The use of medication in the treatment of Anorexia Nervosa

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Workshop structure

The evidence base for medication usage

Discussion regarding use

Case discussion

What would you like to know??

What have been used and why?

Medications that will be discussed

1. Antipsychotics
2. Antidepressants

Antipsychotics

Why could they be helpful?

- Blockage of Dopamine receptors
- Blockage of Serotonin Receptors
- Increase in Leptin levels

Antipsychotics

Which have been tried

- ❑ Chlorpromazine
- ❑ Sulpride
- ❑ Risperidone
- ❑ Quetiapine
- ❑ Cisapride
- ❑ Aripiprazole
- ❑ Olanzapine

Evidence for Olanzapine (Adults)

Individual studies reported positive results (e.g. Bissada *et al* 2008)

- Increased BMI (p=<0.001)
- Quicker weight restoration
- Reduce depressive symptoms (p=<0.001)
- Reduced Anxiety symptoms (p=0.02)
- Reduced compulsions (p=0.003)
- Reduced obsessions (p=0.001)

Evidence for Olanzapine (Adults)
Attia *et al*, (2011)

- Double blind n=11 OLZ and n=12 Placebo
- Maximum 10mg a day for 6 weeks
- BMI significant increase (p=0.02)
- No difference in psychopathology

Meta-analysis

Lebow *et al* (2013)

- 499 studies only 7 used Olanzapine
- Marked heterogeneity
- No difference in BMI (WMD= 0.18)
- No effect on drive for thinness (WMD=-0.49)
- Increased anxiety symptoms

Meta-analysis
Dold *et al* (2014)

- Used SGA
- Variety of ages (including adolescent)
- Good quality studies
- Hedges g= 0.13 (p=0.04) for mean BMI change
- No impact on Psychopathology

Evidence base in Adolescents

Leggero *et al* (2010)

- Open label use of Olanzapine (Olz) (mean 4.1mg per day)
- N=13; age =13.7 years
- Response EDI-2 improved by 50%
- Olz group
  - Increased BMI (p=<0.001)
  - Increased CGAS (p=<0.001)
  - Improved EDI-2 (p=0.008)

Evidence base in Adolescents
Kafantaris *et al* (2011)

- Average age =17 years
- 190 approached
- N=7 Olz and n=8 placebo
- 10mg for 10 weeks

- No significant difference

Evidence bas in Adolescents

Spettigue *et al,*

- Open label
- N=33; age 15.48 years; 91% female; 84% inpatients
- Olz more rapid weight gain in weeks 4-6 (p=0.03)
- Side effects sedation is most common in all studies
- In Spettigue 56.5% had abnormal blood tests during the study

Evidence base in Adolescents
Norris et al (2011)

- 10 -17 years
- Retrospective
- 328 individuals approached only n=47 (14%)
- More rapid weight gain (p=0.06)
- Olz double number of treatment days (p=<0.001)
- Olz higher rates of readmission (p=0.031)

Meta-analysis Adolescents
Suarez-Pinilla *et al* (2015)

- Young adults and adolescents
- Global Effects sizes
  - Antipsychotics = 0.32
  - Antidepressants= 0.10
  - Psychotherapy (not FBT) = 0.77
  - Lithium = 0.64
  - Nutrition (cyclic enteral nutrition) 0.44

Conclusion: Antipsychotics

Small groups some benefit (?Type II error)

Meta-analysis no benefits

Risk of significant side effects

Antidepressants

Antidepressants
points of interest

- Thought to be more useful for patients with depressive, obsessive or compulsive symptoms
- No direct effect on weight gain
- Does it increase satiety?
- Reduced tryptopan in underweight to not able to respond to SSRIs

Sertraline

Santonastaso *et al*, 2001

- Open label trial in adults
- 14 weeks treatment; 50 or 100mg a day
- Intention to treat
  - Rate of improvement in Sertraline group =82%
  - Rate of improvement in control group = 45%
- Improved: maturity fears, perfectionism and depression symptoms
- No effect on weight but does effect psychopathology

Citalopram

Fassino *et al*, 2002

- RCT- waiting list control
- N=26 each group
- No difference in pre medication
- Both groups increased in weight but not significant difference
- Did significantly effect:
  - Depressive symptoms
  - Obsessive symptoms
  - Anger
  - Impulsivity

Fluoxetine

Kaye *et al*, 2001/ Sebaaly *et al*, 2013

- Double blind, inpatient post discharge
- Relapse prevention (1 year FU)
- N=39
- Did reduce:
  - Anxiety
  - Depression
  - Core eating disorder symptoms
- No impact before or after weight restoration (Sebaaly)

