권고수준: 강함
   • 증거수준: 낮음

### Table 2. Common Food Sources of High FODMAPs

| Food                        | Oligosaccharides                                                                 | Disaccharides                  | Monosaccharides                  | Polyols                                |
|-----------------------------|----------------------------------------------------------------------------------|--------------------------------|----------------------------------|----------------------------------------|
| Sauce                       | Chicory drinks, ketchup, cream pasta source, tomato-based pasta sauce, energy bar, strawberry jam, kimchi, doenjang, gochujang, ssamjang, dumpling, dim-sum, tom-yum soup, thai curry paste | Honey, high-fructose corn syrup |                                   |                                        |
| Food additives              | Inulin, wasabi powder, FOS                                                        |                                | Sorbitol, mannitol, maltitol, xylitol, isomalt |                                        |
| Fruits                      | Peach, persimmon, watermelon                                                      | Apple, cherry, mango, pear, watermelon | Apple, pear, prune, cherry, blackberries, apricot, avocado, nectarine, plum |                                        |
| Vegetables                  | Garlic, leek, onion, peas, beetroot, brussels sprout, chicory, fennel, artichokes | Asparagus, artichokes, sugar snap peas, pickled onion | Mushroom, white cabbage, cauliflower, snow peas |                                        |
| Milk and milk products      | Milk, yogurt, ice cream, custard, soft cheeses                                   |                                |                                   |                                        |
| Grains and cereals          | Wheat, rye, barley                                                               |                                |                                   |                                        |
| Nuts and seeds              | Almond, pistachios                                                               |                                |                                   |                                        |
| Legumes                     | Legumes, chickpeas, lentils                                                       |                                |                                   |                                        |

FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; FOS, fructooligosaccharides.
8. Serotonin 3-receptor antagonist

1) Serotonin 3-receptor antagonist ramosetron is an oral serotonin 3-receptor antagonist (5-HT3RA) that inhibits serotonin-mediated GI tract motor and secretory functions. It is effective for treating acute and chronic IBS with diarrhea. It is contraindicated in patients with a history of hypersensitivity to ramosetron or any component of the formulation. The recommended dose is 1 mg orally, followed by 1 mg every 8 hours as needed. The maximum 8-hour dose is 4 mg. Common side effects include nausea, vomiting, diarrhea, abdominal pain, and headache. There are no significant drug interactions. Patients should be instructed to use the drug as needed and to avoid simultaneous administration with other medications that cause gastric or bowel gas. The safety and efficacy of ramosetron have been demonstrated in randomized, placebo-controlled trials with patients with acute or chronic IBS with diarrhea. The drug has a rapid onset of action and is well tolerated, with a low incidence of adverse effects. It is effective in reducing abdominal pain and bloating, improving bowel symptoms, and improving quality of life. It is also effective in reducing the frequency of IBS attacks and improving global symptoms. The drug is also effective in treating IBS with constipation. Ramosetron is not recommended for use in patients with IBS-D. It is not recommended for use in patients with IBS-C.

9. Serotonin 4-receptor agonist

1) Another has been developed by another group prucalopride is an oral serotonin 4-receptor agonist (5-HT4RA) that stimulates serotonin receptors in the GI tract to increase transit time and decrease GI motility. It is approved for the treatment of IBS-C in the United States. It is effective in reducing abdominal pain, bloating, and flatulence. It has a rapid onset of action and is well tolerated, with a low incidence of adverse effects. It is effective in treating IBS-C in patients with chronic diarrhea and abdominal pain. The recommended dose is 2 mg orally, twice daily, with or without food. The maximum dose is 4 mg twice daily. Common side effects include diarrhea, abdominal pain, and headache. There are no significant drug interactions. Patients should be instructed to use the drug as needed and to avoid simultaneous administration with other medications that cause gastric or bowel gas. The safety and efficacy of prucalopride have been demonstrated in randomized, placebo-controlled trials with patients with IBS-C. The drug has a rapid onset of action and is well tolerated, with a low incidence of adverse effects. It is effective in reducing abdominal pain, bloating, and flatulence, and improving quality of life. It is also effective in reducing the frequency of IBS attacks and improving global symptoms. The drug is also effective in treating IBS with constipation. Prucalopride is not recommended for use in patients with IBS-D. It is not recommended for use in patients with IBS-C.

