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Research Article

**AN EVOCATIVE RESEARCH TO ASSESS THE MINIMUM  
AMOUNT INDICATIVE EFFICACY OF SYNACTHEN BY  
USING 250 µg OF SYNACTHEN**<sup>1</sup>Dr Sumble Shager, <sup>1</sup>Dr Ayesha Zahoor, <sup>2</sup>Shabeeh e Zahra  
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**Abstract:**

**Objective:** For assessment of indicative efficiency of the minimum amount 1 µg synacthen trial was performed utilizing the recommended amount of 250 µg synacthen was set as standard.

**Patients and Methods:** This detailed evocative research was carried out at Services Hospital, Lahore from February 2017 to March 2018. The survey comprised of about 30 victims suffering from adrenal inadequacy, with a similar number and developmental stage were compared with fit males and females as checks. Related background and overall checkup data were noted. The minute synacthen examination was carried out among 0800-1000 h through the utilization of ACTH drug of 1 µg & 250 µg with a duration of three days in all the victims and checks. 3 type of blood samples were taken regarding cortisol (consisting of the basal, half hour & 1 hour after 1/M ACTH injection).

**Results:** Utilizing 250 µg minute synacthen examination as average, 1 µg minute synacthen examination had 100% compassion, 72% specificity, 71% constructive forecast and 100% destructive forecast value with 83% efficacy.

**Conclusion:** Minute quantity of 1 µg short synacthen examination is really delicate as the quantity of 250 µg short synacthen examination despite having low efficacy in a verdict of adrenal non-adequacy.

**Keywords:** addison 's disease, Delicate, Adequacy, Constructive and Destructive Forecast Values.

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**INTRODUCTION:**

Adrenal inadequacy is an infrequent clinical defect that is caused due to basal scarcity or trauma extent of plasma cortisol. Adrenal inadequacy might deceive the observer making its diagnosis hard. Therefore, its appropriate recognition is of vital importance in order to timely provide cure to victims [2]. Through adequate recognition and treatment by adrenocortical hormone exchange, a patient can resume healthy living [2]. If recognized, detailed recognition can be inveterate through lab analysis of adrenocortical performance via short synacthen examination, insulin acceptance examination and metyrapone evaluation. Conventional orientation examination to evaluate hypothalamic-pituitary adrenal axis for assessment of cortisol reaction towards insulin is comprised of hypoglycemia [3]. This type of examination has been found difficult for the victims, risk-taking, source exhaustive and cautious for victims suffering from ischemic heart disorder as well as epilepsy.[4] The minute synacthen examination was carried out due to its ease of doing and for analysis of efficient remains of adrenals. Huge substantial relation among minute synacthen examination and insulin acceptance examination was observed in studies [5 – 7]. A minute synacthen examination can be utilized for major and minor adrenal inadequacy.

The recommended quantity of synacthen examination uses 250 µg ACTH amount to evaluate cortisol reaction towards the adrenal cortex. Various researchers modify this quantity and found out that cortisol reaction to 1 µg ACTH is equal to the results having 250 µg ACTH utilization in individuals [8, 9]. It is found easier to believe that supraphysiological quantity of 250 µg utilized as recommended amount examination has an influence on moderate atrophied adrenals and gives a misleading passable cortisol reaction. 1 µg ACTH is beneficial due to suitable price, protective nature as well as ignorance towards victim's huge quantity consumption of ACTH as

recommended in synacthen examination. That is the reason behind the strategical application of this survey for assessment of effective 1 µg ACTH.

**PATIENTS AND METHODS:**

This detailed evocative research was carried out at Services Hospital, Lahore from February 2017 to March 2018. Victims suffering from faintness, restlessness, spot formation on skin and mucous membranes, gradual weightlessness and hypotension were considered. Physically fit individuals were included in the survey as checks. Patients recognized with Addison's disorder, receiving medicine for endocrinal diseases like thyroid issues and women that are expecting child were not included in the survey. 0800-1000 hours are required to do minute synacthen examination. A congenital intravenous cannula was inserted in forearm and fluid to perform basal cortisol was drawn. All individuals including checks and victims were treated with 1 µg and 250 µg minute synacthen examination. Followed by a time interval of three days. After ½ and 1 hour from ACTH insertion, 2 more trials were taken regarding serum cortisol. Trial vials were tagged appropriately, and these were shifted into a dispensation section in ½ hour to permit lumping at 25°C. Centrifuge the vials at 2000-3000 g for 10-15 minutes to obtain serum. It was kept at 4°C to assess cortisol into patches. Through the utilization of Chemiluminescence process serum cortisol was evaluated.