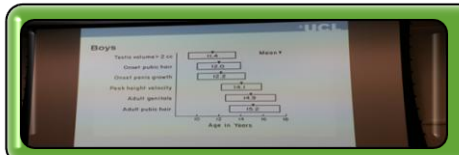
Fluoxetine

Walsh *et al*, 2006

- RCT & double blinded
- Up to Fluoxetine 60mg (also allowed psychotherapy)
- 4 years to recruit n=93
- Large drop out rate= 53
- No difference in BMI or psychopharmacology or time to relapse

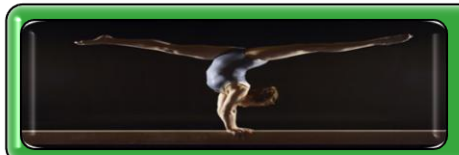
Is there any evidence for medication in AN?

Part 2 - Overview



Out patient Case study – Male

Out patient Case study – Remote/rural



In patient Case Study – Female

Practice aspects

Rationale

Case Study – Tim

Routine GP referral in Mar 14

15 years, 2 months old male

Referred for anxiety and anger issues

Weight 64 kgs (but losing) Height 183 cms (97th Centile)

% weight for height – 95% BMI – 19

Weight loss over several months persistent despite input

Only eats pre packed food (preoccupied with calories)

FBT initiated for anorexia in Sept 14 (% weight for height 85)

Eating very small portion sizes; preoccupation with calories

Excessive uncontrolled exercise ++

Context

Lives with mum and younger brother and stepdad (about 25 miles from base)

Biological father in legal battle for custody

‘my heart will suddenly stop’ (death of baby brother)

On part time timetable at school

Family in financial difficulty; step father diagnosed with depression

Younger brother in P 5 displaying behavioural difficulty

Started on Fluoxetine for anxiety and low mood

JUNIOR MARSIPAN – Physical Risk

Hard to rouse Red

Parent unable to implement meal plan(2 months on) Amber

Uncontrolled Exercise (1hr/day) Amber

Restriction of diet Amber

Pulse – 36 Red

Temp 35 C Red

BMI – Amber

Management of risk

NHS Grampian Junior MARSIPAN joint working pathway

Seen as urgent Paediatric out patient by GI team (decline admission)

Emergency detention- supported decision making carried out by GP

Rest of admission voluntary (seen by MHO once)

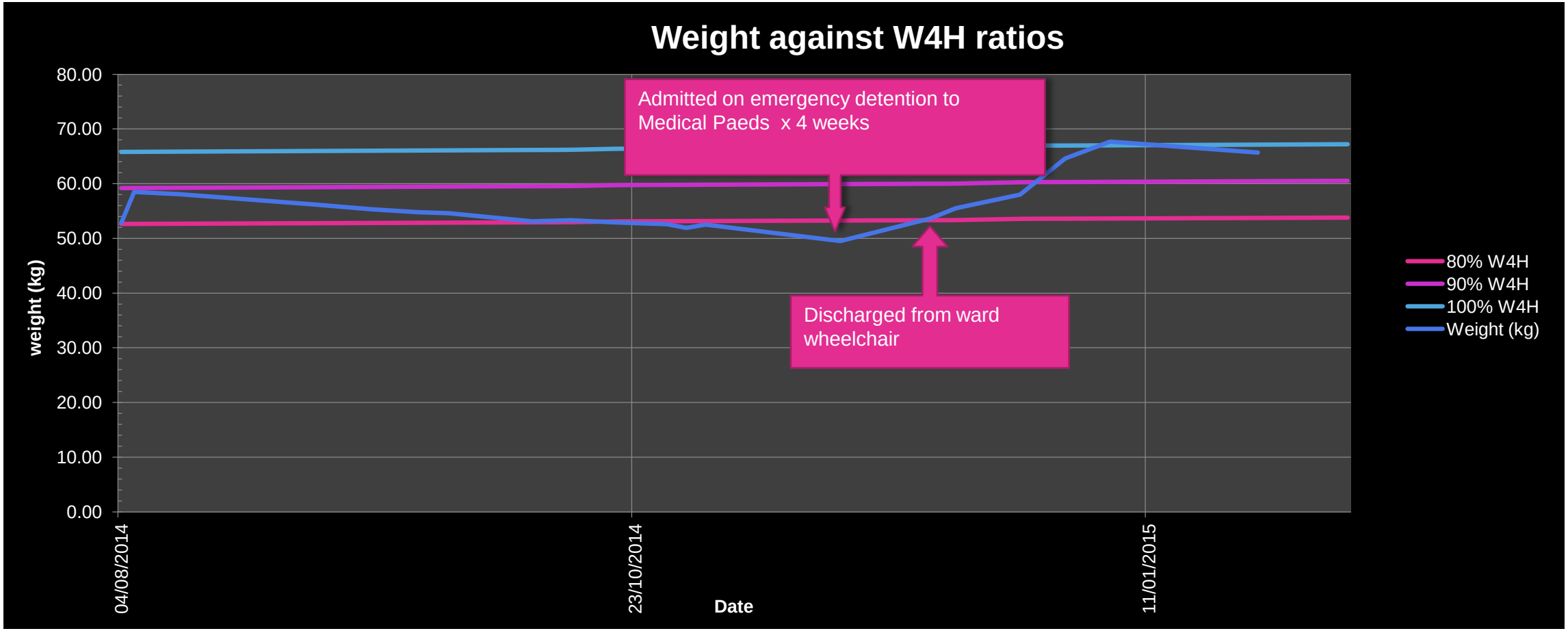
Intensive dietetic input very helpful for mother

