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Letter to the Editor Response

Response to Letter to the Editor from Chee et al: “Prevention of Adrenal Crisis: Cortisol Response to Major Stress Compared to Stress Dose Hydrocortisone Delivery”

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Chee et al (1) enquired about whether we had gathered clinical data on blood pressure or intraoperative hemodynamic instability in the patients undergoing elective surgery. However, our study (2) looked at cortisol responses to major stress in patients with otherwise normal adrenal function, including healthy patients undergoing elective surgery as well as unstressed controls, soldiers exposed to

deployment stress, and patients with severe sepsis. Those were compared to serum cortisol concentrations observed after 4 different modes of hydrocortisone administration in patients with primary adrenal insufficiency.

A clinical study in patients with primary adrenal insufficiency aiming to compare the effects of continuous vs intermittent hydrocortisone delivery on hemodynamic

parameters during elective surgery would be very challenging to execute and, in our opinion, only of theoretical benefit. There is no robust clinical evidence that short-term administration of stress dose hydrocortisone for prevention of adrenal crisis has significant adverse effects, while the potentially fatal consequences of glucocorticoid underreplacement in a stressed patient with adrenal insufficiency, in particular when paired with inflammation, are obvious. We think safety should prevail as first and foremost principle when looking after a patient with adrenal insufficiency who is exposed to major stress and we agree with Chee et al (1) that our pharmacokinetic data indicate that continuous hydrocortisone infusion is best suited to achieve prevention of adrenal crisis in this situation.

Chee et al. rightly enquired whether etomidate, an anesthetic agent that inhibits the crucial cortisol biosynthesis enzyme CYP11B1 (3), formed part of the anesthetic regimens that the patients with normal adrenal function received during elective surgery. We apologize that this information was hidden away in the supplementary information (Suppl. Table 1, (4) and can confirm that, indeed, none of the patients received etomidate. Furthermore, acute or chronic intake of any drug known to impact on cortisol biosynthesis or metabolism during the last 6 months preceding the study procedures were exclusion criteria for study participation.

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Additional Information

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References

1. Chee YJ, Dinesh M, Lim SC. Letter to the Editor from Chee et al: "Prevention of Adrenal Crisis: Cortisol Responses to Major Stress Compared to Stress Dose Hydrocortisone Delivery." *J Clin Endocrinol Metabol*. 2020:dga717.
2. Prete A, Taylor AE, Bancos I, et al. Prevention of adrenal crisis: cortisol responses to major stress compared to stress dose hydrocortisone delivery. *J Clin Endocrinol Metab*. 2020;105(7):2262-2274.
3. Fellows IW, Byrne AJ, Allison SP. Adrenocortical suppression with etomidate. *Lancet*. 1983;2(8340):54-55.
4. Prete A, Taylor AE, Bancos I, et al. Data from: prevention of adrenal crisis: cortisol responses to major stress compared to stress dose hydrocortisone delivery in adrenal insufficiency. *medRxiv*. Deposited February 8, 2020. <https://doi.org/10.1101/2020.02.08.20021246>.