

Best Evidence Summaries of Topics in Mental Healthcare

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Question

“In adults with sexually offending/inappropriate or physically aggressive behaviour, how effective is cyproterone acetate compared with any other intervention in reducing sexually offending /inappropriate behaviour?”

Clarification of question using PICO structure (PICTRO for diagnostic questions)

Patients: Adults with sexually offending/inappropriate or physically aggressive behaviour
Intervention: Cyproterone acetate
Comparator: Any other intervention
Outcome: Reducing sexually offending/inappropriate behaviour

Clinical and research implications

There is insufficient evidence available to make clinical recommendations on the use of cyproterone acetate in adults with sexually offending/inappropriate behaviour. Due to a lack of evidence, the authors of one systematic review stated that anti-libidinal drug treatments should be used with caution. They also stated that it would be worth evaluating this treatment in a well-conducted long-term randomised controlled trial.

What does the evidence say?

Number of included studies/reviews (number of participants)

We identified one systematic review (SR) (0 relevant studies were included), and one cross-over randomised controlled trial (RCT) (n=19) that fulfilled the PICO criteria outlined above. We note that this cross-over RCT is also on the list of 'studies awaiting assessment' for potential inclusion in the SR.

Main findings

No RCTs were identified by the SR that evaluated cyproterone acetate in adults with sexually offending/inappropriate behaviour. In the cross-over RCT conducted in sexual offenders data for all treatment periods were combined, and not evaluated at the first-cross over period (which would minimise any effects of carry-over). This trial reported that the sexual activity score was significantly reduced after treatment with cyproterone acetate compared with placebo ($p < 0.05$), but several other outcomes were not significantly different between treatment groups (e.g. self-reported measures of sexual arousal (after viewing slides), and fantasy after sexual arousal).

Authors conclusions

The authors of the SR did not make any specific conclusions due to a lack of evidence. The authors of the cross-over RCT stated that cyproterone acetate as a treatment for paraphilias was supported by reductions in sexual arousal (physiological and self-report measures), activity, interest and fantasy, and circulation sex hormones. We note, however, that these conclusions appear to be based partly on significant changes from baseline and non-significant differences between placebo and treatment rather than just significant differences between treatment and placebo.

Reliability of conclusions/Strength of evidence

The SR was considered to have a low risk of bias, and the RCT had an unclear risk of bias (i.e. many quality criteria were not reported), thus the reliability of evidence from this trial is uncertain.

What do guidelines say?

There are no guidelines that address this research question.

Date question received: 20/09/2011

Date searches conducted: 22/12/2011

Date answer completed: 01/02/2012

References

Systematic Reviews

White P, Bradley C, Ferriter M, Hatzipetrou L. Managements for people with disorders of sexual preference and for convicted sexual offenders. *Cochrane Database of Systematic Reviews 1998, Issue 4. Art. No.: CD000251. DOI: 10.1002/14651858.CD000251.*

Randomised Controlled Trials

Bradford J M W, Pawlak A. Double-Blind Placebo Crossover Study of Cyproterone Acetate in the Treatment of the Paraphilias. *Archives of Sexual Behavior (1993), Vol. 22, No. 5.*

Results

Systematic Reviews

Author (year)	Search Date	Inclusion criteria	Number of included studies	Summary of results	Risk of bias
White et al. (2009)	1996	<p><i>Participants:</i> Those who have been treated for:</p> <ol style="list-style-type: none"> 1. Sexual behaviours which have resulted in conviction for sexual offences; and/or 2. Disorders of sexual preference: bestiality; child sexual abuse and incest; exhibitionism or indecent exposure; fetishism; frottage or frotteurism; sado-masochism and bondage and discipline; transvestitism and crossdressing; voyeurism; and rape. <p><i>Intervention:</i></p> <ol style="list-style-type: none"> 1. Drug treatment <ol style="list-style-type: none"> a. Testosterone lowering drugs: stilboestrol; oestrogen pellets; medroxyprogesterone acetate; cyproterone acetate. b. Antipsychotics. c. Bromides 2. Surgical castration. 3. Psychological interventions: Behaviour therapy; Relapse 	3 (n= 417)	<p>No trials were included that evaluated cyproterone acetate.</p> <p>The authors reported that at present, there is little data to either support or refute the use of antilibidinal drugs, such as meproxyprogesterone. They also state that it is difficult to justify their use outside of a well-conducted trial.</p>	Low