Two to four times a week input from YPD

Mother supported meals on ward (patient accommodation)

Olanzapine 2.5mg started 2 days following admission and stopped after 8 weeks

Case - Tim


Weight against W4H ratios
80.00
70.00
60.00
50.00
40.00
30.00
20.00
10.00
0.00
weight (kg)
Admitted on emergency detention to Medical Paeds x 4 weeks
Discharged from ward wheelchair
04/08/2014
23/10/2014
11/01/2015
Date
80% W4H
90% W4H
100% W4H
Weight (kg)

Case - Tim

Success of joint working despite difficult context

- Parental mental health
- Very limited social support
- Conflict between biological parents

Taking away choices enabled change (mental health act, hospital food)

Prevented admission to out of area MH provision

Had another period of 4 months of restrictive eating in context of change of house/ school but managed safely in community

Now healthy wt for over 10 months and taking exams

OLZ – a possible role for decrease rigidity of thinking

Trial to decrease FLU lead to drop in mood

Case – Stacy 13 year old

Presented just before Christmas with marked weight loss and intense preoccupation of germs. Refusing to eat and excessive cleaning Excessive pre-occupation with healthy food

Marked distress that her mother (single mum) could not contain and responded with hostility and criticism

Strong family history of psychiatric illness. Youngest of five – only female child. Father has Schizophrenia, One older brother has Bipolar and another has Schizophrenia

Lives on remote island with population of 250

Case – Stacy 13 year old

Considered admission to YPU but decided via supported decision making trial of Tier 4 community input with Olanzapine 2.5 mg and Sertraline 25 mg

Monitored by GP weekly Junior MARSIPAN risk framework reviews – blood tests and ECG

Supported by local practice nurse, social worker/ MHO, VC input from CAMHS clinician

FBT - empowerment of parent/ externalisation of illness

?Validated externalisation for mother/ helped sleep initially

Case 13 y - Stacy

Date of visit	Weight (kg)	Height (cm)	BMI	Weight centile	Height centile	BMI centile	Weight for height
23/12/2014	33.10	148.00	15.11	0.56	5.16	1.38	78.45
30/12/2014	35.20	148.00	16.07	1.62	5.02	5.65	83.38
06/01/2015	35.70	148.00	16.30	1.97	4.89	7.29	84.51
13/01/2015	36.20	148.00	16.53	2.37	4.76	9.21	85.64
12/02/2015	39.70	148.00	18.12	7.63	4.26	29.89	93.68
04/04/2015	40.00	152.00	17.31	7.02	11.56	16.75	89.10
15/08/2015	41.20	154.00	17.37	6.65	13.96	15.12	88.45
03/11/2015	42.30	156.00	17.38	7.46	19.39	13.93	87.95

- Weight restoration pattern established quickly and maintained
- Liver function showed increased ALT (decreasing trend)
- Was seen in Paeds for delayed growth in 2013
- Bone scan showed 2 years delay
- Stopped Olazapine in Feb end (~ 10 weeks)
- Sertraline increased to 50 mg and now tapering dose

Steph- 15y – YPU / YPD

- GP referral for rapid weight loss from 25th centile to 2nd centile in few weeks
- High achiever, excellent ballet dancer, swimmer and family into hill walking. Mother has history of ED and maternal grandmother overly anxious and critical
- BMI 14.6 age 15y WFH 72.2 % seen same week but not able to reverse weight loss trend over 4 weeks; hypothermia, pulse 42; hypoglycemia
- Admitted to YPU Dundee for 5 months and discharged at BMI 18.7 and 90%WFH on OLAZAPINE 5 mg BD (Nov 2012)
- Weight decreased before starting to gain; developed gall stones; gall bladder removed;
- OLZ gradually decreased to 2.5 mg nocte (Feb 2013)
- Tried to stop OLZ but increased difficulty with sleep and more difficulty at breakfast so restarted

