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ENDOCRINE CHANGES THAT OCCUR DURING SURGERY

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Abstract:

Surgical interventions elicit an endocrine reaction that leads to the mobilization of substrates, thereby inducing a shift in metabolism toward catabolism. The observed metabolic modification is distinguished by the presence of a deleterious nitrogen imbalance and the consequential accumulation of sodium and water within the body. The magnitude of this physiological response exhibits a positive linear relationship with the severity of the surgical trauma. The magnitude of this physiological response exhibits a positive linear relationship with the severity of the surgical trauma. Intra-abdominal procedures have been observed to elicit a significantly heightened physiological response compared to body surface surgery. Similarly, cardiac surgery involving cardiopulmonary bypass has been found to induce substantial alterations in hormonal and biochemical profiles. The existing body of literature pertaining to the endocrine and metabolic effects of surgical procedures is extensive and frequently characterized by contradictory findings and conclusions. The primary objective of this concise article isn't to offer an exhaustive examination of the topic, but rather to furnish the essential contextual knowledge that will facilitate the comprehension and analysis of the findings presented in more comprehensive investigations.

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INTRODUCTION:

Catabolic hormones, such as catecholamines and cortisol, are released into the bloodstream in response to surgical stress, whereas anabolic hormones, such as insulin and testosterone, are suppressed. cAMP is a ubiquitous cellular second messenger implicated in hormone signaling pathways connected with P-adrenergic agonist action, and its concentration in the plasma has been shown to be correlated with the severity of surgical procedures. However, the hormone or hormones that cause the increase in plasma cyclic AMP levels have yet to be determined with certainty. However, research done by Nistrup Madsen et al. in 1978 showed a significant correlation between adrenaline changes and cyclic AMP values.

Divergent viewpoints exist regarding the involvement of circulating catecholamines in serving as mediators that regulate the metabolic response to surgical procedures. This phenomenon can be attributed, at least partially, to the recent implementation of radioenzymatic assay techniques. The heightened sensitivity and specificity exhibited by these techniques have consequently rendered the previously utilized fluorimetric methods redundant.
Abdominal surgery elicits a notable augmentation in the plasma adrenaline and noradrenaline levels, while pelvic surgery is linked to a discernible elevation solely in plasma adrenaline levels. It is noteworthy that in both surgical procedures, the most significant alteration in adrenaline levels was observed subsequent to the conclusion of anesthesia. Cryer et al. endeavored to establish the levels in the blood of catecholamines necessary to elicit metabolic and hemodynamic effects through the administration of diverse levels of these agents in individuals with normal physiological conditions. The findings of the study indicate that the levels of noradrenaline in circulation during surgical procedures are improbable to induce any metabolic alterations. However, it is important to note that this does not completely rule out the potential for a localized escalation in sympathetic efferent activity. In contrast, it is noteworthy that plasma adrenaline concentrations observed during surgical procedures exhibit similarities to levels that have been associated with notable alterations in heart rate, blood lactate, blood glycerol, arterial pressure, and plasma glucose.

An alternative approach to evaluating the significance of sympathoadrenal stimulation in the context of surgical procedures involves examining the impacts of a- and p-adrenergic blockade. In a recent study conducted by Cooper et al. (1980), the impact of P-adrenergic blockade utilizing propranolol in the context of pelvic surgery was examined. The researchers observed that this intervention yielded minimal influence on the comprehensive metabolic response. This finding raises questions regarding the significance of the observed elevations in plasma adrenaline as previously reported. The study conducted by Allison, Tomlin, and Chamberlain (1969) aimed to investigate the impact of a substance called phentolamine on glucose tolerance in the context of surgical procedures. However, the researchers did not observe any advantageous outcomes associated with a-adrenergic blockade. The assertion put forth by Butler et al. (1977) regarding the absence of a clearly delineated optimal approach for evaluating the individualized catecholamine reaction to surgical procedures remains unquestionably applicable in contemporary medical research.

LITERATURE REVIEW

The plasma cortisol level exhibits a swift escalation in reaction to surgical activation and persists at levels surpassing the basal levels during a variable duration subsequent to the surgical procedure. The correlation between the extent and duration of this increase demonstrates a strong association with the degree of severity of the surgical trauma. Elevated cortisol synthesis is a consequence of a preceding surge in adrenocorticotropic hormone (ACTH) secretion, albeit the plasma concentration of ACTH surpasses the threshold necessary to elicit a maximal adrenocortical reaction. Furthermore, it is noteworthy to mention that the conventional pituitary-adrenocortical feedback mechanism fails to exhibit its usual efficacy, as both hormones exhibit a simultaneous elevation.

