AUB TR;
ALTERNATIVE TO HYSTERECTOMY

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REPRODUCTIVE-AGE PATIENTS WITH AUB

• TREATMENT BASED UPON:
  • ETIOLOGY
  • SEVERITY OF BLEEDING (ANEMIA, INTERFERENCE WITH DAILY ACTIVITIES)
  • ASSOCIATED SYMPTOMS AND ISSUES (PELVIC PAIN, INFERTILITY)
  • CONTRACEPTIVE NEEDS/ PLANS FOR FUTURE PREGNANCY
  • MEDICAL COMORBIDITIES
  • UNDERLYING RISK FOR DVT AND/OR ARTERIAL THROMBOTIC EVENTS
  • PATIENT PREFERENCES REGARDING
    • MEDICAL VERSUS SURGICAL AND SHORT-TERM VERSUS LONG-TERM THERAPY
GOAL OF TREATMENT

• THE GOAL OF INITIAL THERAPY IS
  • TO CONTROL THE BLEEDING
  • TREAT ANEMIA (IF PRESENT)
  • RESTORE QUALITY OF LIFE
• SOME DESIRED TO CONTINUE CHRONIC MEDICAL THERAPY
• OTHERS; LESS MAINTENANCE OR DEFINITIVE.
ETIOLOGY

• TR ONLY AFTER, THE ETIOLOGY HAS BEEN EVALUATED

• PRE/MALIGNANT DISEASE EXCLUDED
  • EMPIRIC TR WITHOUT EVALUATION
    • MISS A PRIMARY CORRECTABLE ETIOLOGY
    • MASK SYMPTOMS OF NEOPLASTIC DISEASE

• TR OF CERTAIN UNDERLYING CONDITIONS MAY
  • CORRECT THE BLEEDING
  • MAKE FURTHER TR MORE EFFECTIVE.

• INCLUDING:
  • A: STRUCTURAL LESIONS, RESECTABLE VIA HYSTEROSCOPY (POLYP, SUBMUCOSAL FIBROID).
  • B: INFECTIOUS DISORDERS (CHRONIC ENDOMETRITIS)
  • C: ENDOCRINE DISORDERS (PCO)
  • D: BLEEDING DISORDERS
A: STRUCTURAL LESIONS

• SUBMUCOSAL FIBROIDS & ENDOMETRIAL POLYPS
  • CAN BE RESECTED VIA HYSTEROscopy.

• AV MALFORMATIONs CAN BE TREATED
  • INTERVENTIONAL RADIOLOGY PROCEDURES

• C/S SCAR DEFECTS (ISTHMOCELE, NICHE)
  • CAN BE SURGICALLY RESECTED VIA
    • HYSTEROscopy,
    • VAGINAL SURGERY,
    • LAPAROTOMY, LAPAROSCOPY, OR COMBINED
  • STUDY: COMBINED APPROACH (LAPAROSCOPY + HYSTEROscopy); GREATER REDUCTION IN THE DURATION OF AUB
• B: INFECTION
  • AUB DUE TO CHRONIC ENDOMETRITIS: AB THERAPY

• C: ENDOCRINE ABNORMALITIES (ANOVULATORY BLEEDING)
  • HYPOThYROIDISM, HYPERPROLACTINEMIA
    • TR TO RESTORE REGULAR OVULATORY CYCLES
  • PCO
    • TR TO REGULATE OR ELIMINATE BLEEDING EPISODES/ PREVENT ENDOMETRIAL CANCER

• D: BLEEDING DISORDERS
  • WHEN POSSIBLE, BLEEDING DIATHESES SHOULD BE CONTROLLED PRIOR TO OTHER TR
    • MEDICAL TR TO REDUCE MENSTRUAL BLOOD LOSS
HMB

• DEFINITION
  • OVULATORY (CYCLIC), HEAVY BLEEDING.

