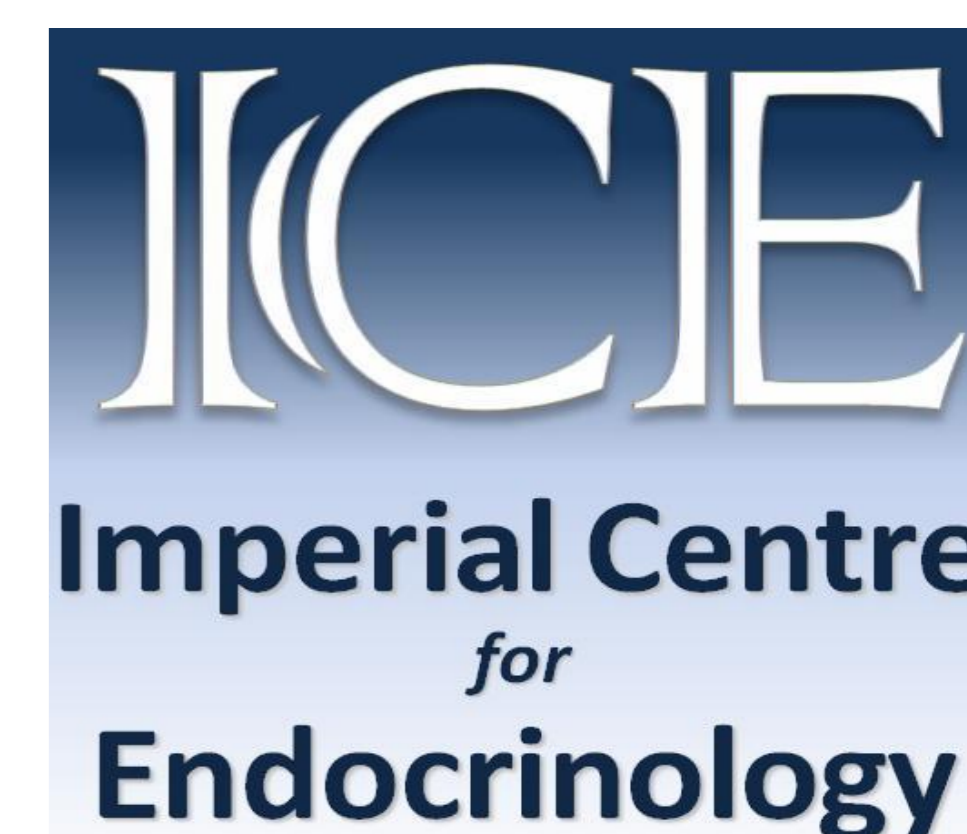




Prednisolone 3mg once daily should be the glucocorticoid replacement for hypopituitarism



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Introduction

Traditionally, hydrocortisone has been the drug of choice for treatment of adrenal insufficiency. Hydrocortisone requires multiple daily dosing, which can be an obstacle to patient compliance. Consequently, this may have a negative impact on a patient's quality of life and may increase the likelihood of an adrenal crisis.

Prednisolone is an alternative glucocorticoid that can be used for steroid replacement therapy¹. It is structurally similar to hydrocortisone with the exception of a double bond between C1 and C2 on the first carbocyclic ring (Figure 1). This double bond gives prednisolone a longer half-life than prednisolone, permitting a one dose per day regimen. We herein present a case highlighting that prednisolone 3mg once daily can be used effectively in hypopituitarism.

