PAROXETINA – propunere protocol

1. Denumire stiintifica:
   Paroxetinum
2. Clasa de medicamente:
   Antidepresive (ATC: N06AB05)
3. Forme farmaceutice (ANMDM):
   - comprimate 10 mg, 20 mg, 30 mg, 40 mg
   - comprimate filmate 20 mg, 40 mg
4. Profil farmacologic : ISRS (inhibitori selectivi ai recaptarii de serotonina) (2 pag. 415)
5. Farmacocinetica :
   - timp de injumatatire de aproximativ 24 de ore, metabolit inactiv, metabolizare hepatica, inhiba CYP 2D6
6. Mecanism de actiune: blocheaza pompa de recaptare a serotoninei, crescand neurotransmisia serotoninergica. Poate avea activitate de blocant slab al recaptarii de noradrenalina. Are si actiune anticolinergica slaba (1 pag 415, 2 pag 298)
   Dozare : 20-60mg
7. Indicatii principale (ANMDM, EMA, FDA) (8, 9, 10):
   Episod depresiv major
   Tulburare obsesiv-compulsiva
   Tulburare de panică cu sau fără agorafobie
   Tulburare de anxietate sociala/Fobie socială
   Tulburare de anxietate generalizata
   Tulburare de stres post-traumatic

8. Alte indicatii:
   - Tulburare disforica premenstruala (FDA, 2 pag 415, 6 pag 1014)
   - Simptome vasomotorii moderat-severe asociate menopauzei (FDA: cps 7,5mg)
   - Episod depresiv din TAB in combinatie cu timostabilizatoare (5)
   - Depresie si Comorbiditati somatice (indicatii ISRS) : Boli cardiovasculare – Boala cardiaca ischemica (11, 12, 13, 14) , AVC (11, 13); Afectiuni oncologice (12, 13); Diabet zaharat (11, 12, 13); Epilepsie (11, 12); Demente (12, 13); Infectie HIV (11, 12).
   - Tulburarea depresiva persistenta (Distimia si Depresia cronica): ISRS (13, 14, 15, 16).
   - Schizofrenie (indicatii antidepresive): - depresia majora comorbida, depresia post-psihotica, TOC (12, 17, 18, 19, 20, 21, 22); simptome depresive severe, care determina disconfort semnificativ sau interfera cu functionarea (17, 22).

9. Efecte secundare : greata, senzatie de gura uscata, ameteli, tremor, constipatie sau diaree, disfunctii sexuale , aplatizare afectiva , lentoare cognitiva , insomnie sau sedare, crestere in greutate , akatisie (2 pag 416, 6 pag 583, 6 pag 1018)
   Intreruperea paroxetinei nu se va face brusc din cauza sindromului de discontinuitate. Simptomele de intrerupere (ameteala, greata, crampe, diaforeza, parestezii, disestezii) tind sa fie mai severe sau mai frecvente decat in cazul

celorlalte ISRS uri. La cei cu reactii severe va intrerupe foartelent (saptamani /luni) sau se va asocia cu un ISRS cu timp lung de injumatatire (ex, fluoxetina) . Mecanismul implica inhibitia propriului metabolism la intreruperea brusca, cu rata de scadere brusca a concentratiei plasmatice la care se adauga readaptarea receptorilor colinergici dupa blocarea lor prelungita.

10. Supradoza:

    - toxicitate scazuta in supradoza; sindrom serotoninergic, sedare, voma, midriaza, tulburari de ritm cardiac. Forte rar s-au raportat cazuri fatale, in combinatie cu alte medicamente/substante psihoactive (2 pag 418) (rcp)

11. Utilizare la grupe de pacienti cu risc crescut:
    - Afectare renala: se recomanda utilizarea unor doze mai scazute, dar poate fi data si pacientilor dializati (2 pag 419, 3 pag 583)
    - Afectare hepatica: se utilizeaza doze scazute (10 mg in insuficienta hepatica severa) (2 pag 419, 3 pag 583)
    - Afectare cardiaca: prezinta siguranta la aceasta categorie de pacienti (2 pag 419)
    - Varstnici: se utilizeaza doze reduse (maxim 40 mg).
    - Sarcina: categorie de risc D, a fost asociata in principal cu malformatii cardiace la fat, desi unele studii au infirmat acest lucru. Au fost raportate complicatii neonatale, inclusiv detresa respiratorie (posibil si datorita sindromului de intrerupere), hipertensiune pulmonara la nou-nascut. Se pare ca este mai putin sigura decat alte ISRS-uri la aceasta categorie. Trebuie evaluate riscurile tratamentului pentru fat fata de riscurile absentei tratamentului atat pentru mama cat si pentru copil .(1 pag 361, 2 pag 420, 3 pag 547)
    - Alaptare: cantitati minime de medicament trec in laptele matern. Se considera ca poate fi dat in alaptare, dar daca sugarul devine iritabil sau sedat, se recomanda trecerea la alimentatie artificiala , intreruperea tratamentului sau utilizarea unui antidepresiv cu un profil mai sigur. In toate cazurile se cantaresc riscurile tratamentului cu beneficiile tratarii depresiei atat pentru mama cat si pentru copil (2 pag 420, 3 pag 563, 4 pag 83).
    - Epilepsie : se recomanda precautie (risc scazut de convulsii). Nu afecteaza farmacocinetica/farmacodinamia anticonvulsivantelor (rcp).

12. Interactiuni medicamentoase :

    - poate creste riscul de hemoragii mai ales la pacientii cu anticoagulante/agenti antiplachetari. Interfereaza cu analgezicele opioide . Nu se administreeaza cu pimozid (creste concentratia plasmatica a pimozidului , iar acesta prelungeste intervalul QTc) (2 pag 419, 6 pag 1014). Nu necesita ajustarea dozei cand se administreaza impreuna cu alte inductoare enzimatice (carbamazepina, rifampicina, fenobarbital, fenitoina) (rcp)

    - creste nivelul plasmatic al unor antipsihotice, beta-blocante, al tioridazinei (2 pag 418-419, 3 pag 332 ,4 pag 83)

    Contraindicatii : tratament cu IMAO, tioridazina, pimozid

    Alte interactiuni : nu se recomanda consumul de alcool

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