• ETIOLOGY
  • MOST COMMON: LEIOMYOMAS OR ADENOMYOSIS.
  • MAY BE TREATED WITH SURGERY, MANY PREFER INITIAL MEDICAL TR
  • HMB + ADENOMYOSIS, EN ABLATION MAY BE LESS EFFECTIVE

• GOAL OF TR: Q OF LIFE, ANEMIA.
HMB TR

• 1<sup>st</sup> LINE THERAPY; MOSTLY OCP (E-P OR LNG 52)
  • EFFECTIVE FOR HMB
  • EFFECTIVE CONTRACEPTION
  • WELL TOLERATED
  • LOW RISK OF ADVERSE EFFECTS

• THE CHOICE BETWEEN THE TWO DEPENDS ON SEVERAL FACTORS.
  • NO CONTRAINDICATION TO E (HTN/ RISK OF THROMBOSIS).
  • PATIENT PREFERENCE.
    • DAILY ORAL, REG BLEEDING
    • PLANNING TO CONCEIVE IN THE NEAR FUTURE
    • LOW MAINTENANCE OF HAVING AN IUD WITH LOW BLEEDING OR AMENORRHEA
HMB OTHER OPTIONS:

• HIGH-DOSE ORAL OR INJECTABLE P-ONLY
  • BUT P-ONLY OCP NOR THE ETONOGESTREL IMPLANT IN TREATING HMB.
  • CONTINUOUS P-ONLY RESULT IN IRREGULAR MENSES

• NSAIDS AND TRANCID
  • IF CONTRAINDICATIONS TO HORMONAL AGENTS.

• ULTRA-LOW-DOSE POSTMENOPAUSAL HT MAY BE AN OPTION.
  • IF CONTRAINDICATIONS TO E DOSE OF OCP

• EXPECTANT MANAGEMENT,
  • REASONABLE IF NOT ANEMIC AND DO NOT DESIRE TR.
    • HCT AND FERRITIN Q 6-12 MO

• SURGERY
  • 8 RCT: 58% OF WOMEN WITH HMB TR UNDERWENT SURGERY BY 2 YRS AFTER MEDICAL TR
HMB TR

• THE COMPARATIVE EFFICACY:
  • LNG 52 MOST EFFECTIVE MEDICAL APPROACH
    • 71 – 95% REDUCTION IN MENSTRUAL BLOOD LOSS.
      • (= EN ABLATION)
    • CYCLICAL ORAL P: REDUCE BLEEDING BY 87%
    • WHILE E-P OCP: 35-69% REDUCTION.

• IN SYSTEMATIC REVIEWS
  • OBSERVATIONAL & RANDOMIZED TRIALS
  • TRANEXAMIC ACID REDUCE 26 -54%
  • NSAIDS REDUCE 10-52%
OVULATORY DYSFUNCTION (AUB-O)

- IRREGULAR, NONOVULATORY BLEEDING
  - OLIGOMENORRHEA, PROLONGED OR HEAVY BLEEDING, EVEN HEMORRHAGE

- ETIOLOGY:
  - SOME CAN BE TREATED (THYROID DISEASE, HYPERPRL)
  - MOSTLY, PCO IS THE ETIOLOGY.
  - SOME SUBMUCOSAL (INTRACAVITARY) FIBROIDS: PROLONGED, IRREGULAR BLEEDING.
AUB-O TR

• GOALS OF TR:
  • REGULAR BLEEDING PATTERN (OR AMENORRHEA),
  • PREVENT HEAVY BLEEDING,
  • PREVENT DEVELOPMENT OF EN HYPERPLASIA/CA
  • IN SOME FERTILITY TR IS REQUIRED

• MOSTLY SHOULD BE TREATED MEDICALLY, AS A MEDICAL DISEASE
  • ALTHOUGH ETIOLOGIES OF PROLONGED AUB-O & HMB DIFFER, MOSTLY SAME TR

• THE EFFICACY OF HORMONAL MANAGEMENT:
  • FEW STUDIES AND NO RANDOMIZED TRIALS
1\textsuperscript{st} LINE TR:

1) E-P CONTRACEPTIVES, 2) ORAL P, 3) LNG 52;
   
   - ALL, REDUCE BLEEDING, DECREASE THE RISK OF ENDOMETRIAL HYPERPLASIA OR CARCINOMA

   1) E-P CONTRACEPTIVES
   
   - CONTRACEPTION

   2) CYCLIC ORAL P (EG, ORAL MPA, 10 MG/D 10-14 D Q MO);
   
   - NO CONTRACEPTION
   
   - MODERATE, PREDICTABLE WITHDRAWAL BLEEDING

   3) LNG 52
   
   - CONTRACEPTION.
   
