FLUOXETINE AND BEYOND, PSYCHOPHARMACOTHERAPY OF BULIMIA NERVOSA

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PHARMACOLOGICAL TREATMENT OF BN

BN therapy ***is not*** exclusively based on pharmacological treatment

International guidelines raccomend a multidisciplinary approach with psychotherapy, nutritional counselling and behavioural intervention

(American Psychiatric Association. 2006; National Institute for Clinical Excellence 2004)

PHARMACOLOGICAL TREATMENT OF BN

drug treatment

psychotherapy

nutritional counselling

medical stabilization

PHARMACOLOGICAL TREATMENT OF BN

In BN there is the best evidence available about pharmacological approach

RCT trials demostrated significant efficacy of drug treatment in BN

BN treatment evidence is different from that of other eating disorders

PHARMACOLOGICAL TREATMENT OF BN

Drug treatment according to indications

Evidence based off label use of drugs

Misuse of drugs

DRUG TREATMENT ACCORDING TO INDICATIONS

Fluoxetine (Flx) is, at the moment, the only drug with specific indication for BN treatment

Flx efficacy in BN have to be distinguished from its effect on depressive disorders

(Goldstein et al 1999)

DRUG TREATMENT ACCORDING TO INDICATIONS

SPECIAL SECTION ARTICLE

Bulimia Nervosa Treatment: A Systematic Review of Randomized Controlled Trials

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ABSTRACT

Objective: The RTI International-University of North Carolina at Chapel Hill Evidence-based Practice Center systematically reviewed evidence on efficacy of treatment for bulimia nervosa (BN), harms associated with treatments, factors associated with treatment efficacy, and differential outcome by sociodemographic characteristics.

Method: We searched six major databases published from 1980 to September 2005 in all languages against a priori inclusion/exclusion criteria; we focused on eating, psychiatric or psychological, and biomarker outcomes.

Results: Forty-seven studies of medication only, behavioral interventions only, and medication plus behavioral interventions for adults or adolescents met our inclusion criteria. Fluoxetine (60 mg/day) decreases the core symptoms of binge eating and purging and associated psychological features in the short term. Cognitive behavioral therapy reduces core behavioral and psychological features in the short and long term.

Conclusion: Evidence for medication or behavioral treatment for BN is strong, for self-help is weak; for harms related to medication is strong but either weak or nonexistent for other interventions; and evidence for differential outcome by sociodemographic factors is nonexistent. Attention to sample size, standardization of outcome measures, attrition, and reporting of abstinence from target behaviors are required. Longer follow-up intervals, innovative treatments, and attention to sociodemographic factors would enhance the literature. © 2007 by Wiley Periodicals, Inc.

Keywords: bulimia nervosa; eating disorders; clinical trials; evidence based review; purging; eating disorder inventory; cognitive behavioral therapy; behavioral intervention trials; second-generation antidepressants

(Int J Eat Disord 2007; 40:321–336)

DRUG TREATMENT ACCORDING TO INDICATIONS

Six RCT trials compared Flx to placebo

Flx (60 mg/day) administered for 8-16 weeks led to significant reduction in binge eating in most of the studies

Flx 60 mg/day performed better than 20 mg/day in decreasing binge eating

DRUG TREATMENT ACCORDING TO INDICATIONS

Flx (60 mg/day) was superior to placebo in decreasing purging behavior

Flx (60 mg/day) was associated with significant improvement in measures of restraint, weight concern, food preoccupation, drive for thinnes and body dissatisfaction

PHARMACOLOGICAL TREATMENT OF BN

Evidence based off label use of drugs

EVIDENCE BASED OFF LABEL DRUG TREATMENT

There's growing evidence about the efficacy of citalopram (20 mg/day) in BN pts with and without comorbid depression

(Leombruni et al 2006 ; Calandra et al 1999)

One study reported contrasting data about the efficacy of citalopram in BN

(Sunblad et al 2005)

EVIDENCE BASED OFF LABEL DRUG TREATMENT

In an open trial with sertraline pts reported improvement in core BN symptoms with good tolerability

(Sloan et al 2004)

Data confirmed in a RCT with Sertraline (100 mg/day) BN pts had significant reduction in binging and purging (Milano et al 2004)

More data about sertraline's efficacy in BED (Leombruni et al 2006; Leombruni et al 2008; Apollinario e McElroy 2004)

EVIDENCE BASED OFF LABEL DRUG TREATMENT

Other evidence support the use of Fluvoxamine (150 mg/day) with one RCT vs placebo (Fichter et al 1991)

Another RCT show significant results with fluvoxamine use in preventing relapses of BN after stabilization of pts (Fichter et al 1996)

EVIDENCE BASED OFF LABEL DRUG TREATMENT

An RCT using Trazodone (400 mg/day) in BN demonstrated a significant decrease of bingeing, vomiting and fear of eating

(Pope et al 1989)

There are no data about paroxetine use in BN treatment (possible weight gain)

(Walsh 1997, Goldbloom et al 1997)

EVIDENCE BASED OFF LABEL DRUG TREATMENT

There are promising data on the efficacy of other SSRIs than Flx in drug treatment of BN

There are wide differencies in available evidence about the efficacy of different SSRIs