		<p>prevention; Any other psychological approaches.</p> <p><i>Comparison:</i> Placebo or standard care.</p> <p><i>Outcome:</i> The primary outcome measures were: recidivism; and people lost to follow up.</p> <p><i>Study type:</i> Randomised controlled trials.</p>			
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RCTs







Author (year)	Inclusion criteria	Number of participants	Summary of results	Risk of bias
<p>Bradford et al. (1993)</p> <p>Cross-over trial</p>	<p><i>Participants:</i> Males between 18 and 60 years of age. All fulfilled the diagnostic criteria for paraphilia, as outlined in DSM-III-R. In addition, they were patients who had a persistence of their condition, that is, it had affected their functioning to the extent that they had been charged with a criminal offense. The paraphilia</p>	19	<p>Data were reported at end of study, and do not appear to be reported at the first cross-over.</p> <p>Outcomes relating to, measures of sexual arousal (physiological, self-reported after viewing slides, and fantasy after sexual arousal) were not significantly different between treatment groups.</p> <p>Regarding the outcome of sexual behaviour, sexual activity scores were significantly higher in the placebo group compared to the treatment group ($p < 0.05$), but no significant difference in sexual interest scores was observed.</p> <p>Endocrine measures of testosterone and follicle stimulating hormone were significantly higher in the placebo group compared to the treatment group ($p < 0.0001$ and $p < 0.005$,</p>	Unclear


	<p>had to be present for at least 12 months prior to their initial presentation.</p> <p><i>Intervention:</i> cyproterone acetate</p> <p><i>Comparator:</i> placebo</p> <p><i>Outcomes:</i> a number of outcomes were evaluated under the broad heading of endocrine measures, sexual arousal, psychopathology assessment, sexual behaviour</p> <p><i>Duration:</i> 3 months treatment for each arm (repeated 4 times)</p>		<p>respectively), but no significant difference in luteinizing hormone was reported.</p> <p>Regarding the measure of psychopathology assessment, the brief psychiatric rating scale scores were significantly higher in the placebo group compared to the treatment group ($p < 0.05$) but no significant differences in the Buss-Durkee hostility inventory scores were reported.</p>	
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Risk of Bias: SRs


Author (year)	Risk of Bias				
	Inclusion criteria	Searches	Review Process	Quality assessment	Synthesis
White et al. (2009)					

RCTs

Study	RISK OF BIAS					
	Random allocation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective Reporting
Bradford et al. (1993)						

 Low Risk

 High Risk

 Unclear Risk

Search Details

Source	Search Strategy	Number of hits	Relevant evidence identified
<i>SRs and Guidelines</i>			
NICE	(offend* OR inappropriate) AND (sex*) AND (cyproterone OR antiandrogen*)	40	0
DARE	(offend* OR inappropriate) AND (sex*)	34	1
<i>Primary studies</i>			
CENTRAL	1 (cyproterone acetate) IN DARE, HTA 18 2 (antiandrogen) IN DARE, HTA 5 3 (behavi*) IN DARE, HTA 2693 4 (sex*) IN DARE, HTA 1003 5 (aggressi*) IN DARE, HTA 310 6 (sex offend*) IN DARE, HTA 14 7 (inappropriate) IN DARE, HTA 584 8 MeSH DESCRIPTOR Sex Offenses EXPLODE ALL TREES 33 9 MeSH DESCRIPTOR Sexual Behavior EXPLODE ALL TREES 143 10 MeSH DESCRIPTOR Paraphilias EXPLODE ALL TREES 4 11 MeSH DESCRIPTOR Aggression EXPLODE ALL TREES 39 12 MeSH DESCRIPTOR Cyproterone Acetate EXPLODE ALL TREES 3 13 MeSH DESCRIPTOR Androgen Antagonists EXPLODE ALL TREES 37 14 #1 OR #12 18 15 #2 OR #13 39 16 #14 OR #15 49	5	3

