A resourceful approach to novel treatment of congenital myasthenia gravis.

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Objective

Cost effective and patient centred access to a novel treatment for congenital myasthenia gravis (CMG).

Clinical Features

CMG is an autosomal recessive condition that causes a mutation in genes that allow signalling between the nerve and muscle cells[1]. This manifests as impaired skeletal muscle movement and muscle weakness[1]. A large number of cases are caused by mutations in the RAPSN, CHAT, COLQ and DOK7 genes.

JM a 29 kg, 8 year old male presented with DOK7+ CMG. His symptoms included weakness and fatigue, facial palsy, dysarthria, intermittent hemiplegia, dysphagia, and reduced walking distances. Treatment with oral salbutamol[2] for 10 months alleviated his symptoms but weakness and dysarthria remained, that worsened with activity and hot weather. A clinical decision was made to trial ephedrine 10 mg orally three times a day and wean oral salbutamol.

Literature Review

β_2 adrenergic receptor agonists have been shown to be effective in the treatment of CMG symptoms. Oral salbutamol provides progressive improvements and doses are titrated over a 6 month period to a maintenance dose of up to 4 mg twice a day as tolerated[2]. The efficacy of salbutamol is often stable between 6 to 24 months of treatment[2].

Ephedrine has been trialled as an alternative treatment. Treatment with 15–90 mg per day has show improved quantitative myasthenia gravis severity (QMG) score and increased muscle strength in patients with DOK7+ CMG[2,3]. Although ephedrine and salbutamol can be used interchangeably, salbutamol is more frequently used in children due to its safety profile, and ease of access.

Pharmacist Interventions

Due to the proposed dose and the age of the patient an oral solution would ensure easy administration and accurate dose delivery. As a commercial oral solution was not available we looked to compounding an oral solution.

Ephedrine is currently available as a 30 mg tablet or as 30 mg/mL ampoules for parenteral use. The 30 mg tablets are a Special Access Scheme (SAS) medication from the United Kingdom. Compounding an oral liquid product with tablets however, is cost prohibitive and there is a lack of a proven formulation with stability data

The ephedrine 30 mg/mL ampoules for parenteral use are readily available and our institution had recently changed our parenteral product from ephedrine sulphate to ephedrine hydrochloride due to a Health Purchasing Victoria contract change. There was also literature demonstrating the stability of parenteral ephedrine solutions stored at 4-40^{O}C for up to 12 months

It was calculated that using the 30 mg/mL ampoules would reduce cost to the organisation by 80% while improving availability for the patient. As we had remaining stock of ephedrine sulphate ampoules, we opted to formulate an oral solution using these.

Initially the ephedrine sulphate solution was drawn up by our non-aseptic compounding area and filtered into a bottle to prepare a quantity sufficient for two weeks' treatment. A conservative two week opened expiry date was assigned to minimise concerns about sterility given there is no preservative. As the family lived over an hour away from the centre this soon became a difficult arrangement.

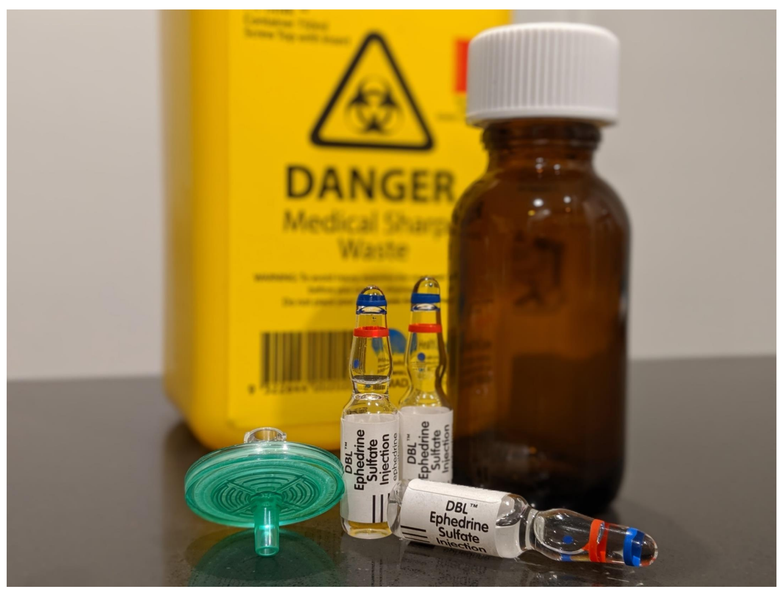
The patient's mother, an intensive care nurse, was educated on the technique of drawing up and filtering the volume of the parental solution. Written instructions were provided, along with all of the necessary equipment and a label for the mother to attach to the bottle once it is prepared.

Outcome

Four weeks after initiation of oral ephedrine J.M has improved in function and in objective measures. He is able to perform his home exercise program and is able to swim 4 lengths of the pool with help, where he had previously only been able to tolerate 1-2 lengths.

Conclusion

This case report highlights a resourceful solution to routine barriers faced in instituting novel therapies, namely cost effectiveness, and logistics. We found this an elegant solution that solved the needs of the patient, the clinicians, and the organisation.



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