Impact of a behavioural sleep intervention on symptoms and sleep in children with attention deficit hyperactivity disorder, and parental mental health: randomised controlled trial

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- Analysis: Attention-deficit/hyperactivity disorder: are we helping or harming? (*BMJ* 2013;347:f6172)
- Views & Reviews: Why are we failing young patients with ADHD? (*BMJ* 2014;349:g6082)
- Research: Melatonin for sleep problems in children with neurodevelopmental disorders (*BMJ* 2012;345:e6664)

STUDY QUESTION

Does a brief, behavioural sleep intervention programme reduce the severity of symptoms of attention deficit hyperactivity disorder (ADHD) and sleep problems in children with ADHD?

SUMMARY ANSWER

The intervention families reported a greater decrease in severity of ADHD symptoms and fewer moderate-severe sleep problems at three months and six months after randomisation compared with the control families.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Sleep problems are common in children with ADHD and are associated with poorer functioning. A brief behavioural sleep programme, encompassing sleep hygiene practices and standardised behavioural strategies, improved the severity of symptoms, sleep, behaviour, quality of life, and daily functioning in children aged 5-12 years with ADHD.

Design

We carried out a randomised controlled trial. A statistician who was not involved with the study generated a randomisation schedule using a computerised random number sequence. Assignment was in a ratio of 1:1 intervention to usual care, stratified by the child's sex. Varying block sizes of 2, 4, and 6 were used to ensure balance between the trial arms and within strata.

Participants and setting

Our study sample comprised 244 children aged 5-12 years with ADHD and attending one of 21 Australian general paediatric practices. 122 participants were assigned to a brief behavioural sleep programme, and 122 were assigned to usual clinical care (control group).

Primary outcome

Parent and teacher reported severity of ADHD symptoms on the ADHD rating scale IV at three months after randomisation.

Main results and the role of chance

The intervention families compared with control families reported a greater decrease in ADHD symptoms at three and six months (adjusted mean difference for change in symptom severity −2.9, 95% confidence interval −5.5 to −0.3, P=0.03, effect size −0.3, and −3.7, −6.1 to −1.2, P=0.004, effect size −0.4, respectively). Compared with control children, intervention children had fewer moderate-severe sleep problems at three months (56% *v* 30%; adjusted odds ratio 0.30, 95% confidence interval 0.16 to 0.59; P<0.001) and six months (46% *v* 34%; 0.58, 0.32 to 1.0; P=0.07). At three months this equated to a reduction in absolute risk of 25.7% (95% confidence interval 14.1% to 37.3%) and an estimated number needed to treat of 3.9. At six months the number needed to treat was 7.8. Intervention families reported greater improvements in all other child and family outcomes except parental mental health. Teachers reported improved behaviour of the children in the intervention compared with control group at three and six months.

Harms

No harms were reported.

Bias, confounding, and other reasons for caution

Parents were aware of whether their child had received the intervention, which may have led to response bias whereby parents overstated improvements in their child in response to the intervention.

Generalisability to other populations

Findings are generalisable to children aged 5-12 years with ADHD from English speaking families.

Study funding/potential competing interests

The study was supported by the Australian National Health and Medical Research Council (project grant No 607362). We have no competing interests.

Trial registration number

Current Controlled Trials ISRCTN68819261.

Comparison of severity of symptoms of attention deficit hyperactivity disorder (ADHD) between intervention and control children as reported by parents on ADHD rating scale IV

	Mean (SD)		Adjusted difference* with multiple imputation (intervention–control)	
Measurement points	Intervention group	Control group	Mean (95% CI)	P value
Baseline	35.6 (9.4), n=120	37.1 (9.9), n=122	—	—
3 months	29.7 (10.7), n=85	33.2 (9.6), n=88	−2.9 (−5.5 to −0.3)	0.03
6 months	28.4 (10.8), n=105	33.8 (9.5), n=98	−3.7 (−6.1 to −1.2)	0.004

*Adjusted for children's age, sex, medication use (yes or no), total number of mental health comorbidities, parental age, parental completion of high school (yes or no), socioeconomic status (index of relative socioeconomic disadvantage).

