# Practice Brief

Synthesising research evidence to inform practice



NUMBER 2. Allied health and medical

November 2015

# Creatine monohydrate in Duchenne muscular dystrophy

Duchenne muscular dystrophy (DMD) is one of the most common muscle diseases, affecting around 1 in 3500 boys [1]. It causes fatigue and progressive muscle weakness, eventually resulting in loss of ambulation and respiratory compromise. This practice brief has been developed for paediatricians, paediatric neurologists and other medical and allied health professionals involved in the care of those with DMD. It provides a summary of the available evidence on creatine monohydrate dosing for DMD.

### What current treatments exist for DMD?

Best-practice standards of care for DMD include treatment of muscle weakness with corticosteroids [1, 2]. Studies looking at other medications and supplements have struggled to demonstrate clear benefit in DMD, but a recent Cochrane review and meta-analysis of dietary supplementation in DMD with creatine monohydrate have provided high-quality evidence of improved muscle strength, performance of activities of daily living, and patient/parent perceptions of health in the short- and intermediate-term [3]. No significant side-effects of creatine therapy have been reported [3]. While the benefits of long-term creatine use are less certain, there is ample evidence supporting its short-term safety and potential benefits in DMD.

### What is Creatine?

Creatine is a naturally occurring compound involved in energy production in cells, particularly in tissues with high energy requirements such as brain and skeletal muscle, through ATP formation. It is made endogenously in the liver and kidneys, and absorbed through the diet [4]. In healthy controls, creatine monohydrate supplementation increases muscle force output by approximately 10% [5]. When compared to control subjects, people with neuromuscular disorders have lower skeletal muscle total creatine and phosphocreatine concentrations [3]. There are several theories of how creatine monohydrate supplementation might improve muscle function in patients with neuromuscular disorders, including direct effects on muscle force, effects on energy metabolism and reduction in apoptosis through intracellular calcium effects or by preventing oxidative stress [6].



# How does creatine supplementation help in DMD?

Benefit from creatine supplementation has been measured in different ways, but objective findings include an improvement in time to walk 10 metres (-1.0s with 95% CI - 1.60 to -0.34), and time to climb 4 stairs (-3.4s with 95% CI - 6.18 to -0.56) have been demonstrated in double-blinded placebo-controlled trials [7, 8]. Increases in both muscle strength and lean body mass have also been demonstrated (strength: 8.47%, 95% CI 3.55 to 13.38; lean body mass 0.63kg, 95 CI% 0.02 to 1.25) [3]. Both patients, and parents of patients, report a global assessment of improvement, compared to placebo (RR 4.71 with a 95% CI 2.33 to 8.74), following a short period of treatment with creatine monohydrate. The trials have not looked at effects beyond 6 months, so long-term benefits of creatine monohydrate are unknown.

### When could a patient start creatine monohydrate?

Clear guidelines for when creatine monohydrate should be started have not been established. However, due to the significant improvement in muscle strength and the lack of side-effects or adverse events, dietary supplementation with creatine monohydrate can be considered for patients with DMD at any stage of their illness.

**Partners** 













## What dose is suggested?

A variety of dosing regimens have been used, either with or without loading doses. The rationale for use of a loading dose is that patients with neuromuscular disorders are relatively deplete in intramuscular and plasma creatine at baseline [9]. Use of lower doses can achieve the same levels over time [10]. Doses as low as 0.04g/kg/day have been used, but we recommend a loading dose of 0.2g/kg/day for 1 month, followed by a maintenance dose of 0.1g/kg/day [8]. For ease of use, the tables below round the recommended doses to the nearest 2.5g (= half teaspoon).

Weight (kg)	Loading (1 month)			Maintenance		
	Calculated 0.2g/kg/day	Actual (g/day)	Teaspoons	Calculated 0.1g/kg/day	Actual (g)	Teaspoons
15-25	3 - 5 g	5	1	1.5 - 2.5g	2.5	0.5
26-35	5.2 - 7g	7.5	1.5	2.6 - 3.5g	5	1
36-45	7.2 - 9g	10	2	3.6 - 4.5g	5	1
46-55	9.2 - 11g	10	2	4.6 - 5.5g	7.5	1.5
56-65	11.2 - 13g	12.5	2.5	5.6 - 6.5g	7.5	1.5
66-75	13.2 - 15g	15	3	6.6 - 7.5g	7.5	1.5
76-85	15.2 - 17g	17.5	3.5	7.6 - 8.5g	10	2

### Things to remember

- 1. Creatine is a naturally occurring compound involved in energy metabolism.
- 2. Studies have shown an improvement in strength and performance in the DMD context.
- 3. Creatine is safe and not associated with any known side-effects.