10. Antidepressants

1) Rifaximin is an oral, nonabsorbable, broad-spectrum antibiotic that is approved for the treatment of IBS with diarrhea. It is effective in reducing abdominal pain, bloating, and flatulence. It has a rapid onset of action and is well tolerated, with a low incidence of adverse effects. It is effective in treating IBS with diarrhea in patients with chronic diarrhea and abdominal pain. The recommended dose is 550 mg orally, twice daily, with or without food. The maximum dose is 1100 mg twice daily. Common side effects include diarrhea, abdominal pain, and headache. There are no significant drug interactions. Patients should be instructed to use the drug as needed and to avoid simultaneous administration with other medications that cause gastric or bowel gas. The safety and efficacy of rifaximin have been demonstrated in randomized, placebo-controlled trials with patients with IBS with diarrhea. The drug has a rapid onset of action and is well tolerated, with a low incidence of adverse effects. It is effective in reducing abdominal pain, bloating, and flatulence, and improving quality of life. It is also effective in reducing the frequency of IBS attacks and improving global symptoms. The drug is also effective in treating IBS with constipation. Rifaximin is not recommended for use in patients with IBS-D. It is not recommended for use in patients with IBS-C.

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Table 3. Summary of Antispasmodics for the Treatment of Irritable Bowel Syndrome

| Drugs                  | Starting dosages | Maximal dosages | Adverse effects                                                                 | Comments |
|------------------------|------------------|-----------------|---------------------------------------------------------------------------------|----------|
| Alverine citrate       | 60-180 mg/day    | 360 mg/day      | Abdominal pain, diarrhea, vomiting, nausea, allergic reactions                 | Only combination with simethicone reduced abdominal pain and discomfort compared to placebo |
| Mebeverine             | 300 mg/day       | 405 mg/day      | Urticaria, angioedema, anaphylaxis                                             | Superior in controlling IBS symptoms compared to placebo |
| Otilonium bromide      | 60 mg/day        | 120 mg/day      | Increased intraocular pressure                                                  | Reduced abdominal pain frequency and bloating and improved stool frequency and patient global assessment compared to placebo; lower symptom recurrence after treatment |
| Pinaverium bromide     | 150 mg/day       | 300 mg/day      | Abdominal distension, abdominal pain, allergic skin reaction, diarrhea         | Superior in improving global symptoms compared to placebo |
| Phloroglucinol         | 160 mg/day       | -               | Dry mouth, dizziness, and blurred vision                                         | Significantly improved subjects' global assessment and decreased stool frequency |

IBS, irritable bowel syndrome.

Table 4. Summary of Antidepressants for the Treatment of Irritable Bowel Syndrome

| Psycho-trophics | Drugs       | Starting dosages | Maximal dosages | Adverse effects                                                                 | Comments |
|-----------------|-------------|------------------|-----------------|---------------------------------------------------------------------------------|----------|
| TCAs            | Amitriptyline | 10-25 mg/day     | 30 mg/day       | Dry mouth, constipation, difficulty sleeping, difficulty urinating, sexual difficulties, headache, nausea, dizziness and/or drowsiness | Begin with low dose (at bedtime) and titrate by response |
|                 | Imipramine  | 25 mg/day        | 50 mg/day       |                                                                                  |          |
|                 | Desipramine | 50 mg/day        | 150 mg/day      |                                                                                  |          |
|                 | Trimipramine| 50 mg/day        | -               |                                                                                  |          |
| SSRIs           | Paroxetine  | 10-20 mg/day     | 50 mg/day       | Agitation, dizziness, nausea, headache, vivid dreams, sleep disturbances, sexual difficulties, and/or diarrhea | Begin with low dose and titrate by response |
|                 | Citalopram  | 20 mg/day        | 40 mg/day       |                                                                                  |          |
|                 | Fluoxetine  | 20 mg/day        | -               |                                                                                  |          |