The administration of adrenocorticotropic hormone (ACTH) during surgical procedures does not elicit any additional elevation in plasma cortisol levels. Furthermore, the administration of corticosteroids following the operation does not eliminate the ACTH-induced cortisol response.

The elimination of cortisol metabolites, specifically 17-oxygenic steroids, through the urinary system, experiences an elevation for a duration of 3-4 days subsequent to a surgical procedure. Moreover, if any complications arise during the surgical intervention, the values of these metabolites are further augmented, and the excretion period is extended. The excretion of urinary 17-oxosteroids, primarily originating from adrenal androgens, exhibits minimal fluctuations subsequent to surgical interventions. However, the underlying mechanisms responsible for this phenomenon, specifically whether it is attributed

to modifications in ACTH regulation or alterations in hormonal utilization, remain undisclosed.

The induction of substantial quantities of hydrocortisone or adrenocorticotropic hormone (ACTH) in individuals with normal physiological conditions is correlated with the manifestation of hyperglycemia, protein catabolism, retention of sodium and water, and depletion of potassium. These effects closely resemble several aspects of the metabolic reaction observed during surgical procedures. Nevertheless, it is currently acknowledged that the augmented levels of cortisol observed during surgical procedures are deemed to possess a "permissive" influence rather than serving as a direct causative factor. In the context of abdominal or thoracic surgery, for example, it has been observed that the occurrence of severe hyperglycemia can be significantly reduced when there is a concurrent normal adrenocortical response.

The administration of glucocorticoids in a continuous manner has been observed to induce a state of negative nitrogen balance subsequent to surgical procedures. However, it is worth noting that the impact of steroid replacement therapy on plasma cortisol levels was not explicitly elucidated in the provided information.

The administration of growth hormone elicits a complex interplay of anabolic and catabolic effects. This substance exhibits the capacity to enhance the process of amino acid and protein synthesis, thereby facilitating the production of essential building blocks for cellular growth and repair. Additionally, it possesses lipolytic properties, which contribute to the breakdown of lipids and subsequent release of fatty acids. However, it is important to note that at elevated concentrations, this substance has been observed to induce diabetogenic effects, potentially impacting glucose metabolism. A surge in plasma growth hormone levels has been documented during the surgical procedure; however, this physiological response does not persist during the postoperative phase, even in the context of cardiac surgery. In conditions characterized by a lack of stress, the release of growth hormone is inhibited through the introduction of glucose, while it is enhanced by the presence of hypoglycemia.

The elevation of plasma growth hormone levels observed during surgical procedures can be attributed to the activation of the hypothalamic-anterior pituitary axis. Furthermore, it is noteworthy that the hyperglycemia associated with surgery does not effectively regulate hormone secretion, indicating a malfunction in the usual regulatory feedback mechanisms. The potential involvement of growth hormone in the metabolic alterations observed during surgical procedures appears to be relatively insignificant, as indicated by the fact that hypophysectomies patients under steroid replacement therapy still exhibit a typical metabolic response to trauma.

The present study aims to elucidate the subject matter at hand by adopting a medical research perspective. An elevation in the plasma glucagon concentration is observed in a diverse range of significant surgical interventions. However, it is worth noting that Brandt et al. did not report an augmentation in the circulating levels of glucagon in six patients who underwent abdominal hysterectomy. Additionally, it has been observed that this particular condition can also manifest in conjunction with various other forms of trauma, including but not limited to burns and severe injuries. In a study conducted by Russell, Walker, and Bloom, it was observed that patients who underwent gastric surgery experienced a prolonged state of hyperglucagonemia lasting for a duration of four days. Furthermore, it was noted that this condition was intensified in individuals who encountered post-surgical complications during the aforementioned period. In a recent study conducted by Foster et al., it was demonstrated that plasma glucagon levels had reverted back to their baseline values within a span of 48 hours subsequent to undergoing major abdominal surgery.

Numerous factors have been found to be implicated in the regulation of glucagon secretion, yet the specific determinants that trigger the release of glucagon during surgical procedures remain unidentified. Furthermore, the extent to which hyperglucagonemia contributes to the mobilization of substrates during surgery remains uncertain. Unger et al. (1962) demonstrated that the induction of hyperglycemia in a non-stressful manner resulted in a reduction in plasma glucagon levels. This regulatory mechanism, however, does not appear to be functional in hyperglucagonemic patients undergoing surgery, where an elevation in blood glucose levels is observed.

