11. Gestione degli effetti collaterali degli antipsicotici

Iperprolattinemia

Per il presente argomento non sono state identificate revisioni sistematiche di studi randomizzati, pertanto non sono state prodotte tabelle GRADE. La raccomandazione è stata formulata sulla base della seguente letteratura.

Bibliografia

Cookson J, Hodgson R, Wildgust HJ. Prolactin, hyperprolactinaemia and antipsychotic treatment: a review and lessons for treatment of early psychosis. Journal of Psychopharmacology 2012; 26: 42-51.

Hoffer ZS, Roth RL, Mathews M. Evidence for the partial dopamine-receptor agonist aripiprazole as a first-line treatment of psychosis in patients with iatrogenic or tumorogenic hyperprolactinemia. Psychosomatics 2009; 50: 317-324.

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Nunes LV, Moreira HC, Razzouk D, Nunes SO, Mari Jde J. Strategies for the treatment of antipsychotic-induced sexual dysfunction and/or hyperprolactinemia among patients of the schizophrenia spectrum: a review. Journal of Sex and Marital Therapy 2012; 38: 281-301.

Richard I, Holt G, Peveler RC. Antipsychotics and hyperprolactinaemia: mechanisms, consequences and management. Clinical Endocrinology 2011; 74: 141–147.

Disturbi metabolici

Question: Should metformin vs placebo be used for weight gain in patients on second generation antipsychotics?

Bibliography: Björkhem-Bergman L, Asplund AB, Lindh JD. Metformin for weight reduction in non-diabetic patients on antipsychotic drugs: a systematic review and meta-analysis. Journal of Psychopharmacology 2011; 25: 299. Ehret M, Goethe J, Lanosa M, Craig I. The effect of metformin on antrhropometrics and insulin resistance in patients receiving atypical antipsychotic agents: a meta-analysis. Journal of Clinical Psychiatry 2009; 71: 10.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Metformin	Placebo	Relative (95% CI)	Absolute		
Body Weight (follow-up 12-16 weeks; Better indicated by lower values)												
6[1]	randomised trials	serious[2]	very serious[3]	serious[4]	no serious imprecision	none	161	167	-	MD 4.82 lower (7.99 to 1.65 lower)	⊕OOO VERY LOW	CRITICAL
BMI (follow-up 12-16 weeks; Better indicated by lower values)												
7[5]	randomised trials	serious[2]	very serious[6]	serious[7]	no serious imprecision	none	171	173	-	MD 1.21 lower (1.84 to 0.59 lower)	⊕OOO VERY LOW	CRITICAL
Waist circumference (follow-up 12-16 weeks[8]; Better indicated by lower values)												
6[5]	randomised trials	serious[2]	very serious[6]	serious[9]	no serious imprecision	none	155	157	-	MD 1.99 lower (3.39 to 0.59 lower)	⊕OOO VERY LOW	CRITICAL
Homeostasis Model Assessment of Insuline Resistance (follow-up 12-16 weeks[8]; Better indicated by lower values)												
6[5]	randomised trials	serious[2]	very serious[6]	serious[7]	no serious imprecision	none	155	157	-	MD 1.71 lower (2.88 to 0.53 lower)	⊕OOO VERY LOW	CRITICAL

[1] These studies are taken from the review by Bjorkhem-Bergman et al. 2011.

[2] Dropout rate is unclear

[3] I-squared=92%; p<0,0001

[4] This meta-analysis included one study with patients treated with lifestyle interventions in addition to metformin

[5] These studies are taken from the review by Ehret et al. 2009, which included the same studies included by Bjorkhem-Bergman et al. 2011 (with the exception of Carrizo et al. 2009) and 2 additional studies on a pediatric population.
[6] Visual inspection of forest plot suggested high level of heterogeneity
[7] Two studies included pediatric patients
[8] These data are not reported by the authors. They are taken from Bjorkhem-Bergman et al. 2011.
[9] One study included pediatric patients

Bibliografia

Björkhem-Bergman L, Asplund AB, Lindh JD. Metformin for weight reduction in non-diabetic patients on antipsychotic drugs: a systematic review and meta-analysis. Journal of Psychopharmacology 2011; 25: 299.

Ehret M, Goethe J, Lanosa M, Craig I. The effect of metformin on antrhropometrics and insulin resistance in patients receiving atypical antipsychotic agents: a meta-analysis. Journal of Clinical Psychiatry 2009; 71: 10.

