Letter

Time-point measurement is critical in hormone characterization

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See related research by Nematy *et al*. in issue 10.1 [http://ccforum.com/content/10/1/R10]

In their recent study 'Changes in appetite related gut hormones in intensive care unit patients: a pilot cohort study' Nematy and colleagues further elucidated intensive care unit (ICU) patients' poor nutritional status. They reported high levels of peptide YY (PYY) and low levels of ghrelin in fasting plasma samples from ICU patients compared with healthy, nonhospitalized controls [1]. While intriguing, this gives only a mere snapshot of PYY/ghrelin physiology in the ICU patient because PYY/ghrelin levels were measured only once per day.

The pattern of plasma ghrelin levels during a 24-hour period in human subjects was previously characterized, in which samples were taken at intervals of 30–60 min throughout the day. Results revealed a preprandial rise and a postprandial decline in ghrelin, characteristic of a natural rhythm related to food intake [2]. PYY secretion was conversely defined as involving a low fasting level followed by a postprandial rise, which peaked 1 hour after food ingestion and was influenced by meal type and meal size [3].

The implications of measuring these gut peptides in fasting individuals only once per day in the morning is an incomplete representation of the physiology of these hormones in the complicated ICU patient. Observing the hormone levels at multiple time points could result in three possible scenarios and could lead to different treatment options. The first hypothesis is a steady baseline state with no rhythmic phenomenon associated with food intake. This possibility, while unlikely, must be considered, since some semblance of normal physiology, albeit inadequate, is usually preserved in the ICU patient.

A second possibility is a rhythmic response in which peaks and troughs reach the same levels as in control subjects while still exhibiting a higher/lower baseline state. This is representative of a suboptimal physiologic response. A rhythmic response may still be present but sufficient hormone levels are not reached, resulting in a less potent stimulus leading to a depressed response. This is the most probable case as it is possible that the hormone response in critically ill patients may be inadequate. This could therefore hold true for PYY/ghrelin responses, in which normal stimuli do not enhance the hormone response.

Finally, these hormones could have baselines that are elevated or depressed relative to controls and could also reach peaks/troughs that are still higher/lower than controls. This would reflect the patients' retention of a normal physiologic rhythm in response to meals even though baseline levels are altered. It is suspected that this final scenario would not be the case as this would yield a normal response to feeding, and possibly a normal nutritional state.

It is therefore essential that preprandial and postprandial measurements be taken to better illustrate this physiology. This would then lend credence to the possibility that the rhythmic release of PYY/ghrelin is more important than baseline levels.

The physiology of ICU patients is a complicated puzzle, one confounded by innumerable variables. To look at a single time point for gut peptide characterization – let alone any hormone – is insufficient and perhaps misleading. With the expansion of time points and sample numbers, consideration of the three aforementioned hypotheses is warranted. It is believed that the new data from these suggestions will help to further unlock the mystery that is the nutritional status of the ICU patient.

ICU = intensive care unit; PYY = peptide YY.

Authors' response

Mohsen Nematy, Jacqui E O'Flynn, Liesl Wandrag, Audrey E Brynes, Stephen J Brett, Michael Patterson, Mohammad A Ghatei, Stephen R Bloom and Gary S Frost

We would like to thank Dr Danna for his interest in our paper. He commented that 'measuring these gut peptides in fasting individuals only once per day in the morning is an incomplete representation of the physiology of these hormones in the complicated ICU patient'. We would therefore like to draw Danna's attention to the following points.

This was a *pilot* study in a group of intensive care patients. The idea of publication was to encourage debate around the role of gut hormones in this area, and to alert colleagues to our early findings. This was the first report in this field. We recognize the weaknesses of measuring one time point for gut hormones, but at the outset of the study we did not even know that interpretable data would be produced.

Previous publications from our group have defined the dynamic relationship between gut hormones, appetite and food intake [4-7]. We are aware that a detailed understanding requires the assessment of response to feeding, often achieved with a test meal. ICU patients tend to be fed continuously, however, thus rendering test meals practically difficult and of arguable significance. What is clear is that our understanding of appetite, food intake and the physiological mechanisms of the regulation of the same are poorly understood, and this is particularly important in recovering patients after discharge. This is a clear avenue for future studies.

We are not claiming to have anything like the whole answer with this pilot study, but suppressed ghrelin and elevated PYY may contribute to a reduced initial motivation to eat. We named this a *pilot* study and subsequently designed two investigations to examine the initial hypothesis and to explore the possible mechanism of observed changes in gut hormones in acute illness. These investigations were performed in elderly patients with a fractured neck of femur and in patients undergoing coronary artery bypass grafting surgery. Results were encouraging and will be submitted shortly for publication.

Competing interests

The authors declare that they have no competing interests.

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