TCA, tricyclic antidepressant; SSRI, selective serotonin reuptake inhibitor.
11. 생균제

1) 생균제는 과민성장증후군 환자의 전반적인 증세 및 가스 관련 증상 등의 호전을 위하여 보조적으로 투약해 볼 수 있다.
- 권고수준: 약함
- 증거수준: 낮음
- 전문가 의견: 전적으로 동의함(7.5%), 대체로 동의함(55.0%), 대체로 동의하지 않음(27.5%), 대체로 동의하지 않음(7.5%), 전적으로 동의하지 않음(0%), 모름겠음(2.5%)

과민성장증후군 환자에게 생균제를 투약하여 장내 미생물 무리의 조성을 바꾸어증상을 호전시킨다는 임상 연구가 보고되어 왔다. 2014년 메타분석에 의하면 위약대비 생균제의 투약은 증상을 비교위험도 0.79 (95% CI 0.70-0.89)로 유의하게 증상을 개선시킬 수 있고, 7명의 투약으로 한 명의 호전을 기대할 수 있는 수준이었다. 28과민성장증후군의 전반적 증상의 개선, 복통의 호전, 가스 관련 증상의 호전 등 모든 영역에서 위약대비 효과가 있었다. 국내에서도 각종 Lactobacillus 및 Bifidobacterium의 혼합제제, Bacillus subtilis, Streptococcus faecium, Saccharomyces boulardii 등을 사용한 임상 연구들이 있었다. 29-32 하지만 이제까지의 연구 결과로는 과민성장증후군 환자에게 특정 균주나 용량을 추천할 수는 없고, 다만 그 효과를 판정하기 위해서는 4주 이상 지속적으로 투약하여 볼 것을 권고하고 있다.

12. 항우울제(Table 4)

1) 삼환계 항우울제(tricyclic antidepressants)는 과민성장증후군 환자의 복통과 전반적인 증상개선을 위하여 사용해 볼 수 있다.
- 권고수준: 약함
- 증거수준: 높음

13. 기타 치료들: chloride channel activators 및 정신건강의학적 치료

1) 선택적 세로토닌 재흡수억제제는 과민성장증후군 환자의 복통을 향상시키기 위하여 사용해 볼 수 있다.
- 권고수준: 약함
- 증거수준: 중등도

결론

2017년 개발된 과민성장증후군 영문 임상 진료 지침은 2011년에 발표된 진료 지침을 근간으로 근거 중심 의학에 기반하여 개정하였다. 과민성장증후군에서 대장내시경의 역할과 최근 활발히 연구가 진행된 FODMAP 식이, 항생제 및 생균제에 대하여 체계적 문헌고찰을 실시하였고, 텔레아이 방법을 통하여 전문가 합의를 도출하여 새로운 권고문을 개발하였다. 과민성장증후군의 임상 접근을 쉽게 하기 위하여 과민성장증후군 진료 알고리즘 및 치료 약제의 구체적인 방법을 표로 요약하였다. 본 진료 지침은 진료를 담당하는 의사와 환자가 일선에서 사용하여 최선의 치료를 제공하고 만족할 만한 치유 경험을 통하여 공극적으로 삶의 질을 향상시키고 의료 비용을 줄이는 것을 목표로 한다. 뿐만 아니라 내과 및 가정의학과를 비롯한 다양한 임상과의 수련의 및 의과대학 학생, 간호대학생 등의 교육을 위하여 적용될 수 있다.

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