   - NO REGULAR WITHDRAWAL BLEEDING;
   
   - AMENORRHEIC OR SCANT BLEEDING,
• ENDOMETRIAL ABLATION?
  • REPRESENTS A PROBLEMATIC CHOICE
    • 1- PREVENT THE CARDINAL SYMPTOM OF EIN: BLEEDING
      • BY INTRAUTERING SCARRING
    • 2- EN BX & SIS NOT BE FEASIBLE FOLLOWING ABLATION
  
• STILL COULD BE AN OPTION
  • IF DO NOT DESIRE FUTURE PREG
  • AND CONSIDERING SURGICAL MANAGEMENT
CHRONIC AUB TR

• 1ST LINE THERAPY
  • USUALLY PHARMACOLOGIC
  • CONTINUED LONG-TERM,
  • SOME PREFER A MANAGEMENT WITH NO FREQUENT DOSING
    • [20 MCG/DAY LNG 52 IUD; MIRENA OR LILETTA]
    • 1ST LINE THERAPY IF DO NOT WISH TO CONCEIVE IN THE NEXT YR
CHRONIC AUB TR

• 2\textsuperscript{ND} LINE
  • INDICATIONS IF:
    • 1\textsuperscript{ST} LINE FAILED AFTER LONG TERM MEDICAL TR
    • CANNOT TOLERATE MEDICAL THERAPY
    • PREFER TR OPTIONS THAT DO NOT REQUIRE FREQUENT DOSING
  • OPTIONS DEPEND ON:
    • FUTURE CHILDBEARING PLAN
    • THE LEVEL OF INVASIVENESS
    • RISK ASSOCIATED WITH THE PROCEDURE

• RCTS: 53\% IN THE MEDICAL TR GROUP HAD RECEIVED A HYSTERECTOMY
1-OCP

• E-P OCP
  • 1\textsuperscript{st} -LINE MANAGEMENT FOR MANY PATIENTS WITH AUB.
  • MAKE BLEEDING MORE REGULAR, LIGHTER, REDUCE DYSMENORRHEA
  • PROVIDE CONTRACEPTION
  • REDUCED MENSTRUAL BLOOD LOSS 35-69%

• TRANSDERMAL CONTRACEPTIVE PATCH (EG, XULANE, TWIRLA)

• VAGINAL CONTRACEPTIVE RING (NUVARING).

• \# ROUTES OF ADMINISTRATION, \# FORMULATIONS, \# TYPE, \# DOSE, \#AND SCHEDULE OF E-P APPEARS TO HAVE THE SAME EFFICACY
1-OCP

• OCS WITH ≤ 4-FREE DAYS PER PILL PACK IS PREFERRED
  • THE FDA-APPROVED OC (NATAZIA) INCLUDES
  • 26 HORMONALLY ACTIVE TABLETS PER Q 28-DAY PILL PACK.
    • E VALERATE (2-3 MG);
      • = TO 1.5-2.25 MG OF MICRONIZED ORAL E
      • = TO <20 MCG OF E
    • THE PROGESTIN COMPONENT IS DIENOGEST (2-3 MG).

• OCS MONTHLY, Q 3 MO, CONTINUOUS.