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High sensitivity cardiac troponin and the under-diagnosis of myocardial infarction in women: prospective cohort study

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● EDITORIAL by Timmis
● RESEARCH, p13

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STUDY QUESTION

Does the use of a high sensitivity cardiac troponin assay with sex specific thresholds improve the diagnosis of myocardial infarction in women?

SUMMARY ANSWER

A high sensitivity troponin assay with sex specific diagnostic thresholds had little effect in men but may double the diagnosis of myocardial infarction in women and identify those at high risk of reinfarction and death.

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Major differences exist in the diagnosis and management of myocardial infarction in men and women presenting with suspected acute coronary syndrome. Our findings with a high sensitivity troponin I assay suggest that the use of contemporary assays with a single diagnostic threshold will disproportionately under diagnose myocardial infarction in women and contribute to sex inequalities in treatment and outcomes.

Participants and setting

Consecutive patients presenting with suspected acute coronary syndrome to a tertiary cardiac centre in Scotland.

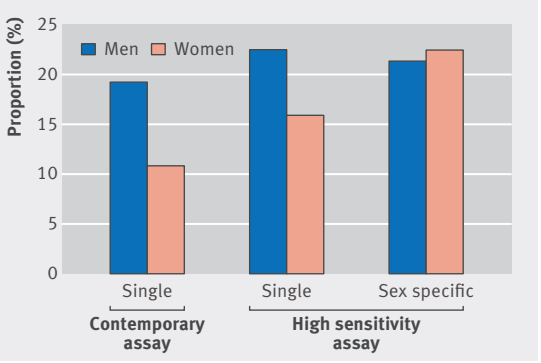
Design, size, and duration

Prospective cohort study of 1126 patients (45% women) over three months with one year follow-up. Two cardiologists independently adjudicated the diagnosis as type 1 myocardial infarction, type 2 myocardial infarction, or myocardial injury using a high sensitivity cardiac troponin I assay with sex specific diagnostic thresholds (men 34 ng/L, women 16 ng/L). They then compared the findings with current practice where a contemporary assay (50 ng/L, single threshold) was used to guide care.

Main results and the role of chance

Use of a high sensitivity troponin I assay noticeably increased the diagnosis of type 1 myocardial infarction in women (from 11% to 22%; P<0.001) but had a minimal effect in men (from 19% to 21%, P=0.002). Women were less likely than men to be referred to a cardiologist or to undergo coronary revascularisation (P<0.05 for both). At 12 months, women with undisclosed increases in troponin concentration (17-49 ng/L) and those with myocardial infarction (≥50 ng/L) had the highest rate of death or reinfarction compared with women without

Proportion of men and women with diagnosis of type 1 myocardial infarction using contemporary (single threshold 50 ng/L) and high sensitivity (single threshold 26 ng/L, sex specific thresholds 34 ng/L for men and 16 ng/L for women) troponin I assays



(≤16 ng/L) myocardial infarction (25%, 24%, and 4% respectively; P<0.001).

Bias, confounding, and other reasons for caution

Implementation of a high sensitivity troponin I assay and use of sex specific diagnostic thresholds will improve the diagnosis of myocardial infarction in women and identify those at highest risk of recurrent myocardial infarction and death. Whether better targeting of treatments for myocardial infarction will improve outcomes remains unknown. Some misclassification of patients with increased plasma troponin concentrations using the high sensitivity assay may have occurred, as many patients with undetectable troponin concentrations using the contemporary assay were reassured and discharged without further cardiac investigation.

Generalisability to other populations

We prospectively included all patients with suspected acute coronary syndrome without case selection. Our findings are therefore both representative and generalisable to most acute secondary and tertiary care centres worldwide.

Study funding/potential competing interests

This research was funded by a special project grant from the British Heart Foundation (SP/12/10/29922) and with support from the legacy of Violet Kemlo. Abbott Laboratories provided assay reagent without charge. ASVS, FSA, and NLM have acted as consultants for Abbott Laboratories.