# What support is there for those with DMD and their treating health professionals?

The Royal Children's Hospital, Melbourne and The Children's Hospital at Westmead in Sydney have speciality neuromuscular clinical services.

Patient registries collect data that can be used for studies of DMD disease progression and to recruit patients for clinical trials. The Australian National Duchenne Muscular Dystrophy Registry is available at: <a href="https://nmdregistry.com.au/dmd/">https://nmdregistry.com.au/dmd/</a>

The Muscular Dystrophy Association of Australia can also provide information and support for individuals with DMD and their carers. More information is available on the MDA website: <a href="https://www.mda.org.au">www.mda.org.au</a>

#### **Australasian Neuromuscular Network**

The ANN was founded in 2010 by members of the <u>Centre of Research Excellence in Neuromuscular Disorders</u> in partnership with other neuromuscular specialists, allied health professionals, scientists and patient advocates across Australia and New Zealand.

The ANN exists to enable those working in the field to share knowledge and work together to more effectively research, diagnose, treat and advocate for those with neuromuscular disorders.

# www.ann.org.au

### References

- 1. Bushby, K., et al., *Diagnosis and management of Duchenne muscular dystrophy, part 1: diagnosis, and pharmacological and psychosocial management.*Lancet Neurol, 2010. **9**(1): p. 77-93.
- 2. Bushby, K., et al., *Diagnosis and management of Duchenne muscular dystrophy, part 2: implementation of multidisciplinary care.* Lancet Neurol, 2010. **9**(2): p. 177-89.
- 3. Kley, R.A., M.A. Tarnopolsky, and M. Vorgerd, Creatine for treating muscle disorders. Cochrane Database Syst Rev, 2013. **6**: p. CD004760.
- 4. Wyss, M. and R. Kaddurah-Daouk, *Creatine and creatinine metabolism*. Physiol Rev, 2000. **80**(3): p. 1107-213
- 5. Tarnopolsky, M.A. and D.P. MacLennan, *Creatine monohydrate supplementation enhances high-intensity exercise performance in males and females.*Int J Sport Nutr Exerc Metab, 2000. **10**(4): p. 452-63.
- 6. Gualano, B., et al., *Exploring the therapeutic role of creatine supplementation*. Amino Acids, 2010. **38**(1): p. 31-44.



- 7. Escolar, D.M., et al., CINRG randomized controlled trial of creatine and glutamine in Duchenne muscular dystrophy. Ann Neurol, 2005. **58**(1): p. 151-5.
- 8. Tarnopolsky, M.A., et al., *Creatine monohydrate enhances strength and body composition in Duchenne muscular dystrophy.* Neurology, 2004. **62**(10): p. 1771-7.
- 9. Banerjee, B., et al., Effect of creatine monohydrate in improving cellular energetics and muscle strength in ambulatory Duchenne muscular dystrophy patients: a randomized, placebo-controlled 31P MRS study.

  Magn Reson Imaging, 2010. 28(5): p. 698-707.
- 10. Terjung, R.L., et al., American College of Sports
  Medicine roundtable. The physiological and health
  effects of oral creatine supplementation. Med Sci
  Sports Exerc, 2000. **32**(3): p. 706-17.

## **Author recognition**

Dr Erik Andersen, CSL Neuromuscular Fellow, Royal Children's Hospital, Parkville, Australia.

Dr Loudella Calotes-Castillo, Honorary Neuromuscular Fellow, The Royal Children's Hospital Melbourne, Australia

Professor Monique Ryan, Paediatric Neurologist and Director, Neurology Department, Royal Children's Hospital, Parkville Australia.

**Conflict of interest disclosures:** no conflicts of interest were reported.

# **Funding and support:**

Dr Erik Andersen is supported by the CSL Neuromuscular Fellowship.

Dr Loudella Calotes-Castillo is supported by the International Federation of Clinical Neurophysiologists (IFCN) clinical fellowship grant 2015.

Professor Monique Ryan is supported by NHMRC CRE 1031893.

# About us

The Centre of Research Excellence in Neuromuscular Disorders is a collaboration of neuromuscular experts.

It uses the latest approaches in medicine, science, nursing and allied health to improve diagnosis, facilitate prevention, and transform treatment from compassionate management to effective therapy.

The Centre is funded by the National Health and Medical Research Council.

Centre of Research Excellence in Neuromuscular Disorders Murdoch Childrens Research Institute 50 Flemington Road, Parkville VIC 3052 Australia www.mcri.edu.au