Respiratory disease

Asthma persisting from childhood to adulthood presents a distinct phenotype

Asthma that starts in childhood and persists throughout adult life tends to be more severe and is associated with poorer lung function compared with adult-onset asthma, a study from Japan has concluded. The difference in clinical characteristics points to a distinct phenotype.

A total of 1,443 patients, aged ≥18 years with asthma, diagnosed using the Global Initiative for Asthma (GINA) guidelines, were recruited to the cross-sectional study from a large specialist centre in Japan.

Patients were classified into three groups: adult onset; relapsed (remitted childhood asthma that had relapsed) and persistent (asthma that had originated in childhood and was still ongoing). Clinical and laboratory data from electronic patient records were analysed.

A higher proportion of patients in the persistent group (40%) had severe asthma compared with the adult-onset group (31%) and relapsing group (34%); P = 0.015. The percentage of patients using high-dose inhaled corticosteroids in the persistent group (40%) was higher than that in the adult-onset group (29%); P = 0.004.

The percentage of patients with a family history of asthma was significantly higher in the persistent group (64%) than in the adult-onset (36%) or relapsed group (52%); P < 0.001.

The comorbidities of allergic rhinitis and atopic dermatitis were significantly higher in the persistent group than in the adult-onset group; 77% vs 64% and 30% vs 7%, respectively (P < 0.001 for both).

Evidence for chronic airway inflammation in the persistent group was also strong with increased eosinophil counts and IgE levels compared with the adult-onset group.

Spirometry showed reduced % forced expiratory flow at 75% of vital capacity (%FEF_{75}) in the persistent group compared with the adult-onset (P < 0.001) and relapsed groups (P < 0.05), and the %FEV_1 and %FEF_{50} values were lower in the persistent group than in the adult-onset group (P < 0.001).

Because %FEV measurements are used as markers for small airway dysfunction, these results suggest that the impairment of the small airways was greater in the persistent group than the other two groups, which is in agreement with previous studies.

The study authors conclude: 'Adult patients with asthma that has persisted from childhood to adulthood have poorer lung function and more severe asthma in adulthood than those with adult-onset asthma based on our findings.

Asthma that persists from childhood to adulthood seems to present a distinct clinical phenotype of adult asthma, and this should be considered when clinicians attempt to optimise treatment for their adult patients with asthma.'

DR PETER SAUL

To M, Tsuzuki R, Katsube O et al. Persistent asthma from childhood to adulthood presents a distinct phenotype of adult asthma. *J Allergy Clin Immunol Pract* 2020;8:1921-27

Mental health

Evaluating therapies for depression in children and adolescents

Fluoxetine, either alone or in combination with CBT, appears to be the most effective treatment for children and adolescents with moderate to severe depression, a systematic review and network meta-analysis has concluded.

Placebo-controlled and head to head trials of 16 antidepressants, seven psychotherapies and five combinations of antidepressant and psychotherapy were identified from databases and trial registers. Double-blind randomised controlled trials (RCTs) of antidepressant monotherapy and observer-blind or self-rated trials of psychotherapy or combination therapy were included.

Trials involving participants with bipolar disorder or subthreshold, treatment-resistant or psychotic depression were excluded.

Overall, 71 trials with a total of 9,510 participants were analysed. Patients ranged in age from 3 to 20, mean 14 years, and 57.2% were female. Three quarters (75.5%) had moderate to severe depression.

The primary outcomes were efficacy and acceptability, defined respectively as the change in the depression symptom score and the all-cause discontinuation rate.

Only two treatments were significantly more effective than pill placebo, namely fluoxetine; effect size i.e. standardised mean difference (SMD) -0.51 (95% CI: -0.84 to -0.18) and fluoxetine plus CBT SMD -0.73, (95% CI: -1.39 to -0.07). Fluoxetine plus CBT was significantly more

effective than both CBT alone SMD -0.78 (95% CI: -1.55 to -0.01) and psychodynamic therapy SMD -1.14 (95% CI: -2.20 to -0.08), but not more effective than fluoxetine alone SMD -0.22 (95% CI: -0.86 to 0.42). Fluoxetine, fluoxetine plus CBT and interpersonal therapy were all significantly more effective than psychological placebo.

