PRACTICAL CONSIDERATIONS IN THE MANAGEMENT OF IBS

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• OR THINGS I ALWAYS WANTED TO SAY AND NOW I CAN

ROME IV CRITERIA FOR IBS

• WHY IN THE WORLD DID WE NEED A ROME IV?
• WHAT DO THE NEW ROME IV DIAGNOSTIC GUIDELINES MEAN FOR PATIENT MANAGEMENT?
ROME IV IBS

• DEVELOPED WITH INCREASED PATHOPHYSIOLOGY KNOWLEDGE
• FELT NOT TO BE HELPFUL TO THE PRACTICING CLINICIAN
• ASPECTS WERE WRONG OR NOT VALID
• DIDN’T DISTINGUISH IBS FROM CHRONIC CONSTIPATION

ROME IV

• THE TERM “FUNCTIONAL” IS REDUCED- IMBALANCE BETWEEN DIFFERENT TYPES OF GUT BACTERIA, INCREASED GUT PERMEABILITY, ALTERED IMMUNE FUNCTION, AND THE IMPORTANCE OF NEURAL AND HORMONAL INTERACTION BETWEEN THE BRAIN AND THE GUT IN PRODUCING AND MODULATING SYMPTOMS
• ABDOMINAL DISCOMFORT IS OUT
• NEED PAIN ONE TIME PER WEEK
• ABDOMINAL PAIN IS ASSOCIATED WITH DEFECATION BUT NOT NECESSARILY RELIEVED BY DEFECATION
ROME IV IBS

RECURRENT ABDOMINAL PAIN, ON AVERAGE, AT LEAST 1 DAY PER WEEK IN THE LAST 3 MONTHS, ASSOCIATED WITH 2 OR MORE OF THE FOLLOWING CRITERIA:

• 1. RELATED TO DEFECATION
• 2. ASSOCIATED WITH A CHANGE IN FREQUENCY OF STOOL
• 3. ASSOCIATED WITH A CHANGE IN FORM (APPEARANCE) OF STOOL
• CRITERIA FULFILLED FOR THE LAST 3 MONTHS WITH SYMPTOM ONSET AT LEAST 6 MONTHS BEFORE DIAGNOSIS.

• WILL HAVE A SUBSTANTIAL IMPACT ON WHETHER PATIENTS WITH LESS FREQUENT SYMPTOMS ARE DIAGNOSED IBS.
DIAGNOSIS

• IBS-C PREDOMINANT-EASY

• IBS-MIXED TYPE-EASY BECAUSE WHAT ELSE CAN GIVE YOU DIARRHEA ONE DAY AND CONSTIPATION THE NEXT?

• IBS-D-NOT QUITE AS EASY-CHECK CELIAC SEROLOGIES, CRP AND FECAL CALPROTECTIN

WAS THERE A PRIOR HISTORY OF A GI INFECTION?

• POST-INFECTIONOUS (PI) IBS CAN ACCOUNT FOR UP TO 11% OF ALL IBS CASES

• MOST COMMONLY IBS-D AND IBS-MIXED TYPE
WHAT ABOUT IBSDETEX?

• QUEST LAB—NOT CLEARED/APPROVED BY FDA
• CHECKS CDT AB (CITOLETHAL DISTENDING TOXIN) AND ANTI VINCULIN
• ANTI CDT CAN FORM AFTER AN INFECTIOUS GASTROENTERITIS AND BECAUSE OF MIMICRY ANTI VINCULIN CAN THEN FORM
• SPECIFICITY 90% BUT SENSITIVITY 40%
• NOT YET READY FOR PRIME TIME

WHAT DO WE KNOW ABOUT THE GUT MICROBIOME IN IBS?

