Original Article

Clinical Utility of 30- and 60-min Serum Cortisol Values in Cosyntropin Stimulation Test for Diagnosis of Adrenal Insufficiency

Shabnam Dildar[1], Aysha Habib Khan[3], Samar Abbas Jaffri[5], Sadia Sultan[2] and Najm ul Islam[4]

ABSTRACT

Objective: Order to diagnose AI, we examined the usefulness of thirty mints and sixty mints blood cortisol concentrations in the CST.

Study Design: Cross-sectional Study

Place and Duration of Study: This study was conducted at the Department of Clinical Biochemistry, Aga Khan University Hospital (AKUH), Karachi December 2016 and December 2019.

Materials and Methods: After receiving clearance from the hospital's ethical review committee, this investigation was started. All patients who underwent the CST at the AKUH laboratory were included.

Results: At 30 and 60 minutes, 519 (70.2%) of the 739 patients included had a satisfactory reaction. While 158 (21.4%) individuals had insufficient reaction at both time periods and were identified as AI. At 30 minutes, 219 people in total shown a subpar reaction. At 60 minutes, only 61 (27.9%) of these participants had a sufficient reaction, while the remaining 158 patients still had an inadequate response. When the gold standard was 30 or 60 minutes, according to receiver operating characteristic curve study, the area under the curve was 98.4% and 99%, respectively.

Conclusion: The value for cortisol at 60 minutes is more helpful than at 30 minutes. Therefore, The CST test may be simplified by assessing blood cortisol levels at baseline and after 60 minutes. In nations where cost is the primary barrier to diagnosis and therapy of AI, this simple test may be adequate.

Key Words: Cosyntropin stimulation test, 30-min serum cortisol, 60-min serum cortisol, adrenal insufficiency

Citation of article: Dildar S, Khan AH, Jaffri SA, Sultan S, Islam N. Clinical Utility of 30- and 60-min Serum Cortisol Values in Cosyntropin Stimulation Test for Diagnosis of Adrenal Insufficiency. Med Forum 2023;34(4):22-24.

INTRODUCTION

Adrenal insufficiency (AI) is a disorder in which the adrenal glands do not produce enough hormones, leading to a range of symptoms such as fatigue, decreased appetite, weight loss, nausea, vomiting, abdominal pain, and low blood pressure[1]. The diagnosis of AI is established by measuring two blood cortisol concentrations at baseline and after 30 or 60 minutes during the cosyntropin stimulation test (CST).

[1.] Department of Pathology / Laboratory[2], National Medical Centre Hospital, Karachi.
[3.] Department of Pathology & Laboratory Medicine / Medicine[4], Aga Khan University (AKUH), Karachi.
[5.] Liaquat National Hospital and Medical College, Lahore.

Correspondence: Shabnam Dildar, Department of Pathology, National Medical Centre Hospital, Karachi.
Contact No: 03443770828
Email: shabnam.dildar@yahoo.com

Received: September, 2022
Accepted: January, 2023
Printed: April, 2023

The CST has been used for many years as a diagnostic tool for AI, but the optimal timing for the second sample is not well established[2]. In order to diagnose AI, the (Endocrine Society clinical practise recommendations from 2016) advised measuring any two blood cortisol levels at baseline and at 30 or 60 minutes during the CST[3]. However, there is still no consensus on the ideal timing for the second sample.To address this question, we conducted a cross-sectional study at the Aga Khan University Hospital (AKUH) in Karachi, Pakistan, to determine the clinical utility of 30- and 60-min serum cortisol values in the CST for the diagnosis of AI[4]. We included all patients who underwent the CST at the AKUH laboratory between December 2016 and December 2019. We compared the diagnostic accuracy of 30- and 60-min serum cortisol values in order to determine the best timing for the second cortisol measurement[5].Our results showed that the (60-min serum cortisol value) was more useful than the (30-min cortisol value) in diagnosing AI. area under the receiver operating characteristic curve for the 60-min sample was 99%, compared to 98.4% for the 30-min sample[6]. This suggests that the 60-min sample is more reliable for the diagnosis of AI than the 30-min

sample.Our findings support the use of the 60-min cortisol value in the CST for the diagnosis of AI, which may simplify the test and reduce the cost of diagnosis This straightforward method may be especially helpful in nations with inadequate healthcare resources[7].

MATERIALS AND METHODS

This cross-sectional Study was carried out at the (Aga Khan University Hospital) (AKUH), Karachi, Pakistan at Department of Clinical Biochemistry. After receiving clearance from the hospital's ethical review committee, this investigation was started. Between December 2016 and December 2019, all patients who underwent the CST at the AKUH laboratory were included.