**RESULTS:**

The survey includes 30 victims of Addison's disorder which comprises of 14(47%) men and 16(53%) women with developmental stage at 2-62 years having an average of 32 years and body mass between 7-75 kg with the regular value of 41kg. 250 µg ACTH lead to huge cortisol augmentation in case of suspicious Addison's disorder victims at ½ and 1 hour from baseline ( $p < 0.05$ ) while 1 µg leads to substantial cortisol increase within ½ hour ( $p < 0.05$ ).

**Table – I:** Increment of cortisol from baseline after 250 microgram ACTH stimulation test and 1 microgram ACTH stimulation in suspected Addison's disease patients.

	Basal cortisol mean (SD)	Cortisol after 30 min mean (SD)	Cortisol after 60 min mean (SD)
250 microgram ACTH stimulation test	202 (67)	349 (86)*	419 (96)*
1 microgram ACTH stimulation test	210 (70)	332 (72)*	293 (40)

p-value is significant at less than 0.05 as compared to baseline.

Checks category is comprised of fourteen men and sixteen women with developmental stages of 6-62 years having an average of 34 and body mass of 22-82 kg having a regular value of 52. Checks having recommended amount of 250 µg ACTH incentive examination leads to huge incentive adrenal glands in

order to form substantial cortisol augmentation at ½-1 hour. Meanwhile, enough adrenal motivation was performed by 1 µg ACTH that leads to substantial cortisol augmentation.

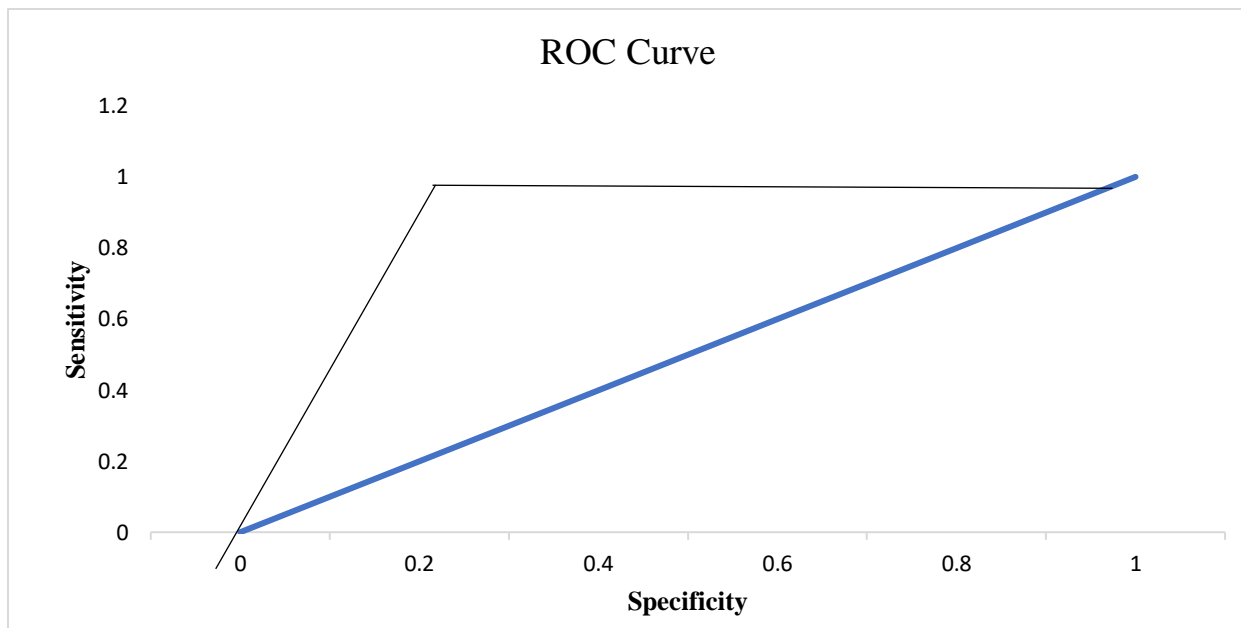
**Table – II:** Increments of cortisol from baseline after 250 microgram ACTH stimulation and 1 microgram ACTH stimulation tests in controls.

	Cortisol basal mean (SD)	Cortisol after 30 min mean (SD)	Cortisol after 60 min mean (SD)
250 microgram ACTH stimulation test	349 (53)	682 (69)*	793 (78)*
1 microgram ACTH stimulation test	348 (61)	598 (60)*	502 (59)*

p-value is significant at less than 0.05 as compared to baseline.

The reaction of 13 victims out of 30 showed disappointment regarding 1&250 µg ACTH amount of minute synacthen examination (accurate +ve).12 victims responded cortisol augmentation more than 200nmol/L in response to 1 and 250 µg ACTH (inaccurate –ve). Some victims (about 5) reacted towards 250 µg ACTH but showed no reaction towards 1 µg (inaccurate +ve). None of inaccurate –ve examination outcome was reported in victims that reacted towards 1 µg ACTH but not towards 250 µg.