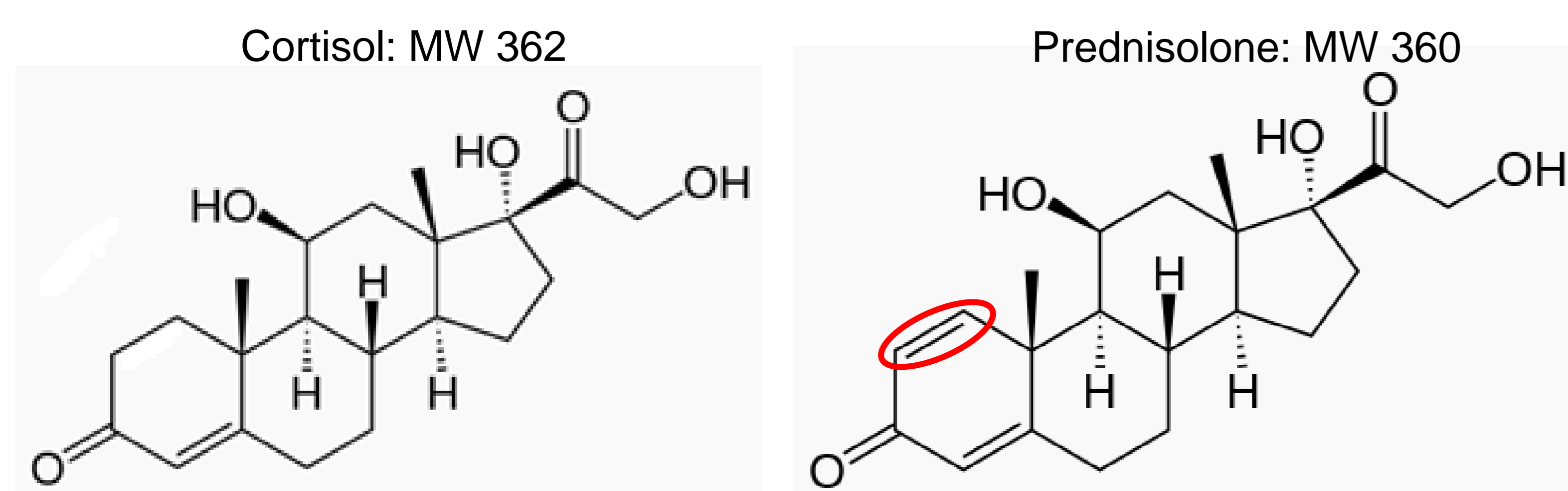


Figure 1: Prednisolone is structurally the same as cortisol except for the C1-C2 double bond (ringed) which increases its binding affinity and its half life.

Case Report

♦ A 33 year-old male bus driver with long standing pemphigus requiring high dose prednisolone, presented with acromegaly in 2001. MRI pituitary revealed a 2x2x0.5cm pituitary adenoma and his GH levels of 14.8-16.4 nmol/L throughout and were not suppressible with glucose. His IGF1 was 191 nmol/L (reference range: 13-64 nmol/L), Prolactin 6,557 mU/L, testosterone 2 nmol/L and cortisol uninterpretable given prednisolone therapy.

♦ Trans-sphenoidal hypophysectomy and external beam radiotherapy to the pituitary were undertaken in 2001 with good response. He was started on levothyroxine and testosterone. Prednisolone for his pemphigus was continued. As he remained on prednisolone, there was no opportunity or reason to check his cortisol reserve, as it was presumed that he would stay on prednisolone for life.

♦ In 2015 he began to respond to alternative therapies for his pemphigus that was being reviewed at another dermatological centre, who were unaware of his hypopituitarism. They began to wean him off the prednisolone using a standard protocol to 5mg, then reducing by 1mg per month.

♦ He remained well even on 3mg, but on 2mg he felt very tired. When the dose was reduced to 1mg daily, he started vomiting and was unable to go to work. Without seeking medical advice he then increased the dose and improved.

References:

(1) Funder JW, Carey RM, Mantero F, et al. The Management of Primary Aldosteronism: Case Detection, Diagnosis, and Treatment: An Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab.* 2016;101(5):1889-916.

(2) Hahner S, Allolio B. Therapeutic management of adrenal insufficiency. *Best Pract Res Clin Endocrinol Metab.* 2009;23(2):167-79.

Investigation and Management

A short synacthen test confirmed a sub-optimal adrenal response (<20, 59, 79 nmol/L)

A prednisolone day curve was performed on 3mg (Table 1 and Figure 2). The target range is 10-20µg/L at 8 hours post prednisolone administration, indicating adequate steroid replacement. The patient remains well on 3mg of prednisolone once daily.