Leucht S, Cipriani A, Spineli L, Mavridis D, Orey D, Richter F, Samara M, Barbui C, Engel RR, Geddes JR, Kissling W, Stapf MP, Lässig B, Salanti G, Davis JM. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. Lancet 2013; 382: 951-962.

Disturbi extrapiramidali

Question: Should benzodiazepines vs placebo be used for EPS?

Bibliography: Lima AR, Soares-Weiser K, Bacaltchuk J, Barnes TRE. Benzodiazepines for neuroleptic-induced acute akathisia. Cochrane Database of Systematic Reviews 1999, Issue 4. Bhoopathi PS, Soares-Weiser K. Benzodiazepines for neuroleptic-induced tardive dyskinesia. Cochrane Database of Systematic Reviews 2006, Issue 3.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	**Design**	**Risk of bias**	**Inconsistency**	**Indirectness**	**Imprecision**	**Other considerations**	**Benzodiazepines**	**Placebo**	**Relative (95% CI)**	**Absolute**		
Parkinsonism reduction												
0	No evidence available					none	-	-	-	-		CRITICAL
Akathisia remission (follow-up 7-14 days; assessed with: ESRS, Barnes Rating Scale for Drug Induced Akathisia)												
2[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3]	none	13/13 (100%)[4]	2/13 (15.4%)	RR 0.09 (0.01 to 0.58)	140 fewer per 1000 (from 65 fewer to 152 fewer)	⊕OOO VERY LOW	CRITICAL
Tardive dyskinesia reduction (assessed with: GDS, AIMS, AMS)												
3[5]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[3,6]	none	8/19 (42.1%)[7]	5/11 (45.5%)	RR 1.08 (0.57 to 2.05)	36 more per 1000 (from 195 fewer to 477 more)	⊕OOO VERY LOW	CRITICAL
Dropouts (follow-up 6-10 weeks; assessed with: patients leaving before end of study)												
3[5]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[6]	none	2/33 (6.1%)[7]	0/23 (0%)	RR 2.73 (0.15 to 48.04)	-	⊕OOO VERY LOW	CRITICAL
Adverse events (follow-up 7-14 days; assessed with: at least one adverse event)												
2[1]	randomised trials	serious[2]	no serious inconsistency	no serious indirectness	very serious[6]	none	1/13 (7.7%)[4]	0/13 (0%)	RR 3.00 (0.15 to 61.74)	-	⊕OOO VERY LOW	IMPORTANT

[1] Data from Lima 1999
[2] Allocation concealment is unclear
[3] Number of patients is less than 50
[4] Intervention = clonazepam
[5] Data from Bhoopathi 2006
[6] 95% CI ranges from substantial benefit with benzodiazepines to substantial benefit with placebo; number of patients is less than 50
[7] Intervention = diazepam, alprazolam, clonazepam

Question: Should anticholinergics vs placebo be used for EPS?

Bibliography: Tammenmaa I,McGrath J, Sailas EES, Soares-Weiser K. Cholinergic medication for neuroleptic-induced tardive dyskinesia. Cochrane Database of Systematic Reviews 2002, Issue 3.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Anticholinergics	Placebo	Relative (95% CI)	Absolute		
Parkinsonism reduction												
0	No evidence available					none	-	-	-	-		CRITICAL
Akathisia remission												
0	No evidence available					none	-	-	-	-		CRITICAL
Tardive dyskinesia reduction (follow-up 1-12 weeks; assessed with: improvement assessed by rater)												
8	randomised trials	serious[1]	serious[2]	no serious indirectness	serious[3]	none	39/94 (41.5%)	24/76 (31.6%)	RR 0.84 (0.68 to 1.04)	51 fewer per 1000 (from 101 fewer to 13 more)	⊕OOO VERY LOW	CRITICAL
Dropouts (follow-up 1-12 weeks; assessed with: number of patients leaving the study early)												
10	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	serious[3,4]	none	5/129 (3.9%)	9/111 (8.1%)	RR 0.52 (0.21 to 1.33)	39 fewer per 1000 (from 64 fewer to 27 more)	⊕⊕OO LOW	CRITICAL
Adverse events (follow-up 1-12 weeks)												
9	randomised trials	serious[1]	serious[2]	no serious indirectness	serious[5]	none	15/104 (14.4%)	5/86 (5.8%)	RR 2.34 (0.96 to 5.73)[6]	78 more per 1000 (from 2 fewer to 275 more)	⊕OOO VERY LOW	IMPORTANT

[1] Allocation concealment is unclear
[2] I squared = 70%
[3] 95% CI ranges from substantial benefit with anticholinergics to no difference; number of patients is less than 200
[4] 95% CI ranges from substantial benefit with anticholinergics to substantial benefit with placebo

[5] 95% CI ranges from no difference to substantial harm with anticholinergics; number of patients is less than 200
[6] Our calculation using RevMan software

Question: Should beta-blockers vs placebo be used for EPS?