Setting 250 µg ACTH incentive examination as a recommendation, the severity of minute quantity of 1 µg synacthen examination i.e., % of victims were accurately determined as hundred percent, while the precision of minute quantity 1µg synacthen examination i.e., the value of healthy population was recorded as 71%.



Diagonal segments are produced by ties.

Sensitivity 100%  
Specificity 72%

**Figure:** ROC Curve for 1 microgram ACTH test in suspected cases of Addison's disease

Optimistic forecast rate of 1 µg minute synacthen examination i.e., probability that an individual having constructive outcomes would suffer from infection was seventy-two percent. Destructive forecast rate of 1 µg minute synacthen examination i.e., chances of the population having false outcome have no chances of getting an infection of about 100%. Precision i.e., the quantity of all the examined individuals accurately recognized through 1µg minute synacthen examination was eighty-three percent.

### DISCUSSION:

Absence of clinical distrust is the leading cause in recognition of major adrenal inadequacy as this state is sporadic and the symbols & indications are not adequate [10]. Value of adrenal inadequacy leads to subclinical hypoadrenalism as well as major adrenal inadequacy. Consideration of subclinical hypoadrenalism is done through the usual cortisol reaction towards ACTH as well as selected basal ACTH value. On the other hand, major adrenal inadequacy is considered as ignorable cortisol reaction towards artificial ACTH insertion [11]. Instead of augmented guarding glucocorticoids & mineralocorticoids exchange treatment, fitness regarding values of life in adrenal inadequacy has less influence than former [12]. If found doubtful, the descriptive recognition could be established through lab analysis of adrenocortical performance via minute synacthen examination, insulin acceptance as well as metyrapone [13]. Guideline to evaluate hypothalamic-pituitary-adrenal axis is to determine cortisol reaction towards insulin persuaded hypoglycemia regardless of its unhappy, source exhaustive examination leading to various problems in victims of older age having heart disorders, epilepsy or hypothyroidism despite any care that needs strict clinical observation [13].

The recommendation was made to utilize minute synacthen examination despite insulin acceptance in order to assess hypothalamic-pituitary-adrenal axis having the formation of various destructive outcomes concerning major penalties [14]. Timely recognition of major adrenocortical inadequacy has a vital function in hypothalamic-pituitary infections. Functional application of 1µg ACTH enhances fragility of synacthen examination. This was observed with individuals of minute adrenal inadequacy which permits evaluation of pituitary-adrenal conquest after huge cure through glucocorticoids [15]. The rationality of less quantity of about 1 µg minute synacthen examination is noted in order to determine minor adrenocortical inadequacy [16]. 1µg is regarded as the minimal amount to determine adrenal gland performance, this examination is not recommended

because of causing various troubles regarding non-specific stations lacking sufficient working drill of members in the intravenous insertion of a small dosage of medicine.

Current survey assures the management of 1µg ACTH has the capacity to persuade persistent cortisol increase in physically fit individuals. Results for compassion regarding 1µg minute synacthen examination were 100% (-ve forecast ratio) and 72% (+ve forecast ratio) in relation to 250 µg minute synacthen examination as the average for recognition of Addison's disease having 83% precision.

Outcomes of 1µg minute synacthen trial leading to cortisol reaction maximum at 500 nmol/l and augmentation of 200 nmol were inveterate by a number of research projects including Dickstein et al[9], Tordjman et al[15] and Weintrob N et al [17]. Suitability, harmlessness and cheapness of 1µg ACTH were guaranteed by Ambrosi et al. in order to determine early hypothalamic-pituitary adrenal performance [18].

Determination of saliva cortisol reaction towards 25 µg corticotrophin inserted in deltoid muscle was narrated by Contreras et al that leads to a beneficial clinical approach for determination of hypoadrenal conditions [19]. Maximum cortisol reaction was obtained at 1 hour in checks due to 250µg minute synacthen examination in terms of distrusted Addison's disorder based on the continual reaction towards a huge quantity of ACTH. There is a correlation existing among the survey held at Aga Khan University clinic at Karachi performed by Mansoor et al. according to him 1-hour cortisol treatment at 250 µg minute synacthen examination was consistent to recognize usual individuals and to extract adrenal inadequacy [20]. Highest cortisol rate can be achieved at ½ hour with 1 µg minute synacthen examination in checks as well as sustained Addison's disorder victims based on low life span reaction of a minute quantity of ACTH. Beneficial aspects of little quantity of 1 µg minute synacthen examination include cheapness and usefulness for the victim by imperilling them towards the maximum quantity of artificial ACTH.

### CONCLUSION:

The survey showed that less quantity of 1µg minute synacthen examination is delicate towards the recommended quantity of 250µg minute synacthen trial having poor precision for recognition of adrenal inadequacy.