• OCS CONTRAINDIcATED IF AT ELEVATED RISK FOR THROMBOSIS
1-OCP

• CONTRAINDICATIONS
  • ≥35 YRS + SMOKING ≥15 CIGARETTES/D
  • MULTIPLE RFS FOR ARTERIAL CARDIOVASCULAR DISEASE
    • (OLDER AGE, SMOKING, DIABETES, HTN)
  • VTE, KNOWN THROMBOGENIC MUTATIONS
  • HTN, KNOWN IHD, HX OF STROKE
  • COMPLICATED VALVULAR HEART DISEASE
    • (PULMONARY HTN, RISK FOR AF, HX OF SUBACUTE BACTERIAL ENDOCARDITIS)
  • SYSTEMIC LUPUS ERYTHEMATOSUS (+ OR UNKNOWN ANTIPHOSPHOLIPID ABS)
  • MIGRAINE WITH AURA AT ANY AGE
  • IN OBESE PATIENTS 40 YEARS AND OLDER.
2-NON OCP FORMULATIONS

• ULTRA-LOW E
  • MARKETED FOR THE TR OF MENOPAUSAL SYMPTOMS
  • USEFUL IN SELECTED PATIENTS WITH AUB
    • IF RELATIVE CONTRAINDICATIONS TO OCP DOSES OF E
    • OLDER PATIENTS WHO ARE OBESE, HYPERTENSIVE, DIABETIC, OR SMOKERS
    • SUCH USE REQUIRES CAREFUL ASSESSMENT
    • PATIENT COUNSELING
    • POSSIBLE MEDICAL CONSULTATION REGARDING THROMBOTIC RISK.
2-ULTRA LOW ESTRADIOL

• EG: EE 5 MCG + 1 MG OF [NORETHINDRONE] ACETATE (JINTELI 1/5)
  • APPROVED FOR TR OF VASOMOTOR SYMPTOMS
  • ALSO USED IN PATIENTS WITH AUB
  • OFTEN RESULTS IN AMENORRHEA AFTER SEVERAL MONTHS
    • AUB-O + OBESITY AND/OR HYPERTENSION
    • HMB + LEIOMYOMAS + OBESITY AND/OR HYPERTENSION
    • AUB-O OR HMB + SMOKE CIGARETTES
  • P-RELATED SIDE EFFECTS ARE LESS COMMON AND SEVERE WITH THE EE 5 MCG/NEA 1 MG & HIGHER-DOSE ORAL P
3-LNG IUD

- **LEVONORGESTREL IUD- THE LNG 52**
  - HIGHLY EFFECTIVE AND EASY-TO-USE
  - FDA: FOR TR OF HMB.
- **THE LNG 52; 1ST LINE OPTION FOR TR OF HMB**
  - IF DO NOT DESIRE PREG
- **REVERSIBLE CONTRACEPTION**
- **CAN BE LEFT IN PLACE FOR 5-6 YRS**
- **OVER TIME DECREASING VOLUME OF BLEEDING**
  - UNTIL THE PATIENT HAS SCANT BLEEDING OR AMENORRHEA.
3-LNG IUD

• REDUCTION OF BLEEDING –
  • AFTER 3 MO, MOSTLY SPOTTING.
  • AFTER 6 MO, MOSTLY AMENORRHEA
  • MEDIAN HB 7.5% AND FERRITIN 68.8% INCREASED
  • STUDIES: COMPARED WITH OTHER HORMONAL OR NONHORMONAL TR,
    • IMPROVED Q OF L
    • LESS ADDITIONAL INTERVENTIONS: ORAL TRANEXAMIC ACID, ORAL P, HYSTERECTOMY

• RISK OF EXPULSION
  • HIGHER IN THE TR OF HMB VS FOR CONTRACEPTION
    • WITH ADENOMYOSIS, 25%
  • CONTRAINDUCTION: DISTORTION OF THE EN CAVITY (EG, FIBROIDS)
4-PROGESTERONE: DEPO-MPA

- **DEPOT MPA:**
  - IF CONTRAINDICATIONS TO E
  - IF PREFER TO AVOID E
  - IF PREFER FOR CONTRACEPTION.
  - CONTRACEPTION PERSISTS 3-MO DOSING INTERVAL

- **EFFICACY**
  - IF NO AUB AT BASELINE, 50% AMENORRHEIC AFTER 4 INJECTIONS (1 YR), 75% 8 INJECTIONS
  - IF AUB-O OR HMB 49% REDUCTION AFTER 2 MO
5- PROGESTERONE: HIGH-DOSE

• HIGH-DOSE ORAL P:
  • **NORETHINDRONE** ACETATE (NEA) 5 MG 1-3 TAB DAILY OR **MPA** 5-30 MG DAILY
  • + BARRIER CONTRACEPTIVES

• SIDE EFFECTS: DYSPHORIA, BLOATING, INCREASED APPETITE.