Bibliography: Barnes TRE, Soares-Weiser K, Bacaltchuk J. Central action beta-blockers versus placebo for neuroleptic-induced acute akathisia. Cochrane Database of Systematic Reviews 2004, Issue 4.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Beta-blockers	Placebo	Relative (95% CI)	Absolute		
Parkinsonism reduction												
0	No evidence available					none	-	-	-	-		CRITICAL
Akathisia remission (follow-up mean 3 days; assessed with: IMEPS, SAS)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	1/6 (16.7%)	1/5 (20%)	RR 1.04 (0.59 to 1.83)	8 more per 1000 (from 82 fewer to 166 more)	⊕OOO VERY LOW	CRITICAL
Tardive dyskinesia reduction												
0	No evidence available					none	-	-	-	-		CRITICAL
Dropouts (follow-up mean 3 days; assessed with: number of patients leaving the study early)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/16 (0%)	0/15 (0%)	-	-	⊕OOO VERY LOW	CRITICAL
Adverse events (follow-up mean 3 days; assessed with: any adverse event)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	0/10 (0%)	0/10 (0%)	-	-	⊕OOO VERY LOW	IMPORTANT

[1] Allocation concealment is unclear
[2] 95% CI ranges from substantial benefit with beta-blockers to substantial benefit with placebo; number of patients is minimal
[3] Number of patients is minimal with no events

Question: Should antipsychotic reduction vs standard dose be used for EPS?

Bibliography: Soares-Weiser K, Rathbone J. Neuroleptic reduction and/or cessation and neuroleptics as specific treatments for tardive dyskinesia. Cochrane Database of Systematic Reviews 2006, Issue 1.

Quality assessment							No of patients		Effect		Quality	Importance
No of studies	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Antipsychotic reduction	Standard dose	Relative (95% CI)	Absolute		
Parkinsonism reduction												
0	No evidence available					none	-	-	-	-		CRITICAL
Akathisia remission												
0	No evidence available					none	-	-	-	-		CRITICAL
Tardive dyskinesia reduction (follow-up 44-52 weeks)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[2]	none	6/9 (66.7%)	1/8 (12.5%)	RR 0.42 (0.17 to 1.04)	73 fewer per 1000 (from 104 fewer to 5 more)	⊕OOO VERY LOW	CRITICAL
Dropouts (follow-up 52 weeks; assessed with: number of patients leaving the study early)												
1	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/4 (25%)	3/4 (75%)	RR 0.33 (0.06 to 1.99)	502 fewer per 1000 (from 705 fewer to 743 more)	⊕OOO VERY LOW	CRITICAL
Adverse events (follow-up 44-52; assessed with: adverse effects: dyskinesia deterioration)												
2	randomised trials	serious[1]	no serious inconsistency	no serious indirectness	very serious[3]	none	1/9 (11.1%)	2/8 (25%)	RR 0.61 (0.11 to 3.31)	97 fewer per 1000 (from 222 fewer to 577 more)	⊕OOO VERY LOW	IMPORTANT

[1] Allocation concealment is unclear
[2] 95% CI ranges from substantial benefit with antipsychotic reduction to no difference; number of patients is very low
[3] 95% CI ranges from substantial benefit with antipychotic reduction to substantial benefit with standard dose; number of patients is very low

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Barnes TRE, Soares-Weiser K, Bacaltchuk J. Central action beta-blockers versus placebo for neuroleptic-induced acute akathisia. Cochrane Database of Systematic Reviews 2004, Issue 4.

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Leucht S, Cipriani A, Spineli L, Mavridis D, Orey D, Richter F, Samara M, Barbui C, Engel RR, Geddes JR, Kissling W, Stapf MP, Lässig B, Salanti G, Davis JM. Comparative efficacy and tolerability of 15 antipsychotic drugs in schizophrenia: a multiple-treatments meta-analysis. Lancet 2013; 382: 951-962.

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