Fluoxetine was associated with fewer dropouts than sertraline, imipramine, and desipramine.

The non-significant findings for other antidepressant monotherapies may in part simply reflect that there were more fluoxetine trials compared with trials for other antidepressants.

The authors highlight a number of limitations. Most of the included studies were of low or very low quality, and there was some evidence of publication bias. A further difficulty is the high placebo response rate in children.

Psychological placebo usually involves a non-directional and neutral discussion so satisfactory blinding may not be possible.

The authors conclude: 'The findings suggest that fluoxetine (alone or in combination with CBT) might be considered the best option to treat acute symptoms in children and adolescents with major depression.'

The NICE guideline currently recommends a psychological intervention for initial management of moderate to severe depression in children and adolescents,[1] and this may now need to be reviewed.

NICE recommends that antidepressant treatment should not be initiated in primary care.[1] Children and adolescents with moderate to severe depression should be referred to child and adolescent mental health services (CAMHS).

DR PHILLIP BLAND

Zhou X, Teng T, Zhang Y et al. Comparative efficacy and acceptability of antidepressants, psychotherapies, and their combination for acute treatment of children and adolescents with depressive disorder: a systematic review and network meta-analysis. *Lancet Psychiatry* 2020; 7:581-601

REFERENCE

1 National Institute for Health and Care Excellence. NG134. Depression in children and young people: identification and management. NICE. London. 2019

See also Special report: Optimising the management of depression in children, p21

Addiction

Patient safety incidents in opioid substitution therapy analysed

Errors in prescribing, supervised or non-supervised dispensing, and monitoring and communication, were responsible for patient safety incidents in opioid substitution treatment, a study from England and Wales has shown.

Data on patient safety incidents involving patients receiving either methadone or buprenorphine treatment in community services between 2005 and 2015 were extracted from the National Reporting and Learning System. This is a national database of patient safety incident reports maintained by the NHS in England and Wales.

Eligible reports were manually reviewed to check that they fitted study criteria, and the resulting study population comprised 2,284 safety incident reports.

Methadone was the most commonly reported drug (n = 1,862; 82%) followed by buprenorphine (n = 394; 17%) and buprenorphine and naloxone in combination (28; 1%).

Most incident reports from opioid substitution treatment came from failure in one of four processes of care delivery: non-supervised dispensing (n = 1,544) examples included dispensing incorrect doses and dispensing to the wrong patient; supervised dispensing (n = 318) e.g. incorrect dose, wrong patient and failure to supervise consumption; monitoring and communication (n = 248) e.g. failing to stop dispensing when appropriate; and prescribing opioid substitution treatment (n = 151) e.g. incomplete or inaccurate prescriptions and prescriptions for the wrong dose.

For incidents associated with harm, prescribing opioid substitution had the highest proportion (14 of 151; 9%), followed by monitoring and communication-related incidents (22 of 284; 8%), and failures with supervised dispensing (24 of 318; 8%). Non-supervised dispensing had the lowest proportion resulting in harm (57 of 1,544; 4%).

Overall, 94% (n = 2,155) of incidents resulted in no harm, while 6% (n = 129) caused low or moderate harm to the patient. There were no incidents resulting in severe harm or death.

Contributory factors (categorised as staff; organisational; patient; medication storage and packaging; or information technology) were identified in 75% of incidents with 40% involving more than one factor.

Opioid substitution therapy is an effective harm reduction strategy in the management of opioid dependence and reduces illicit drug use and associated morbidity. Substitution therapy is widespread and evaluating the safety of treatment programmes is vital.

Based on their findings the authors conclude that priority areas to promote safe opioid substitution include prescriber education, implementing and strengthening electronic prescribing systems, strengthening dispensing and monitoring systems and developing specific procedural and educational interventions for pharmacy staff.

DR JEZ THOMPSON

Gibson R, McLeod N, Donaldson LJ et al. A mixed-methods analysis of patient safety incidents involving opioid substitution treatment with methadone or buprenorphine in community-based care in England and Wales. *Addiction* Epub ahead of print 9 March 2020 doi:10.1111/add.15039

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