Time	Time of Prednisolone Dose	Time from Prednisolone dose (h)	Cortisol concentration nmol/L	Prednisolone concentration µg/l
09:00	06:00	03:00	53	53
10:00	06:00	04:00	35	42
12:00	06:00	06:00	25	26
14:00	06:00	08:00	24	20
15:45	06:00	09:45	<20	11
16:15	06:00	10:15	59	7
16:45	06:00	10:45	79	6

Table 1: Results of the prednisolone day curve- the 8 hour prednisolone concentration is 20µg/L (within target range)

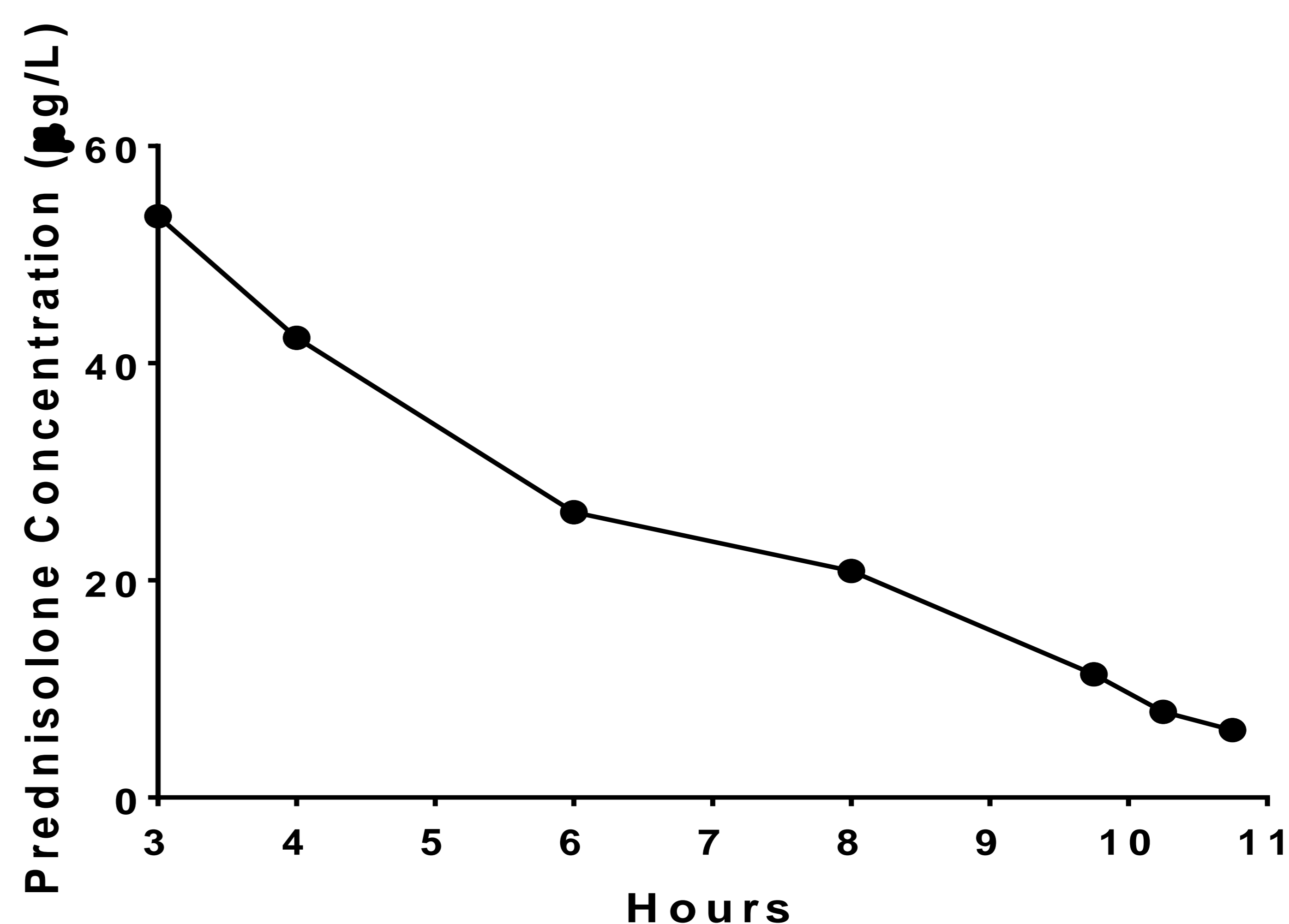


Figure 2: Graph of the prednisolone day curve. Terminal half-life was calculated at 3.01 hours.

Conclusion

Prednisolone 3 – 4 mg daily is an adequate replacement dose and, is given once daily. This is more convenient than hydrocortisone, which is given thrice daily. Previous recommendations have suggested 5mg to 7.5mg daily², but this dose is supraphysiological and may be more likely to cause adverse effects such as osteoporosis, diabetes and cardiovascular disease in the long term.