5HT reuptake inibition ***do not*** imply necessarely any efficacy in BN treatment

EVIDENCE BASED OFF LABEL DRUG TREATMENT

Anticonvulsants in BN:

"…Phenytoin has been effective in some cases, suggesting that bulimia may be a neurologic disorder analogous to epilepsy…"

(Conner CS, 1983)

EVIDENCE BASED OFF LABEL DRUG TREATMENT

Topiramate (Tpr) is indicated in epilepsy and in migraine profilaxys

There is good evidence about Tpr use in Bed complicated with Obesity

(Claudino et al 2008; McElroy et al 2007; Mc Elroy et al 2004)

Two RCT reported extremely interesting results about Tpr efficacy in BN features (reduction in binge/purge days, body dissatisfaction, drive for thinnes) and in general anxiety

(Hoopes et al 2003, Edges et al 2003)

EVIDENCE BASED OFF LABEL DRUG TREATMENT

Topiramate appears to have the broadest spectrum of action as an anti-binge eating, anti-purging and weight loss agent with 2 placebo-controlled studies in BN and 3 placebo-controlled studies in BED with obesity

(McElroy et al 2009; Arbaizar et al 2008)

EVIDENCE BASED OFF LABEL DRUG TREATMENT

Lamotrigine has been studied in an open study (add on with Flx) in BN pts (Marilov et al 2010) and in a RCT in BED pts with obesity

(Guerdjikova et al 2009)

There are interesting results as for weight control but also contrasting data about efficacy in core BN features

EVIDENCE BASED OFF LABEL DRUG TREATMENT

Since the ’80 triciclic antidepressant (Tca) have been used in BN treatment (desipramine)

(Pope et al 1983; Mitchel e Groat 1984; Hughes et al 1986)

Possible cardiotoxicity with TCA treatment

(Crome 1986, Thanacoody e thomas 2005)

High risk of cardiotoxicity in pts with hypokaliemya, electrolyte imbalance and repeated vagus stimulation (Pentel e Benowitz 1986)

EVIDENCE BASED OFF LABEL DRUG TREATMENT

Tca have to be considered as second choice drug treatment being available drugs with better tolerability profile and given the peculiar cardiological risk of BN patients

AUGMENTATION STRATEGIES

Data suggests that the combination of an antidepressant plus CBT is superior to either treatment alone. Further pharmacological research is needed, particularly in pharmacological augmentation strategies, for patients not responding to primary therapies

(Pederson et al 2003)

PHARMACOLOGICAL TREATMENT OF BN

Misuse of drugs in BN

MISUSE OF DRUGS IN BN

Some anti obesity drugs are used in BN treatment in order to allow patients to control their weight

Efficacy in Weight control DO NOT imply any efficacy in BN treatment

Risk/benefit ratio must be accurately assessed, given the vulnerability of BN pts

MISUSE OF DRUGS IN BN

Orlistat (Ort) is an inibitor of lipasis that can be unproperly used in BN treatment (case reports) (Fernandez-Aranda et al 2001)

Side effects of Ort derive from uncontrolled assumption of lipids that cannot be enzimatically digested

Pts with BN ***by definition*** lose control on their diet resulting in steatorrea, fecal incontinency

MISUSE OF DRUGS IN BN

Rimonabant (Rbt) is an endocannabinoid CB1 receptor antagonist with indication in methabolic syndrome

There are NO data about its efficacy or tolerability in pts with BN

The European Drug Agency (EMEA) recently retired it from the trade due to suicidality risk

MISUSE OF DRUGS IN BN

Sibutramine (Sbm) is a NA and 5HT reuptake inibitor with some efficacy in weight reduction

Blood pression and cardiac rithm instability reported with its use (Italian trade stopped in 2002 because of reports of cardiac failure)

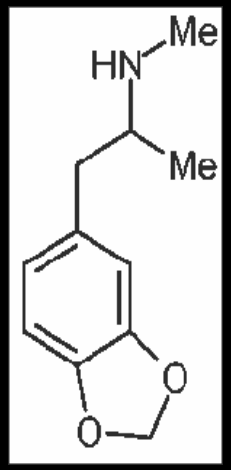
No evidence of efficacy and significant risk in BN pts

MISUSE OF DRUGS IN BN

Amphetamines have psychostimulating properties with compromission of sleep, increased vigilance, changes in cognitive and attention parameters and impairment of impulse control

MISUSE OF DRUGS IN BN

In United States some amphetamines have been approved for obesity treatment



In Europe nearly all of them have been retired from trade due to their unfavourable risk/benefit ratio

CONCLUSIONS

Augmentation strategies for pharmacological treatment and RCT on new drugs are the main targets to improve the outcome of BN

There are drugs with good evidence of efficacy and tolerability that can be used in the integrated treatment of BN

Weight control is an item, but it cannot be the main goal in BN treatment

CONCLUSIONS

Drugs to control weight and anti obesity treatment are unproperly used in BN with significant risk for this special population of Pts

There is no reason to endanger BN pts with the use of drugs with unfavourable safety profile given the tolerability of existing treatments

THANK YOU

Donwload available from websites:

WWW.PSYTER.NET

WWW.NEUROFARMACOLOGIA.NET