Diagnostic accuracy of single baseline measurement of Elecsys Troponin T high-sensitive assay for diagnosis of acute myocardial infarction in emergency department: meta-analysis

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EDITORIAL by Timmis
RESEARCH, p12

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Research: Off-hour presentation and outcomes in patients with acute myocardial infarction (*BMJ* 2014;348:f7393)
Views & Reviews: Bad medicine: non-ST elevation myocardial infarction (*BMJ* 2013;347:f5967)

STUDY QUESTION

What is the diagnostic accuracy of a single baseline measurement of the Elecsys Troponin T high-sensitive assay (Roche Diagnostics) for the diagnosis of non-ST segment elevation acute myocardial infarction in patients presenting to the emergency department with symptoms suggestive of acute coronary syndrome?

SUMMARY ANSWER

If 14 ng/L is used as a positivity threshold the sensitivity would be 89.5% (95% confidence interval 86.3% to 92.1%) and the specificity 77.1% (68.7% to 83.7%), whereas using 3 ng/L or 5 ng/L would result in a sensitivity of 97.4% (94.9% to 98.7%) and a specificity of 42.4% (31.2% to 54.5%).

WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Patients who present to the emergency room with suspected acute coronary syndrome but have very low baseline troponin concentrations have a very low risk of acute myocardial infarction. A single baseline measurement of the Elecsys Troponin T high-sensitive assay could rule out acute myocardial infarction in a significant proportion of patients if a low cut-off value (<5 ng/L) is used.

Selection criteria for studies

We searched Medline, Embase, and other relevant electronic databases for papers published between January 2006 and December 2013. We included studies in the meta-analyses reported here if they evaluated the diagnostic accuracy of a single baseline measurement of the Elecsys Troponin T high-sensitive assay (Roche Diagnostics) for the diagnosis of acute myocardial infarction in patients presenting to the emergency room with symptoms suggestive of acute coronary syndrome.

Primary outcome(s)

The main outcomes were summary sensitivity and specificity.

Main results and role of chance

Twenty three studies reported the performance of the high sensitivity troponin T assay at presentation. We pooled the data for cut-off values at 14 ng/L (20 studies) and at 3 or 5 ng/L (six studies). The table shows the summary estimates for sensitivity and specificity. In a population of 100 with a 21% prevalence of the target condition, using 14 ng/L as a cut-off value will miss 2 (95% confidence interval 2 to 3) patients with acute myocardial infarction (false negatives) and will misdiagnose 18 (13 to 25) who do not have the target condition (false positives). If the combined 3-5 ng/L cut-off value is used, <1 (0 to 1) patient with acute myocardial infarction will be missed and 46 (36 to 54) patients without acute myocardial infarction will test positive.

Bias, confounding, and other reasons for caution

Use of a single baseline measurement of the evaluated high sensitivity troponin T assay to rule out acute myocardial infarction should be part of a comprehensive triage strategy and may not be appropriate for patients who present less than three hours after onset of symptoms. Care must also be exercised because of the higher imprecision of the high sensitivity troponin T assay and the greater effect of lot-to-lot reagent variation at low troponin concentrations.

Study funding/potential competing interests

This research was funded by the South West Academic Health Science Network and the National Institute for Health Research (NIHR) Collaboration for Leadership for Applied Health Research and Care for the South West Peninsula. ZZ and CH received financial support from the NIHR Collaboration for Leadership in Applied Health Research and Care for the South West Peninsula.

Summary estimates of sensitivity and specificity at different cut-off values

Cut-off value	No of studies	Sensitivity (%) (95% CI)	Specificity (%) (95% CI)	Positive likelihood ratio (95% CI)	Negative likelihood ratio (95% CI)
14 ng/L	20	89.5 (86.3 to 92.1)	77.1 (68.7 to 83.7)	3.9 (2.8 to 5.4)	0.14 (0.10 to 0.18)
3 ng/L or 5 ng/L (combined)	6	97.4 (94.9 to 98.7)	42.4 (31.2 to 54.5)	1.69 (1.40 to 2.05)	0.06 (0.04 to 0.10)

EDITORIAL by Sacks

Glibenclamide, metformin, and insulin for the treatment of gestational diabetes: a systematic review and meta-analysis

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STUDY QUESTION

What are the short term relative risks and benefits of insulin, glibenclamide, and metformin for treating women with gestational diabetes requiring drug treatment?

SUMMARY ANSWER

Glibenclamide is clearly inferior to both insulin and metformin, while metformin (with added insulin when required) performs slightly better than insulin.