• IBS CAN RESULT FROM A DYSFUNCTIONAL INTERACTION BETWEEN THE ENDOGENOUS FLORA AND THE INTESTINAL MUCOSA THAT LEADS TO IMMUNE ACTIVATION IN THE COLONIC MUCOSA
• SOME INVESTIGATORS PROPOSE A ROLE FOR BACTERIAL OVERGROWTH (SMALL BOWEL) AS A CAUSATIVE FACTOR IN THE PATHOGENESIS OF SYMPTOMS WHEREAS OTHER INVESTIGATORS SUGGEST THAT QUALITATIVE CHANGES IN THE COLONIC FLORA MAY BE MORE RELEVANT
• THESE THEORIES HAVE LEAD TO THE INVESTIGATION OF THE THERAPEUTIC UTILITY OF PROBIOTICS
APPROACH TO TREATMENT

WHAT I HEAR FROM MY IBS PATIENTS

• “I FELT LIKE THE DOCTOR DIDN’T LISTEN TO ME”
• “I WAS NEVER GIVEN A DIAGNOSIS”

AND FINALLY......
• “THE DOCTOR SAID THERE WAS NOTHING ELSE HE (OR SHE) COULD DO”
AGA GUIDELINES ON IBS 2014

AGA OFFERS RECOMMENDATIONS ABOUT PHARMACOLOGICAL THERAPY FOR IBS-C (CONSTIPATION) AND IBS-D (DIARRHEA).

AMERICAN COLLEGE OF GASTROENTEROLOGY MONOGRAPH ON THE MANAGEMENT OF IRRITABLE BOWEL SYNDROME AND CHRONIC IDIOPATHIC CONSTIPATION 2014

ALEXANDER C. FORD, MB CHB, MD ET AL AM J GASTROENTEROL 2014; 109:S2 – S26; DOI: 10.1038/AJG.2014.187
GUIDELINES VERSUS REAL LIFE

DIET

• TRY LACTOSE ELIMINATION

• FOR REALLY DESPERATE PATIENTS—TRIAL OF THE FODMAP DIET—SHORT CHAIN CARBOHYDRATES THAT CAN ARE POORLY ABSORBED, OSMOTICALLY ACTIVE AND RAPIDLY FERMENTED BY BACTERIA
FODMAP DIET

RECENT STUDIES (CHEY ET AL) HAVE SHOWN THE FODMAP (EXCLUSION) DIET TO BE EFFECTIVE IN IBS-D PATIENTS

FODMAP DIET

• DDW 2017-BELLINI ABS 132-LOW FODMAPS DIET SAFE, EFFECTIVE UNDER GUIDE OF EXPERT NUTRITIONIST
ANTI-GLIADIN ANTIBODIES MAY INDICATE GLUTEN-FREE DIET WILL HELP IN IBS

• SANCHEZ, MARIA INES AT MCMASTER UNIVERSITY DDW ABSTRACT 2017
• IMPROVEMENT IN CONSTIPATION, DIARRHEA AND ABDOMINAL PAIN ON GLUTEN FREE DIET

FIBER

• NOT STRAIGHT FORWARD
• USE SOLUBLE NOT INSOLUBLE FIBER-PSYLLIUM VERSUS BRAN
• MORE EFFECTIVE IN IBS-CONSTIPATION
PEPPERMINT

- IBGARD- "REDUCES SYMPTOMS WITHIN 24 HOURS- GOOD FOR IBS-MIXED TYPE-CASH, BROOKS ET AL ABSTRACT TU 1600/1601
- MENTHOL-XL
- PEPPERMINT DROPS

WHAT ABOUT PROBIOTICS IN IBS

- OVER 35 RCTS
- OVERALL IMPROVE GLOBAL SYMPTOMS, BLOATING AND FLATULENCE IN IBS PATIENTS
GUT MICROBIOME

- Efficacy of an encapsulated probiotic Bifidobacterium infantis 35624 in women with Irritable Bowel Syndrome Whorwell 2006

- *B. infantis* 35624 is a probiotic that specifically relieves many of the symptoms of IBS. At a dosage level of $1 \times 10^8$ CFU, it can be delivered by a capsule making it stable, convenient to administer, and amenable to widespread use. The lack of benefits observed with the other dosage levels of the probiotic highlight the need for clinical data in the final dosage for the lack of benefits observed with the other dosage levels of the probiotic highlight the need for clinical data in the final dosage form and dose of probiotic before these products should be used in practice.