	17 #3 AND #4 287 18 #9 AND #17 70 19 #5 OR #11 316 20 #6 OR #18 81 21 #8 OR #9 OR #10 OR #20 176 22 #7 OR #19 OR #21 1054 23 #16 AND #22 5		
MEDLINE	Search History: 1. MEDLINE; CYPROTERONE ACETATE/; 1570 results. 2. MEDLINE; "cyproterone acetate".ti,ab; 2252 results. 3. MEDLINE; 1 OR 2; 2686 results. 4. MEDLINE; exp ANDROGEN ANTAGONISTS/; 11445 results. 5. MEDLINE; Antiandrogen*.ti,ab; 4146 results. 6. MEDLINE; 4 OR 5; 12981 results. 7. MEDLINE; 3 OR 6; 13351 results. 8. MEDLINE; exp SEX OFFENSES/; 16338 results. 9. MEDLINE; exp PARAPHILIAS/; 4301 results. 10. MEDLINE; sex*.ti,ab; 424280 results. 11. MEDLINE; offend*.ti,ab; 9779 results. 12. MEDLINE; 10 AND 11; 2465 results. 13. MEDLINE; exp AGGRESSION/; 25599 results. 14. MEDLINE; aggressi*.ti,ab; 113318 results. 15. MEDLINE; 13 OR 14; 124469 results. 16. MEDLINE; inappropriate.ti,ab; 35284 results. 17. MEDLINE; behavi*.ti,ab; 651952 results. 18. MEDLINE; 8 OR 9 OR 12 OR 15 OR 16; 178402 results. 19. MEDLINE; 17 AND 18; 32856 results.	65	

	<p>20. MEDLINE; 7 AND 19; 129 results.</p> <p>21. MEDLINE; "randomized controlled trial".pt; 324576 results.</p> <p>22. MEDLINE; "controlled clinical trial".pt; 84254 results.</p> <p>23. MEDLINE; randomized.ab; 240171 results.</p> <p>24. MEDLINE; placebo.ab; 135452 results.</p> <p>25. MEDLINE; "drug therapy".fs; 1521571 results.</p> <p>26. MEDLINE; randomly.ab; 175715 results.</p> <p>27. MEDLINE; trial.ab; 249012 results.</p> <p>28. MEDLINE; groups.ab; 1152861 results.</p> <p>29. MEDLINE; 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28; 2910963 results.</p> <p>30. MEDLINE; 20 AND 29; 65 results.</p>		
EMBASE	<p>Search History:</p> <p>81. EMBASE; "cyproterone acetate".ti,ab; 2284 results.</p> <p>82. EMBASE; Antiandrogen*.ti,ab; 4590 results.</p> <p>83. EMBASE; sex*.ti,ab; 464397 results.</p> <p>84. EMBASE; offend*.ti,ab; 12558 results.</p> <p>85. EMBASE; 83 AND 84; 3208 results.</p> <p>86. EMBASE; exp AGGRESSION/; 53001 results.</p> <p>87. EMBASE; inappropriate.ti,ab; 40751 results.</p> <p>88. EMBASE; behavi*.ti,ab; 696615 results.</p> <p>89. EMBASE; CYPROTERONE ACETATE/; 5785 results.</p> <p>90. EMBASE; 81 OR 89; 6296 results.</p> <p>91. EMBASE; ANTIANDROGEN/; 8354 results.</p> <p>92. EMBASE; 82 OR 91; 10805 results.</p> <p>93. EMBASE; 90 OR 92; 15079 results.</p> <p>94. EMBASE; exp SEXUAL CRIME/; 13277 results.</p> <p>95. EMBASE; 83 OR 94; 469727 results.</p>	25	