WHAT IS KNOWN AND WHAT THIS STUDY ADDS

Information on the safety of oral agents for treating gestational diabetes is limited. This review of short term effects showed that glibenclamide is clearly inferior to both insulin and metformin and should not be used for treating gestational diabetes if insulin or metformin is available.

Selection criteria for studies

We searched Medline, CENTRAL, and Embase until 20 May 2014 for randomized controlled trials that compared use of glibenclamide, metformin, and insulin for women with gestational diabetes requiring drug treatment and that provided maternal or fetal outcomes. We conducted three meta-analyses to compare glibenclamide with insulin, metformin with insulin, and metformin with glibenclamide.

Primary outcome(s)

Primary maternal outcomes were HbA_{1c} level in the third trimester, severe maternal hypoglycaemia, pre-eclampsia, total weight gain during pregnancy, caesarean section, and (for trials of metformin *v* glibenclamide) treatment failure. Primary fetal outcomes were gestational age at delivery, preterm birth, birth weight, macrosomia (≥4000 g), large for gestational age newborn (birth weight >90th centile), small for gestational age newborn (birth weight <10th centile), neonatal hypoglycaemia, and perinatal mortality.

Main results and role of chance

We analyzed 15 articles, including 2509 subjects. In the trials of glibenclamide versus insulin, we found significant differences in birth weight (mean difference 109 g (95% confidence interval 35.9 to 181)), macrosomia (risk ratio 2.62 (1.35 to 5.08)), and neonatal hypoglycaemia (risk ratio 2.04 (1.30 to 3.20)). With metformin versus insulin, significance was reached for weight gain (mean difference −1.14 kg (−2.22 to −0.06)), gestational age at delivery (mean difference −0.16 weeks (−0.30 to −0.02)), and preterm birth (risk ratio 1.50 (1.04 to 2.16)), with a trend for neonatal hypoglycaemia (risk ratio 0.78 (0.60 to 1.01)). With metformin versus glibenclamide, significance was reached for weight gain (mean difference −2.06 kg (−3.98 to −0.14)), birth weight (mean difference −209 g (−314 to −104)), macrosomia (risk ratio 0.33 (0.13 to 0.81)), and large for gestational age newborn (risk ratio 0.44 (0.21 to 0.92)).

Point estimates are reasonably robust, and the results of the metformin versus glibenclamide comparison support those of the other two comparisons. We think the results are unlikely to be due to chance.

Bias, confounding, and other reasons for caution

Sensitivity analysis to address risk of bias did not affect treatment estimates in any substantial way, and publication bias assessed after funnel plot inspection was deemed to be low.

In the metformin versus insulin comparison, prepregnancy body mass index was 0.78 higher in the metformin arm. As maternal body mass index itself is a predictor of most outcomes addressed, this could have an influence on the significance or magnitude of the differences observed.

Study funding/potential competing interests

MB, AGP, and RC declare no financial relationships with organisations that might have an interest in the submitted work in the previous three years, but they have received travel grants from Lilly, NovoNordisk, and Sanofi Aventis.

Differences in birth weight after treatment of maternal gestational diabetes

Mean (SD) birth weight (g)	No of births		Mean (SD) birth weight (g)	No of births
Glibenclamide		*v*	Insulin	
3256 (543)	201		3194 (598)	203
2720 (340)	10		2600 (430)	13
3460.5 (741)	48		3395.6 (542)	49
3372.18 (501.04)	32		3082.78 (423.23)	36
3603.7 (607)	41		3363.2 (385)	41
3010 (400)	30		2980 (390)	30
3200 (420)	32		3100 (540)	32
Total	394			404
Metformin		*v*	Insulin	
3451.8 (727.5)	32		3500.2 (700.5)	31
3372 (572)	363		3413 (569)	370
3712 (432)	47		3558 (593)	50
3300 (400)	80		3400 (400)	80
3143.7 (446.6)	46		3237.6 (586.8)	46
3604 (488)	110		3589 (448)	107
Total	678			684
Metformin		*v*	Glibenclamide	
3103 (600)	75		3329.6 (334)	74
3193.87 (521.22)	104		3387.98 (512.16)	96
Total	179			170