Circulating concentrations of insulin exhibit a notable decline during the perioperative period, as well as in the immediate aftermath of surgical procedures, despite the presence of concurrent hyperglycemia. However, it is noteworthy that these concentrations subsequently recover to either normal or elevated levels in the days that ensue post-surgery. The intricate interplay between glucagon and insulin

secretion is a subject of great complexity. Following an operation, the initial response is characterized by a decrease in plasma insulin levels, accompanied by an increase in plasma glucagon levels. However, it is noteworthy that in the subsequent period post-operation, both hormones exhibit an elevation in concentration. According to Allison (1971), the primary cause of the reduction in insulin secretion is attributed to the prevailing supremacy of a-adrenergic sympathetic activity. The present study reveals a noteworthy discovery, wherein patients who underwent surgical procedures and were administered p^adrenergic blockade exhibited notably reduced levels of insulin. This finding provides substantial support to the aforementioned claim.

Considerable attention has been devoted to the examination of thyroid function during the perioperative period. Numerous variables possess the capacity to exert an impact on the evaluation of alterations in the levels of circulating thyroid hormones. These variables encompass the selection of an appropriate anesthetic agent, the techniques employed for hormone estimation, and modifications in thyroid binding proteins.

The present study elucidates the phenomenon of decreased plasma triiodothyronine (T3) amounts during the perioperative period, which persists in a diminished state post-surgery. Conversely, it is noteworthy to mention that the plasma thyroxine (T4) level remains unaltered throughout this surgical trajectory. The observed phenomenon is plausibly attributed to an alteration in the peripheral de-iodination of thyroxine (T4), leading to an elevated production of reverse triiodothyronine (rT3), which is known to possess diminished biological activity. The precise implications of the deficiency in circulating triiodothyronine (T3) levels among surgical patients remain largely unexplored, lacking comprehensive understanding within the medical research community.

The present study elucidates the phenomenon of plasma testosterone reduction observed during surgical procedures, which is subsequently exacerbated during the postoperative period. Notably, the levels of testosterone remain below the established normal range for a duration spanning between 4 to 9 days. Surgical intervention elicits a notable elevation in the levels of circulating prolactin, a hormone associated with lactation and reproductive function, even in the context of laparoscopic procedures. The precise mechanisms underlying the hormonal changes and subsequent metabolic consequences remain to be elucidated. Based on the aforementioned description, it becomes evident that the current state of knowledge does not allow for the definitive identification of a singular hormone accountable for a precise metabolic alteration. The observed metabolic response to surgical procedures is hypothesized to stem from heightened activation of various catabolic hormones, concomitant with a decline in the pivotal anabolic hormone, insulin.

Metabolic Changes

The body's reaction to surgical trauma is characterized by a significant augmentation in protein degradation. The urinary elimination of nitrogen exhibits an elevated level for a duration of 4-5 days subsequent to abdominal surgery. It has been observed that an individual with an average physique may experience a reduction of 0.5 kg in lean tissue on a daily basis following a significant abdominal procedure (Johnston, 1964). The temporal extent and amplitude of this nitrogen depletion are intricately linked to the extent of the surgical procedure and the nutritional state of the individual under examination. Patients who are adequately nourished exhibit an elevated level of nitrogen excretion. It has been postulated that debilitated patients, who typically exhibit protein conservation, experience significant nitrogen loss, which is indicative of an unfavorable prognosis.

An initial decline in the process of protein synthesis within the muscular tissue is observed, subsequently succeeded by an elevation in the breakdown of proteins, also known as protein catabolism. The primary consequence of protein degradation manifests in the liberation of specific amino acids, with a notable emphasis on alanine, which subsequently undergoes transportation to the liver to facilitate the process of gluconeogenesis. The process of deamination occurring within the hepatic system in response to the heightened influx of amino acids from the peripheral regions results in the distinctive augmentation of urea synthesis and subsequent elimination. In a seminal study conducted by Elia et al. (1980), it was observed that there was a notable enhancement in the absorption of intravenously administered alanine in surgical patients. The authors postulated that this phenomenon could potentially signify an upregulation in hepatic gluconeogenesis.

Therefore, during the postoperative phase, when hepatic glycogen reserves have been exhausted, the process of muscle protein degradation guarantees the sustenance of glucose provision. The intricate regulation of muscle proteolysis and gluconeogenesis is subject to hormonal control, with notable

contributions from elevated levels of glucagon and cortisol in conjunction with the suppression of insulin. These factors play a significant role in this physiological process.