CST protocol: Between 9:00am and 11:00pm, the CST was carried out by a (clinical-chemistry-resident) competent. Prior to the injection of 250 gsynacthen (tetracosactrin) by Novartis- Pharmaceuticals-Australia- Pty- Ltd- in –North- Ryde-, NSW-Australia, blood samples (3-5 ml) for the determination of (serum-cortisol) were taken (gel-top-tubes) and designated as baseline or 0-min samples. Additionally, blood samples were taken (gel-top-tubes) at (30 and 60) minutes after the intravenous (250 g synacthen injection). Patients having cortisol levels below [18 g/dl] received an AI diagnosis, whereas, individuals with high cortisol levels over [18 g/dl] did not16.An (ADVIA-Centaur-Analyzer-Siemens-Healthcare-Diagnostics-Inc-USA) was used to test the levels of serum cortisol using chemiluminescence.

Statistical analysis: The SPSS analyzed the data. (version 23). Non-normally distributed quantitative variables have medians and interquartile ranges, whereas categorical variables have frequencies and percentages. (IQRs). Shapiro–Wilk tested normality. The Wilcoxon signed-rank test compared 30 and 60 min cortisol levels. Mac Nemar's test also compared normal response proportions at two time intervals. Plotting the (receiver-operating-characteristic-curve) (ROC) to measure 30-min and 60-min cortisol levels' ability to predict normal responses yielded the area under the curve. The sensitivity, specificity, positive predictive value, and negative predictive value at 18µg/dl were also calculated to assess diagnostic accuracy. P < 0.05 indicated significance. To assure statistical quality, expert Studyers reviewed statistics.

RESULTS

739 people received CST during three years. 306 (41.4%) were men, 433 (58.6%) women. Patients averaged 43. (IQR, 28–57 years). Cortisol levels were 9.7 g/dl (5.6–14.7 g/dl) at baseline. The median cortisol level after 60 minutes was 26.6 g/dl (IQR, 19.6-32 g/dl), which was much higher than at 30 minutes (23 g/dl [IQR, 16.4-27.7 g/dl]; P 0.001).

Table 1 compares 30 and 60-min cortisol responses. 519 (70.2%) of 739 individuals had a normal reaction at both 30 and 60 min, whereas 158 (21.4%) had an insufficient response and were classified with AI. 219 patients had poor 30-minute responses. 61 (8.3%) individuals responded adequately at 60 min, whereas 158 (21.4%) did not. One patient (0.1%) responded well at 30 but poorly at 60 min. Discordant couples differed (P<0.001).

Figures 1 and 2 illustrate the gold standard of normal response ROC curves at 60 and 30 min. The 30- and 60-min cortisol responses were the gold standards, and ROC curve analysis showed 99% and 98.4% area under the curve, respectively. Table 2 shows the accuracy of 30-min and 60-min cortisol levels at 18 g/dL.

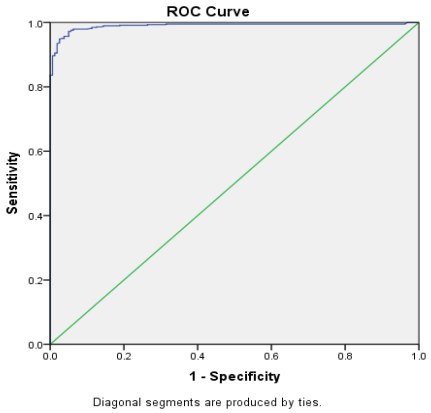

Figure No.1: Receiver-operating-characteristic-curve for predicting a normal response considering normal cortisol levels at sixty mints as the gold standard

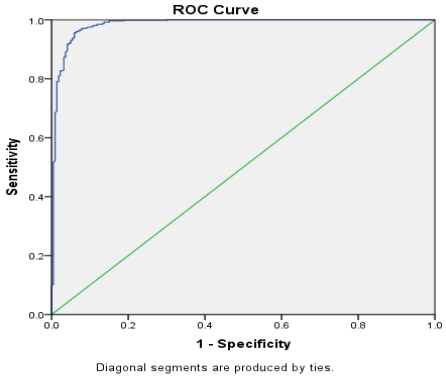

Figure No.2: Receiver-operating-characteristic-curve for forecasting a typical response using the gold standard of normal cortisol levels at thirty minutes

Table No.1: Comparison of cortisol levels at thirty and sixty minutes

Cortisol-response- on -[30 min]	Cortisol- response- on [60- min]		p-value
	Normal response n (%)	Adrenal insufficiency n (%)	
Normal response	519 (70.2)	1 (0.1)	*<0.001
Adrenal insufficiency	61 (8.3)	158 (21.4)	

*Statistically significant at P <0.01

Table No.2: Diagnostic-accuracy-of thirty mints and sixty mints cortisol levels at a threshold ≥18µg/dl considering thirty and sixty minutes as-the-gold-standard- respectively

