along with the occasional presence of subcutaneous nodules.[2,7,11,13] Within synovial joints, the synovium and the tidemark region of articular cartilage are particularly susceptible to iron deposition. This makes the cartilage matrix stiffer and more predisposed to fragmentation. In addition, iron salts promote the formation and precipitation of calcium pyrophosphate dihydrate crystals within the joint, contributing to subsequent joint degeneration.[2]

Individuals with more severe iron overload may develop liver disease with fibrosis or cirrhosis. Hepatocellular carcinoma has been reported to develop in about 30% of individuals with untreated cirrhosis caused by hereditary haemochromatosis.[7] Diabetes also occurs more frequently in hereditary haemochromatosis, especially in advanced disease; overall, 20–50% of those with symptomatic disease have diabetes.[7]

Treatment of hereditary haemochromatosis is through removal of iron, so that total body iron stores return to normal. Usually, this can be achieved most efficiently by venesection of 500 mL blood (which depletes about 250 mg of iron), initially every week or fortnight until the serum ferritin concentration is reduced to 50–100 microg/L. Maintenance phlebotomy may then be scheduled to maintain haemoglobin concentrations above 11–12 g/dL and the serum ferritin concentration between 50–100 microg/L,[11] with most patients requiring phlebotomy every two to four months.[3,5,7,10,14] Each venesection should be preceded by measurement of haemoglobin and haematocrit. Venesection should only go ahead if the haematocrit is within 20% of the previous measurement and/or haemoglobin is greater than 11g/dL.[5,7] Venesection treatment is performed through the Australian Red Cross Blood Service, many public hospitals and some private pathology providers; if the individual has no contraindications, the blood can be used for donation purposes.[7]

While the evidence is not definitive, chronic use of proton pump inhibitors by individuals with hemochromatosis may decrease iron absorption, diminishing the severity of overload that would otherwise occur as the result of excess absorption of iron from dietary sources, or reduce requirements for maintenance phlebotomy.[7,15,16] Conversely, vitamin C increases iron mobilisation; individuals with hemochromatosis should limit their intake of supplemental vitamin C to 500 mg daily.[7,15] Patients with haemochromatosis should not consume raw shellfish, owing to an increased susceptibility to infection with Vibrio vulnificus.[7,15]

While phlebotomy is very effective, there are potential adverse effects, including fatigue, fainting, pain at the venous access site, haematomas, and anaemia.[15,17] Negative experiences such as travel, loss of time, and discomfort by the procedure itself have been reported by between one-third and one-half of patients, and there tends to be a constant rate of decline in the percentage of patients who comply with maintenance therapy.[15,17,18] Not surprisingly, most patients would prefer to take medication rather than undertake phlebotomy.[17]

Some patients with hereditary haemochromatosis are intolerant of phlebotomy because of baseline anaemia, poor venous access (e.g. with severe heart failure), intolerance to phlebotomy, or coexisting haematological disorders. These patients should be considered for iron chelation therapy, such as deferasirox.[3,5] A more expensive alternative to phlebotomy is erythrocytapheresis, or the removal of erythrocytes only rather than whole blood. Here, blood is centrifuged, separating the erythrocytes from plasma. The red cells are removed while the plasma is returned to the treated individual. In addition saline can be infused during the process to minimise the risk of vasovagal symptoms.[7] More than twice as much iron can be removed per session compared with phlebotomy. In addition, side effects are reduced and it's preferred by patients.[17] However, it's likely that venesection will remain the mainstay of treatment because of its efficacy, tolerance, and low cost.[11]

Useful resources for pharmacists and consumers are available from the website of Haemochromatosis Australia: http://haemochromatosis.org.au.