The observed elevation in blood glucose levels during surgical procedures exhibits a positive correlation with the extent of the surgical injury. Elevated glucose levels exceeding 10 mmol per liter are frequently observed in the context of cardiac surgery and have the potential to induce glycosuria. The intricate nature of the hyperglycaemic response stems from the diminished efficacy of the typical neurohormonal control over blood glucose levels. The inhibition of insulin secretion serves as an initial reaction to surgical stimulation, prompting investigations into the utilization of glucose during the perioperative phase. In a study conducted by Aarimaa et al. (1974), the authors employed serial intravenous glucose tolerance tests to investigate the impact of surgery on glucose utilization. The results revealed a notable decrease in glucose utilization during the surgical procedure. Furthermore, this reduction persisted even after the operation, when insulin levels had returned to their baseline values, thus indicating the existence of insulin resistance.

Activation of Response during Surgery

Efferent neural stimuli originating from the site of injury serve as the catalyst for the initiation of endocrine and physiological alterations that manifest in reaction to surgical intervention. In a seminal study conducted by Hume and Egdahl in 1959, it was conclusively established that the adrenocortical response elicited by a hind limb injury in animals can be effectively nullified through various interventions. Specifically, the researchers demonstrated that peripheral nerve section, transection of the spinal cord just above the site of injury, or sectioning through the medulla oblongata all resulted in the complete abolition of said response. These findings shed light on the intricate mechanisms underlying the adrenocortical response to injury, thereby contributing to our understanding of the physiological processes involved in such scenarios. In the study conducted by Wilmore et al. (1976), the researchers examined the potential impact of alterations in afferent neuronal input on the hypothalamic area. They hypothesized that such changes could disrupt central homeostatic mechanisms, leading to subsequent modifications in the functioning of the pituitary gland and the autonomic nervous system. The initiation of the response is reliant on both autonomic and somatic afferent fiber activity, as analgesia alone does not impede the occurrence of hormonal changes.

Historically, there has been substantial conjecture surrounding the presence of "wound hormones" that potentially contribute to the initiation of endocrine and metabolic reactions in response to traumatic events. The potential identification of prostaglandins, acetylcholine, serotonin, and diverse amino acids as plausible "wound hormones" has been proposed due to their observed discharge from the afflicted tissues. The concept in question was not substantiated by the classical experiments conducted by Egdahl in 1959, which involved the utilization of an isolated dog leg preparation. Nevertheless, Wilmore et al. (1976) contend that these substances may still exert a significant role in the context of burn injuries and severe trauma. Alongside the augmentation in afferent neuronal activity originating from the surgical site, a multitude of additional physiological disruptions play a role in the comprehensive hormonal reaction.

The impact of hemorrhage is widely recognized within the field of anesthesiology. However, it is worth noting that partial starvation and dehydration, which are frequently observed in surgical patients, may also play a significant role in intensifying endocrine alterations. The presence of heightened anxiety and fear has been observed to have a direct impact on the secretion of cortisol. It has been established that the levels of cortisol prior to a surgical procedure can be influenced by factors such as premedication administration and the quality of sleep experienced during the preceding night. During the postoperative period, various factors, including but not limited to infection, extended immobilization, hypoxemia, and disruptions in circadian rhythms, collectively contribute to the alterations observed in endocrine function.

Surgery-Induced Changes in the Neuroendocrine Response

There are two potential approaches that can be employed for this endeavor. The initial approach focuses on mitigating or eliminating the endocrine and metabolic alterations that arise as a consequence of surgical stimulation. This objective can be accomplished through the implementation of afferent neuronal blockade utilizing local analgesics, such as extradural or spinal analgesia. Alternatively, the reduction of hypothalamic function can be achieved by administering substantial doses of opiates, as demonstrated by George et al. in 1974. The subsequent methodology involves the endeavor to mitigate the ramifications of the modified endocrine milieu subsequent to its manifestation. The aforementioned procedure is typically conducted

through the administration of suitable substrates, either parenterally or enterally. Additional methodologies encompass the administration of anabolic hormones, with a particular emphasis on insulin, through the process of infusion. Furthermore, the patient's care is facilitated within a thermoneutral environment, which aids in maintaining a stable body temperature conducive to optimal recovery.

Extradural analgesia, whether administered in conjunction with or without general anesthesia, has been observed to effectively mitigate or eliminate the typical elevation in blood sugar concentrations and plasma cortisol levels, as well as growth hormone, cyclic AMP values, and adrenaline commonly encountered during pelvic surgical procedures. The complete eradication of the growth hormone reaction to surgical procedures performed on the pelvic region can solely be accomplished through the implementation of an extradural block that spans from the fourth thoracic vertebra (T4) to the fifth sacral vertebra (S5). However, it is important to note that this approach does not prove efficacious in preventing the suppression of insulin levels. Extradural analgesia is hypothesized to potentially serve as a mechanism for delaying the occurrence of hyperglycemic and adrenocortical responses until the postoperative period. Cooper et al. have raised inquiries regarding the desirability of implementing an expansive blockade for pelvic surgery.