• IF GOOD RESPONSE, TAPER SLOWLY, AS LOW AS 2.5 MG/D

• IN PROMOTING EN SUPPRESSION, NEA MORE POTENT THAN MPA
6-TRANEXAMIC ACID

• IF HMB, SHOULD NOT USE HORMONAL TR. (HX OF BR CA)

• ANTIFIBRINOLYTIC
  • COMPETITIVELY BLOCKS THE CONVERSION OF PLASMINOGEN TO PLASMIN,
  • REDUCING FIBRINOLYSIS.

• FDA APPROVED FOR THE TR OF HMB IN 2009;

• ADVANTAGES
  • WHILE TRYING TO CONCEIVE
  • TAKEN ONLY DURING MENSES

• DISADVANTAGES
  • INCREASED RISK OF THROMBOSIS?? IS CONTROVERSIAL
6-TRANEXAMIC ACID

• FDA CONTRAINDICATION:
  • HX OF DVT, ELEVATED RISK OF THROMBOSIS (OCP CURRENT USE)

• IF NORMAL RENAL FUNCTION
  • TR OF HMB IS 1300 MG (TWO 650 MG TABLETS)
  • X3/D (A TOTAL OF 3900 MG)
  • 5 DAYS DURING MENSTRUATION
7-NSAIDS

• TR OF HMB, NOT AUB-O

• NONHORMONAL, NONCONTRACEPTIVE

• NO KNOWN CONTRAINDICATION TO USE WITH TRANEXAMIC ACID.

• REDUCE THE VOLUME OF MENSTRUAL BLOOD LOSS
  • DECLINE PGE2 & PGF2Å SYNTHESIS IN THE EN, VASOCONSTRICTION
8-OTHER MEDICAL TREATMENTS

• ADVANTAGES
  • NO RISK OF THROMBOSIS
  • LESS DYSMENORRHEA
  • LOW COST
  • NO NEED TO BE TAKEN DAILY

• LESS EFFECTIVE THAN THE LNG 52 AND TRANEXAMIC ACID

• START : 1ST D OF BLEEDING, 4-5 D OR UNTIL MENSTRUATION CEASES
  • ●MEFENAMIC ACID 500 MG TDS
  • ●NAPROXEN 500 MG AT ONSET, 3-5 HR LATER, THEN 250 TO 500 MG BD
  • ●IBUPROFEN 600 MG/D
8-OTHER MEDICAL TREATMENTS

• MAY BE:
  • LESS EFFECT
  • MORE ADVERSE EFFECTS

• DANAZOL

• THE SHORT-TERM IV E ACUTE AUB

• GNRHA IF UNDERGO CHEMOTHERAPY.
NON-MEDICAL TR

• MAIN INDICATION FOR SURGERY
  • HMB DUE TO STRUCTURAL LESIONS (LEIOMYOMAS, ADENOMYOSIS)
  • AUB-O ONLY IF THE PATIENT DESIRE HYSTERECTOMY

• THE CHOICE OF SURGICAL THERAPY
  • PATIENT'S CHARACTERISTICS,
  • THERAPEUTIC GOALS,
  • PLANS FOR FERTILITY
NON-MEDICAL TR

- IF DESIRE FUTURE CHILDBEARING,
  - SURGICAL OPTIONS ARE LIMITED.
  - MYOMECTOMY
- IF NO DESIRE FERTILITY
  - ENDOMETRIAL ABLATION
  - UTERINE ARTERY EMBOLIZATION
- HYSTERECTOMY
  - IF FAILED OTHER SURGICAL TREATMENTS
  - IF DESIRE DEFINITIVE TR.