**REFERENCES:**

1. Gold PW, Kling MA, Khan I, Calabrese JR, Kalogeras K, Post RM et al. Corticotropin-releasing hormone: relevance to normal physiology and to the pathophysiology and differential diagnosis of hypercortisolism and adrenal insufficiency 1987;43:183-200.
2. Greenwood FC, Landon J, Stamp TCB. The plasma sugar, free fatty acid, cortisol and growth hormone response to insulin in control subjects. *J Clin Invest* 1996; 45:429-36.
3. Hurel SG, Thompson CJ, Watson MJ, Harris NM, Baylis PH, Kendal-Taylor P. Audit of short synacthen and insulin stress test in the assessment of the hypothalamo-pituitary-adrenal axis. *Clin Endocrinol Oxf* 1996; 44:141-46.
4. Lindholm J, Kehlet H. Re-evaluation of the clinical value of the 30 min ACTH test in assessing the hypothalamic-pituitary-adrenocortical function. *Clin Endocrinol Oxf* 1987; 26:53-9.
5. Hagg E, Hassel U, Lithner F, Asplund K. Hypothalamopituitary-adrenal function: can a short ACTH test replace insulin tolerance test? *Lakaridningen* 1981. 78:4027-30.
6. Kane KF, Emery P, Sheppard MC, Stewart PM. Assessing the hypothalamic-pituitary-adrenal axis in patients on long-term glucocorticoids therapy: the short synacthen test vs. the insulin tolerance test. *Q J Med* 1995; 88:263-7.
7. Crowley S, Hindmarsh PC, Honour JW, Brook CGD. Reproducibility of the cortisol response to stimulation with a low dose of ACTH: the effect of basal cortisol levels and comparison of low-dose with high dose secretory dynamics. *J Endocrinol* 1992; 136:167-72.
8. Daidoh H, Morita H, Mune T. Responses of plasma adrenocortical steroids to low dose ACTH in normal subjects. *Clin Endocrinol Oxf* 1995; 43:311-5.
9. Dickstein G, Shechner C, Nicholson WE, Rosner I, Shenorr Z, Adawai F et al. Adrenocorticotrophin stimulation test: effects of basal cortisol level, time of day, and suggested new sensitive low dose test. *J Clin Endocrinol Metab* 1991; 72:773-8.
10. Burke CW. Adrenocortical insufficiency. *Clin Endocrinol Metab* 1985; 14:947-76.
11. Grinspoon SK, Biller BM. Laboratory assessment of adrenal insufficiency. *J Clin Endocrinol Metab* 1994; 79:923-31.
12. Arlt W, Allolio B. Division of Medical Sciences, UNIVERSITY OF Birmingham, UK. *Lancet*.2003;31;361(9372):1881-93.
13. Clayton RN. Short synacthen test versus insulin stress test for assessment of the hypothalamopituitary-adrenal axis: a controversy revisited. *J Clin Endocrinol*; 44:147-9.
14. Schlaghecke R, Kornely E, Santen RT, Ridderskamp P. The effect of long-term glucocorticoid therapy on pituitary-adrenal responses to exogenous corticotropin-releasing hormone. *N Engl J Med* 1992; 326:226-30.
15. Tordjman K, Jaffe A, Grazas N, apter C, Stern N. The role of the low dose 1 µg adrenocorticotropin test in the evaluation of patients with pituitary disease. *J Clin Endocrinol Metab* 1995; 80:1301-5.
16. Pura M, Kreze Jr A, Kentos P, Vanuga P. The low dose 1 short synacthen test for primary adrenocortical insufficiency. Defining the normal cortisol response add a report on first patients with Addison's disease confirmed with low dose test. *Exp Clin Endocrinol Diabetes*.2009;8.
17. Weintrob N, Sprecher E, Josefsberg Z, Weiningger C, Aurbach-Klipper Y, Lazard D et al. Standard and low-dose short adrenocorticotropin test compared with insulin-induced hypoglycemia for assessment of the hypothalamic-pituitary-adrenal axis in children with idiopathic multiple pituitary hormone deficiencies. *J Clin Endo and Metab* 1998; 83:88-92.
18. Ambrosi B, Barbeta L, Tiziana Re et al. The one microgram adrenocorticotropin test in the assessment of the hypothalamic-pituitary-adrenal function. *European Journal of Endocrinology* 1998; 139:575-79.
19. Contreras LN, Arregger AL, Persi GG, Gonzalez NS, Cardoso EM. A new less intensive and more informative low dose ACTH test. Salivary steroids in response to corticotrophin. *Clin Endocrinol Oxf* 2004;61(6):675-82.
20. Mansoor S, Islam N, Siddiqui I, Jabbar A. Sixty-minute post-Synacthen serum cortisol level: a reliable and cost-effective screening test for excluding adrenal insufficiency compared to the conventional short synacthen test. *Singapore Med J* 2007; 48:6:519-23.