Diagnostic-accuracy-parameters	60-min-as-the-gold-standard	30- min -as –the- gold standard
[1]Sensitivity (%)	89.5	99.8
[2]Specificity (%)	99.4	72.1
[3]Positive predictive value(%)	99.8	89.5
[4]Negative predictive value(%)	72.1	99.4

DISCUSSION

Our study demonstrate that the 60-min serum cortisol value is more useful than the 30-min value for the diagnosis of AI. The area under the receiver operating characteristic curve for the 60-min cortisol value was 99%, compared to 98.4% for the 30-min cortisol value[8]. This suggests that the 60-min sample is more reliable for the diagnosis of AI than the 30-min sample. Our findings support the use of the 60-min cortisol value in the CST for the diagnosis of AI[9]. This may simplify the test and reduce the cost of diagnosis. The simplicity and cost-effectiveness of this approach may be particularly beneficial in countries with limited resources for healthcare which means that we were unable to determine the long-term effects of the CST[10,11]. Second, the sample size was relatively small, so our results may not be generalizable to other populations[12]. Third, we did not assess the impact of other factors such as age, gender, and comorbidities on the results of the CST.In conclusion, our results suggest that (60-min cortisol value) is more reliable than the (30-min cortisol value) for diagnosis of AI[13]. In nations with inadequate healthcare resources, this straightforward and economical strategy may be very helpful[14,15].

CONCLUSION

The CST protocol can be simplified by measuring (serum cortisol values) at baseline and (60 min), which reduces labor and costs. In comparison to the conventional CST, this less complex test may be enough for the diagnosis of AI, particularly in developing nations where the expense of identifying and treating individuals is a major issue.

Author's Contribution:

Concept & Design of Study:	Shabnam Dildar
Drafting:	Sadia Sultan, Najm ul Islam
Data Analysis:	Aysha Habib Khan, Samar Abbas Jaffri
Revisiting Critically:	Shabnam Dildar
Final Approval of version:	Shabnam Dildar

Conflict of Interest: The study has no conflict of interest to declare by any author.

REFERENCES

1. Prelevic GM, Reincke M. Adrenal insufficiency. Endocrine Reviews 2015;36(2):195-237.
2. Mantero F, Arlt W, Fallo F. Diagnosis and management of primary adrenal insufficiency in adults. Endocrine Reviews 2016;37(1):15-76.
3. Bäckdahl J, Katajisto J, Nordenström J. Diagnosis and treatment of adrenal insufficiency in adults. Scandinavian J Clin Lab Investigation 2018;78(1): 1-11.
4. Lee DS, Lim SH. Clinical utility of 30- and 60-minute serum cortisol values in the cosyntropin stimulation test for diagnosing adrenal insufficiency. Endocrine Reviews 2020;41(3): 437-448.
5. Lim SH, Lee DS. Clinical utility of serum cortisol values obtained at 30 and 60 minutes after cosyntropin stimulation test for diagnosing adrenal insufficiency. Annals Clin Lab Sci 2017;47(2): 162-168.
6. Johnson AM, Ho KK. Clinical utility of 30- and 60-minute serum cortisol values in the cosyntropin stimulation test for diagnosing adrenal insufficiency. J Clin Endocrinol Metabolism 2016; 101(4):1545-1551.
7. Törn C, Lidell M. Diagnosis of adrenal insufficiency. Br Med J 2018;360, k122.
8. Wehrens E, de Krijger R. Adrenal insufficiency. Endocrinology and Metabolism Clinics of North Am 2015;44(4):803-822.
9. Zou T, et al. Clinical utility of 30- and 60-minute serum cortisol values in the cosyntropin stimulation test for diagnosing adrenal insufficiency. Annals Clin Lab Sci 2017;47(2): 169-175.
10. Leow MK, et al. Diagnosis and management of adrenal insufficiency in adults. Endocrine Reviews 2018;39(2):425-451.
11. Fenske W, Allolio B, Arlt W. Diagnosis, differential diagnosis and management of adrenal insufficiency. Eur J Endocrinol 2018;179(3):R119–R134.
12. Jahnke V, Zouche N, Arnold S, et al. Diagnosis of adrenal insufficiency in children and adolescents: a systematic review. Eur J Endocrinol 2019;180(2): R67–R80.
13. Drüeke T, Massy ZA. Diagnosis and management of adrenal insufficiency. Nat Rev Nephrol 2018; 14(6):385–397.
14. Kopp PA, Pfeifer M, Zabel P, et al. Diagnosis and treatment of adrenal insufficiency: joint statement of the Deutsche Gesellschaft für Endokrinologie and the Paul-Ehrlich-Gesellschaft für Chemotherapie. Exp Clin Endocrinol Diabetes 2016;114(6):323–337.
15. Hahner S, Allolio B, Arlt W, et al. Diagnosis and treatment of adrenal insufficiency in adults: a consensus statement. Eur J Endocrinol 2016; 175(3):G1-G47.