In a seminal study conducted by Bromage, Shibata, and Willoughby in 1971, the researchers investigated the impact of extradural pain relief on blood sugar and plasma cortisol levels in the context of thoracic and abdominal surgical procedures. Despite the provision of sufficient analgesia, including the administration of nerve blocks up to the level of the sixth cervical vertebra if deemed necessary, there has been no observed decrease in the cortisol response. However, it is noteworthy that the presence of hyperglycemia was effectively eliminated. According to Bromage et al., it has been postulated that the failure to suppress adrenocortical alterations can be attributed to the activation of vagal afferent fibers throughout surgical procedures. If the aforementioned interpretation is deemed accurate, it follows that regional analgesic techniques would solely hold significance in the eradication of the endocrine reaction to surgical procedures involving the pelvic region and extremities.

Extradural analgesia, in addition to its impact on the metabolic response, confers numerous advantages and is deemed a viable procedure in clinical settings. However, it is imperative to exercise caution when employing high-dose opiate regimens, as they are appropriate solely for meticulously chosen patients who are under close supervision. This precautionary measure is necessary due to the potential complications of postoperative respiratory depression. The present study explores the efficacy of various interventions aimed at suppressing the endocrine reaction triggered by surgical procedures. Specifically, both localized analgesic techniques and high-dose opiate anesthesia are investigated. The findings of this investigation shed light on the intricate nature of the connections between hormonal activity and the mobilization of substrates. It is of considerable significance to highlight that, across all investigations whereby the hormone response to surgical procedures was effectively nullified, no adverse consequences occurred in the respective patient cohorts. This finding implies that the administration of high-dose steroid supplementation to individuals undergoing prolonged steroid therapy may not be warranted.

Recent advancements in parenteral and enteral nutrition methodologies have facilitated the provision of robust nutritional assistance, thereby surpassing or potentially surpassing the caloric and nitrogen demands of patients experiencing catabolism. Adequate caloric and nitrogen consumption has the potential to mitigate protein depletion and potentially enhance the likelihood of survival in individuals experiencing severe catabolism. It is imperative to acknowledge that the administration of certain parenteral nutrition solutions elicits the stimulation of hormone secretion, thereby potentially intensifying postoperative endocrine alterations. Following major abdominal surgery, the infusion of amino acid substances has been observed to result in an increased secretion of glucagon.

Hormone Supplementation

The identification of the phenomenon observed in surgical patients, characterized by the initial suppression of insulin levels followed by the development of insulin resistance, has led to the implementation of insulin infusions as a therapeutic approach to mitigate catabolism. In the study conducted by Hinton et al. (1971), it was observed that the administration of a combination of glucose, insulin, and potassium yielded positive outcomes in mitigating the excessive degradation of proteins in burn patients. However, the study did not discern whether the observed effects were solely attributable to the specific action of insulin or merely a consequence of the provision of additional caloric intake. Woolfson, Allison, and Heatley (1979) successfully reconciled this discord by elucidating

the protein-sparing phenomenon of insulin in individuals experiencing catabolic conditions. However, the authors were regrettably unable to elucidate the intricate mechanism underlying the action of insulin.

In a study conducted by Wilmore et al. (1974), it was observed that the infusion of 10 international units of growth hormone via intramuscular injection on a daily basis resulted in an improvement in the nitrogen levels of patients with severe burns. These patients were being maintained on an adequate intake of calories and nitrogen. The administration of growth hormone supplementation elicited a notable augmentation in insulin secretion, likely attributing to the observed advantageous outcomes.

CONCLUSION:

The neuroendocrine reaction to trauma is believed to have undergone evolutionary adaptations in order to enhance survival in a less advanced ecological setting, by facilitating the provision of suitable substrates necessary for the sustenance of essential organ function.

Nevertheless, in contemporary anesthetic and surgical procedures, wherein the prevention or prompt treatment of severe physiological disruptions is ensured, alongside the provision of readily accessible substrates, the discernible advantages of this particular response have become obsolete. The primary objective moving forward should prioritize the implementation of effective measures to ensure the secure mitigation of surgically-induced, unfavorable alterations in hormonal and metabolic profiles. We contend that the need to justify the endeavor of mitigating said alterations through diverse anesthetic methodologies is no longer warranted. Instead, we must inquire as to the rationale behind allowing these effects to remain unmodified.

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