<p>96. EMBASE; 85 OR 94; 14320 results.</p> <p>97. EMBASE; 95 OR 96; 469727 results.</p> <p>98. EMBASE; aggressi*.ti,ab; 131063 results.</p> <p>99. EMBASE; 86 OR 98; 161627 results.</p> <p>100. EMBASE; 87 OR 97 OR 99; 660390 results.</p> <p>101. EMBASE; 88 AND 100; 89979 results.</p> <p>102. EMBASE; 93 AND 101; 344 results.</p> <p>103. EMBASE; exp SEXUAL DEVIATION/; 5162 results.</p> <p>104. EMBASE; 83 OR 85 OR 94 OR 103; 472170 results.</p> <p>105. EMBASE; 87 OR 97 OR 103 OR 104; 511291 results.</p> <p>106. EMBASE; 87 OR 99 OR 105; 662552 results.</p> <p>107. EMBASE; 88 AND 106; 90178 results.</p> <p>108. EMBASE; 93 AND 107; 347 results.</p> <p>109. EMBASE; random*.ti,ab; 671179 results.</p> <p>110. EMBASE; factorial*.ti,ab; 17573 results.</p> <p>111. EMBASE; (crossover* OR cross-over*).ti,ab; 57365 results.</p> <p>112. EMBASE; placebo*.ti,ab; 162603 results.</p> <p>113. EMBASE; (doubl* ADJ blind*).ti,ab; 119852 results.</p> <p>114. EMBASE; (singl* ADJ blind*).ti,ab; 11323 results.</p> <p>115. EMBASE; assign*.ti,ab; 188035 results.</p> <p>116. EMBASE; allocat*.ti,ab; 63257 results.</p> <p>117. EMBASE; volunteer*.ti,ab; 147020 results.</p> <p>118. EMBASE; CROSSOVER PROCEDURE/; 31378 results.</p> <p>119. EMBASE; DOUBLE BLIND PROCEDURE/; 102103 results.</p> <p>120. EMBASE; RANDOMIZED CONTROLLED TRIAL/; 294155 results.</p> <p>121. EMBASE; SINGLE BLIND PROCEDURE/; 14552 results.</p>		
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	<p>122. EMBASE; 109 OR 110 OR 111 OR 112 OR 113 OR 114 OR 115 OR 116 OR 117 OR 118 OR 119 OR 120 OR 121; 1114654 results.</p> <p>123. EMBASE; 108 AND 122; 25 results.</p>		
PsycINFO	<ol style="list-style-type: none"> 1. Search History: 2. 37. PsycINFO; "cyproterone acetate".ti,ab; 119 results. 3. 38. PsycINFO; Antiandrogen*.ti,ab; 209 results. 4. 39. PsycINFO; sex*.ti,ab; 207339 results. 5. 40. PsycINFO; offend*.ti,ab; 23005 results. 6. 41. PsycINFO; 39 AND 40; 7481 results. 7. 43. PsycINFO; inappropriate.ti,ab; 11517 results. 8. 44. PsycINFO; behavi*.ti,ab; 585919 results. 9. 45. PsycINFO; aggressi*.ti,ab; 54542 results. 10. 46. PsycINFO; ANTIANDROGENS/; 173 results. 11. 47. PsycINFO; 37 OR 38 OR 46; 338 results. 12. 48. PsycINFO; exp SEX OFFENSES/; 24992 results. 13. 49. PsycINFO; exp PARAPHILIAS/; 6503 results. 14. 50. PsycINFO; 39 OR 41 OR 48 OR 49; 211902 results. 15. 51. PsycINFO; exp AGGRESSIVE BEHAVIOR/; 98889 results. 16. 52. PsycINFO; AGGRESSIVENESS/; 3136 results. 17. 53. PsycINFO; 45 OR 51 OR 52; 127972 results. 18. 54. PsycINFO; 43 OR 50 OR 53; 327752 results. 19. 55. PsycINFO; BEHAVIOR/; 18648 results. 20. 56. PsycINFO; 44 OR 55; 587669 results. 21. 57. PsycINFO; 54 AND 56; 101866 results. 22. 58. PsycINFO; 47 AND 57; 160 results. 	26	

	<p>23. 59. PsycINFO; CLINICAL TRIALS/; 5645 results.</p> <p>24. 60. PsycINFO; random*.ti,ab; 104550 results.</p> <p>25. 61. PsycINFO; groups.ti,ab; 315182 results.</p> <p>26. 62. PsycINFO; (double adj3 blind).ti,ab; 15452 results.</p> <p>27. 63. PsycINFO; (single adj3 blind).ti,ab; 1142 results.</p> <p>28. 64. PsycINFO; EXPERIMENTAL DESIGN/; 8098 results.</p> <p>29. 65. PsycINFO; controlled.ti,ab; 65431 results.</p> <p>30. 66. PsycINFO; (clinical adj3 study).ti,ab; 6542 results.</p> <p>31. 67. PsycINFO; trial.ti,ab; 54997 results.</p> <p>32. 68. PsycINFO; "treatment outcome clinical trial".md; 20697 results.</p> <p>33. 69. PsycINFO; 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68; 482549 results.</p> <p>34. 70. PsycINFO; 58 AND 69; 26 results.</p>		
Summary	NA	NA	

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