References

1. Axford JS, Bomford AB, Revell P, Watt I, Hamilton ED. A case of haemochromatosis arthritis. Br J Rheumatol 1992;31(8):547–53.
2. Davies MB, Saxby T. Ankle arthropathy of hemochromatosis: a case series and review of the literature. Foot Ankle Int 2006;27(11):902–6.
3. Mohamed M, Phillips J. Hereditary haemochromatosis. BMJ 2016;353:i3128.
4. Emery J, Rose P. Hereditary haemochromatosis: never seen a case? Br J Gen Pract 2001;51(466):347–8.
5. Salgia RJ, Brown K. Diagnosis and management of hereditary hemochromatosis. Clin Liver Dis 2015;19(1):187–98.
6. Bentley P, Bell B, Olynyk J. Therapeutic venesection at the Australian Red Cross Blood Service: impact of the High Ferritin Application on management of hereditary haemochromatosis. Aust Fam Physician 2015;44(8):589–92.
7. Delatycki M, Allen K. Hereditary haemochromatosis. Australian Doctor 2013; Apr 12:25–32.
8. Ogilvie C, Gaffney D, Murray H, Kerry A, Haig C, Spooner R, et al. Improved detection of hereditary haemochromatosis. J Clin Pathol 2015;68(3):218–21.
9. Goot K, Hazeldine S, Bentley P, et al. Elevated serum ferritin – what should GPs know? Aust Fam Physician 2012;41(12):945–9
10. Ekanayake D, Roddick C, Powell LW. Recent advances in hemochromatosis: a 2015 update : a summary of proceedings of the 2014 conference held under the auspices of Hemochromatosis Australia. Hepatol Int 2015;9(2):174–82.
11. Powell LW, Seckington RC, Deugnier Y. Haemochromatosis. Lancet 2016. DOI: 10.1016/S0140-6736(15)01315-X
12. Borch-Iohnsen B, Hauge A. Should iron preparations be available only by prescription?. Tidsskr Nor Laegeforen 2001;121(4):460–2
13. Barbosa FB, Callegari A, Sarinho JC, Lucena J, Casagrande R, de Souza BD. Hemochromatosis simulating rheumatoid arthritis: a case report. Rev Bras Reumatol 2014;54(1):62–4.
14. Genetic haemochromatosis. Therapeutic Guidelines Ltd (eTG March 2016 edition).
15. Adams PC, Barton JC. How I treat hemochromatosis. Blood 2010;116(3):317–25.
16. Hutchinson C, Geissler CA, Powell JJ, Bomford A. Proton pump inhibitors suppress absorption of dietary non-haem iron in hereditary haemochromatosis. Gut 2007;56(9):1291–5.
17. Rombout-Sestrienkova E, Winkens B, Essers BA, Nieman FH, Noord PA, Janssen MC, et al. Erythrocytapheresis versus phlebotomy in the maintenance treatment of HFE hemochromatosis patients: results from a randomized crossover trial. Transfusion 2016;56(1):261–70.
18. Hicken BL, Tucker DC, Barton JC. Patient compliance with phlebotomy therapy for iron overload associated with hemochromatosis. Am J Gastroenterol 2003;98(9):2072–7.

References (Evidence summaries, page 41)

1. Hirsch LE, Pringsheim T. Aripiprazole for autism spectrum disorders (ASD). Cochrane Database of Systematic Reviews 2016, Issue 6. Art. No.: CD009043. DOI: 10.1002/14651858.CD009043.pub3.
2. Kogan MD, Blumberg SJ, Schieve LA, Boyle CA, Perrin JM, Ghandour RM, et al. Prevalence of parent-reported diagnosis of autism spectrum disorders among children in the US, 2007. Pediatrics 2009;124(5):1395–403.
3. Lecavalier L. Behavioral and emotional problems in young people with pervasive developmental disorders: relative prevalence, effects of subject characteristics, and empirical classification. Journal of Autism and Developmental Disorders 2006;36(8):1101–14. [PUBMED: 16897387].
4. Posey DJ, Stigler SKA, Erickson CA, McDougle CJ. Antipsychotics in the treatment of autism. Journal of Clinical Investigation 2008;118(1):6–14.
5. Findling RL, Mankosi R, Timko K, Lears K, McCartney T, McQuade RD, et al. Randomized controlled trial investigating the safety and efficacy of aripiprazole in the long-term maintenance treatment of pediatric patients with irritability associated with autistic disorder. Journal of Clinical Psychiatry 2014;75(1):22–30. [PUBMED: 24502859]

» EVIDENCE SUMMARIES

The effectiveness of Aripiprazole for ASD

BY DR HANAN KHALIL

The prevalence of Autism spectrum disorder (ASD) in Australia is about one in 50 in children under 15 years according to the latest Australian Bureau of Statistics data and the carer's allowance provided by the Australian government. The three main characteristics of Autism spectrum disorder include; compromised social interaction, impaired communication and restricted repetitive and stereotyped patterns of behaviour.[2,3]

Management of ASD includes both pharmacological and non-pharmacological treatments. Non pharmacological treatment rely on enhancing the person's communication and academic learning and behaviour. Examples of interventions used are educational, behavioural and social communication. Pharmacological interventions address the behavioural aspects of ASD. Both typical (first) and second (atypical) generation antipsychotics have been used in clinical practice. Typical antipsychotics are associated with extrapyramidal side effects despite their efficacy in improving learning. Risperidone has also been effective in reducing aggression and irritability but is also associated with adverse events such as sedation and weight gain. Aripiprazole is a relatively newer antipsychotic that has not been widely used in ASD. This evidence summary will summarise the latest on the effectiveness of aripiprazole for ASD.[4,5]

Characteristics of the studies

Randomised controlled trials (RCTs), including both parallel group and cross-over designs, of any duration including children and adults diagnosed with ASD. Diagnosis of ASD includes individuals with autistic disorder, Asperger's disorder and pervasive developmental disorder.