PROBIOTIC BIFIDOBACTERIUM LONGUM NCC3001 REDUCES DEPRESSION SCORES AND ALTERS BRAIN ACTIVITY: A PILOT STUDY IN PATIENTS WITH IRRITABLE BOWEL SYNDROME

PINTO-SANchez, MARIA ET AL GASTRO AUG 2017
CANNABIS

- MAKES SENSE THAT IT COULD HELP
- COLONIC MUCOSA AND NEUROMUSCULAR LAYERS CONTAIN CANNABINOID TYPE 1 RECEPTORS EXPRESSED IN PLASMA CELLS WHICH INFLUENCE MUCOSAL INFLAMMATION
- NO DATA

ONE MEDICATION ONE SOLUTION
**IBS-MIXED TYPE**

- WHAT A PAIN
- TRIAL OF ANTI-SPASMODIC/ANTI-CHOLINERGIC SUCH AS METHSCOPOLAMINE OR TCA
- UNFORTUNATELY CAN WORSEN CONSTIPATION
- TRIAL OF FIBER
- TRIAL OF PEPPERMINT

**IBS-C**

- POLYETHYLENE GLYCOL - NO EVIDENCE THAT IT IMPROVES PAIN
- AMITIZA - CHLORIDE CHANNEL 2 ACTIVATOR - 8MCG BID WITH FOOD
**IBS-C**

- **LINACLOTIDE (LINZESS)-GUANYLATE CYCLASE-C RECEPTOR AGONIST-SECRETAGOGUE THAT WORKS IN THE COLON-290MCG DAILY BEFORE BREAKFAST**

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**PLECANATIDE**

- **WITH THE EXCEPTION OF A SINGLE AMINO ACID SUBSTITUTION FOR GREATER BINDING AFFINITY, TRULANCE IS STRUCTURALLY IDENTICAL TO HUMAN UROGUANYLIN**

- **HUMAN UROGUANYLIN ACTIVATES GUANYLATE CYCLASE-C (GC-C) RECEPTORS IN A PH-SENSITIVE MANNER**

- **UROGUANYLIN MODULATES ITS ACTIVITY WITHIN THE CHANGING PH ENVIRONMENT OF THE INTESTINE, STIMULATING FLUID SECRETION AND MAINTAINING STOOL CONSISTENCY NECESSARY FOR REGULAR BOWEL FUNCTION**
TENAPANOR-IN DEVELOPMENT

• TENAPANOR—AN INHIBITOR OF GASTROINTESTINAL NA+/H+ EXCHANGER NHE3 -IN PHASE 3 TRIALS

IBS-D

• ALOSETRON (LOTRONEX)
• RIFAXIMIN (XIFAXAN)
• ELUXADOLINE (VIBERZI)
ALOSETRON

• 5HT3 ANTAGONIST
• NOW GENERIC AND EASIER TO GET
• START LOW AND GO HIGH WITH DOSE

RIFAXIMIN

• NON-ABSORBABLE ANTIBIOTIC FOR NON-CONSTIPATED IBS PATIENTS
• TWO WEEKS OF TREATMENT AND CAN REPEAT TWICE MORE IF EFFICACIOUS
RIFAXIMIN (XIFAXAN)

- DDW 2017 PIMENTAL ET AL ABS 1619
- YOUNGER PATIENTS MORE LIKELY TO RESPOND AND HAVE A SUSTAINED RESPONSE
- SEVERE IBS LINKED TO RELAPSING SOONER ONCE TREATED

ELUXADOLINE (VIBERZI)

- MU/KAPPA OPIOID RECEPTOR AGONIST AND DELTA-OPIOID RECEPTOR ANTAGONIST
- FANTASTIC
- UNLESS YOU DON'T HAVE A GALLBLADDER
- LACK OF ABUSE POTENTIAL
ELUXADOLINE: IMPORTANT DRUG WARNING

• 120 REPORTS OF SERIOUS CASES OF PANCREATITIS
• OF 68 WHO REPORTED GALLBLADDER STATUS, 56 DID NOT HAVE A GALLBLADDER
• ALCOHOL INTAKE WAS UNCLEAR
• 76 CASES HOSPITALIZED AND 2 PATIENTS DIED
• USUALLY WITHIN 3 DAYS OF TAKING MEDICATION BUT COULD BE LONGER
SOCIETY LEADERSHIP AND DIVERSITY: HAIL TO THE WOMEN!

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