Steph – (YPU/YPD)

- WFH 85.8% involvement of psychology ; trial without OLZ but unsuccessful (dec 13)
- In June 14 to discuss alternatives to OLZ
- Also reported intrusive thoughts that predated anorexia and started Sertraline 50 mg
- Stopped OLZ after one month – decrease in 'ruminative thinking' 'laid back' (Oct 14)
- Sert 100mg made transition to Uni WFH 87.5 % (Dec 14)
- Periods started WFH 89% and willing to gain weight; increased flexibility in thinking (Feb 15)
- WFH 91.97% BMI 19.43 wt 50.5 (in recovery)
- Schema based and compassion focussed individual intervention
- Family based treatment / involvement of 'Dad'

NHS Scotland - Values

Safe

Effective

Person centred

Off label use

- Consent – not a one off event / Information
- Target symptom – e.g. ‘distress’ ?cognitive flexibility
- Very close monitoring - effectiveness
  - Adherence
  - Symptom specific psychometric e.g. MFQ, EDE, SCARED
- Monitor side effect e.g. Glasgow antipsychotic side effects scale
- Blood tests and ECG as indicated (If WFH <75%; medical history; family history)
- When to stop
  - OLZ – as soon as regular weight increase pattern leading to >85% WFH
  - SSRI – 6 months after recovery

To consider

Attitude of young people to psychotropic medication

Preparation for appointment worksheet (Brien et al CAMH 2015 pg 107-111)

Hands on tool based on several focus groups with families and clinicians

Tool illustrates variation in needs of teens and parents

To assist in communication ; amplify teen voice; empower both parents and teens

3Q on today's apt

Share worries ; Get inform – diagnosis/ medication; share what is going well

4Q on 'since last appt'

Innovations in Practice: Supporting parent and teen communication during outpatient psychotropic medication appointments

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Background: Encouragement of youth participation in mental health treatment is relatively new and there have been few specific interventions to improve engagement, particularly as it relates to medication management. This article describes the development of a tool to support engagement during medication appointments by identifying areas of agreement/disagreement between parents and teens. **Method:** Data were analyzed from 240 parent/teen dyads visiting an outpatient community mental health center for medication management. Frequencies and percentages were calculated for all items. Kappa scores were used to assess agreement between parent and teen dyads. **Results:** The level of agreement between parents and teens was low. Overall, teens expressed preference for discussion of 'positive' aspects of treatment such as what is going well, whereas parents preferred to focus on 'negative' aspects of treatment such as problematic symptoms. The lowest level of agreement was found for the item: 'My teen seems to be having problems with energy levels' (Kappa = .19; 95% CI = .05–.34). The strongest level of agreement was for the question 'How has your teen been using the medication since the last appointment?' (Kappa = .56; 95% CI = .44–.69). **Conclusions:** The findings support the utility of the tool for illustrating the variation in needs of teens and parents during medication appointments. Knowledge of these differences can be used by providers to encourage teen participation and may enhance overall communication.

Key Practitioner Message

- Parents and teens often have different agendas for medical appointments and value hands-on tools to assist with communication during psychiatric medication appointments.
- The *Preparing for the Appointment* worksheet represents one hands-on option clinicians can use to reveal divergent parent/teen perspectives.
- Clinicians can use the worksheet to facilitate communication, to amplify teen voice and to empower both parents and teens to communicate with one another and with providers.

Keywords: Teen; psychiatric medication; kappa score; communication

To conclude

- Weight restoration often necessary before use of medication
- Use reserved for co-morbidities and refractory cases
- SSRI has not shown to benefit anorexia or bulimia nervosa (in YP)
- Use of Olazapine has very little evidence
  - Off label use / unlicensed should be limited to extreme presentations
  - More research necessary

More information

NICE clinical guidance 9 (2004) (under revision)

QIS Scotland Eating disorder guidance (2006)

Junior MARZIPAN CR168 RCPsych (2012)

Australian and New Zealand clinical practice guidelines for eating disorders (2014)

Practice Parameter for the Assessment and Treatment of Children and Adolescents With Eating Disorders AACAP (May 2015)

British Columbia eating disorder guidance (2015)

Useful website

http://www.choiceandmedication.org/nhs24/

http://www.headmeds.org.uk/