Quality of the research

Studies included in the report had a low risk or an unclear risk of bias. Attrition bias was a major drawback.

Results

The following databases were searched; Cochrane Central Register of Controlled Trials (CENTRAL; 2015, Issue 9; part of The Cochrane Library), Ovid MEDLINE (1946 to Oct Week 1, 2015), Embase (1980 to Week 41, 2015; Ovid), CINAHL Plus (1937 to current; EBSCOhost), PsycINFO (1806 to October Week 1, 2015; Ovid), Cochrane Database of Systematic Reviews (CDSR; 2015, Issue 10; The Cochrane Library), Database of Abstracts of Reviews of Effects (DARE; 2015, Issue 2; The Cochrane Library), Conference Proceedings Citation Index - Science (CPCI-S; 1990 to current; Web of Science), Autism Data (all available years), ZETOC (limited to conference proceedings; all available years), WorldCat (limited to theses and dissertations; all available years), ClinicalTrials.gov (all available years), World Health Organisation International Clinical Trials and Registry Platform (WHO ICTRP; all available years).

The primary outcomes measures include; emotional and behavioural symptoms, , irritability, hyperactivity, sterotypy, Inappropriate speech, lethargy, withdrawal, aggression, clinical improvement as measured by validated clinician- or parent-reported scales and extrapyramidal adverse events.

Secondary outcomes include; obsessive compulsive behaviour, weight gain, metabolic side effects and other side effects.

A total of 579 citations were identified from the search strategy. Only three studies evaluating aripiprazole were included in the review with a total number of 401 participants. Two studies were included in the meta-analysis and the third did not because of its low quality.

Aripiprazole showed a significant improvement in the irritability scale measured by the Aberrant behaviour checklist (ABC); MD =-6.17 (-9.07 to -3.26). There was also an Improvement on both the hyperactivity (MD=-7.93 (-10.98 to 4.88) and the sterotypy scale (MD=-2.26 (3.55 to -1.77).

There was a significant increase in weight gain in children and adolescents taking aripiprazole MD= 1.13 (0.71 to 1.54). Sedation and tremor were also increased.

Relapse rate of symptoms was only reported in one study and was found to be 37% in the aripiprazole group compared to 52% in the placebo group (HR 0.57; 95%CI 0.28 to 1.12).

Implications for practice

There is insufficient evidence addressing the efficacy of aripiprazole for the management of ASD. Only two small studies were found to address the review. Studies focussing on long term effectiveness should provide more evidence for its use. Constant evaluation of the medications is appropriate to determine its continued efficacy.

Conclusion

Aripiprazole is effective in the management of the symptoms of ASD in the short term however longer term use of aripiprazole might be associated with relapses of symptoms.

References located on page 41.

Professor Lisa Nissen – School of Clinical Sciences, Queensland University of Technology
Dr Esther Lau – School of Clinical Sciences, Queensland University of Technology

The purpose of this evidence summary is to provide the best available evidence for the effectiveness of aripiprazole for the management of the symptoms of autism spectrum disorders (ASD). For the full review, please refer to: Hirsch LE, Pringsheim T. Aripiprazole for autism spectrum disorders (ASD). Cochrane Database of Systematic Reviews 2016, Issue 6. Art. No.: CD009043. DOI: 10.1002/14651858.CD009043.pub3.1

CONTENTS

» NEWS

PSA16 HIGHTLIGHTS

Read full coverage of PSA16 – Award winners, the Federal Minister's speech to delegates and more.

» NEWS

HEALTH IN TRANSITION

Pharmacists and pharmacy, like many in the health sector, are in transition, Federal Health Minister Sussan Ley told delegates at PSA16.

» CANBERRA COMMENTARY

LEY SETS SCENE FOR NEXT THREE YEARS

The election count is over the new Senate has been elected and the Turnbull Government is getting down to business. On the surface it certainly appears to be business as usual for the reappointed Health Minister Sussan Ley, *Andrew Daniels* writes.

REGULARS

NATIONAL PRESIDENT SAYS	5
NEWS	6
BE OUR GUEST	22
EARLY CAREER PHARMACIST	26
APSIG	28
AGED CARE	38
EVIDENCE SUMMARIES	41
ETHICAL DILEMMAS	68
BUSINESS	70
PRODUCT	78

AUSTRALIAN
Pharmacist
AUSTRALIA'S MOST CLOSELY READ PHARMACY JOURNAL
SEPTEMBER 2016

CPD: Respiratory
A nagging case of persistent cough

Aged Care
Haemochromatosis: not all joint pain is arthritis

V35#9
SEP 2016
PRINT POST APPROVED
100007595

Pharmaceutical Society of Australia