European Journal of Pediatrics

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INDISA - NEORED

Un Nuevo Concepto en Medicina Perinatal

European Journal of Pediatrics
https://doi.org/10.1007/s00431-019-03544-z

ORIGINAL ARTICLE

Higher C-peptide levels and glucose requirements may identify neonates with transient hyperinsulinism hypoglycemia who will benefit from diazoxide treatment

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- *Objetivo:*
  - *Caracterizar los factores que pueden servir como herramientas clínicas para identificar a los recién nacidos con HH neonatal transitoria que pueden beneficiarse del tratamiento con diazóxide*

- *Método:*
  - *Estudio retrospectivo, con información recabada de la dicha de los pacientes*
  - *Enero 2015- Abril 2018, en el Tel Aviv Sourasky Medical Center*
  - *Criterios de inclusión: hipoglicemia (< 50 mg/dl) + insulina elevada y/o evidencia de su elevación (ej: CG > 8, test de glucagon +).*
  - *Criterios de exclusión: pacientes con mutaciones genéticas en genes implicados ene a secreción de insulina o síndromes con HH*

24%

Table 1 Characteristics of diazoxide-treated and non-treated neonates

Characteristics	Treated (n = 34)	Non-treated (n = 107)	P value
Male, n (%)	25 (73.5)	68 (63.6)	0.28
Prematurity (< 37 weeks)	21 (61%)	66 (61%)	0.99
Gestational age, weeks	36.0 ± 3	36.1 ± 2	0.82
Birth weight, g	2152 ± 696	2182 ± 703	0.83
Birth weight, SDS	− 1.07 ± 0.96	− 0.98 ± 1.13	0.69
Maternal factors			
Maternal age, years	34.0 ± 5.4	34.5 ± 5.8	0.61
Pregnancies, n	2.1 ± 1.7	2.3 ± 1.5	0.50
Deliveries, n	1.4 ± 0.8	1.8 ± 1.1	0.53
GDM only, n (%)	4 (11.8%)	16 (15.0%)	0.96
HTN only, n (%)	4 (11.8%)	13 (12.1%)	
GDM + HTN, n (%)	2 (5.9%)	5 (4.7%)	
Postnatal factors			
Max. glucose infusion rate, mg/kg/min	16.6 ± 3.4	10.4 ± 4.0	*< 0.001**
Duration of IV fluids, days	15.9 ± 19.3	7.8 ± 6.5	*0.02**
Hospitalization, days	32.8 ± 22.7	20.4 ± 13.4	*0.01**
Duration of carbohydrate supplementation, days	38.9 ± 40.4	17.8 ± 21.4	*0.004**
Glucose levels, mg/dl	37.9 ± 6.1	39.0 ± 6.7	0.39
Insulin levels, μU/ml	3.5 ± 2.9	2.2 ± 3.8	0.07
C-peptide levels, ng/ml	1.4 ± 0.9 (n = 28)	0.8 ± 0.5 (n = 79)	*<0.001**

Data are presented as mean ± standard deviation unless indicated otherwise

GDM, gestational diabetes mellitus; *HTN*, hypertension; *Max.*, maximum; IV, intravenous

* Statistically significant

Diazoxide:
Edad inicio: 14,7 +- 8 d
Suspenden: 49,2 +-40,2 d
D max: 7,1 +- 2,3 mg/Kg/d

Table 2 Stepwise logistic regression analyses for the decision to treat with diazoxide

	OR	95% CI	*P* value
Max. GIR (mg/kg/min)	1.56	1.30–1.88	< 0.001
C-peptide (ng/ml)	3.57	1.30–12.1	0.005

Area under the curve 0.93

OR, odds ratio; *CI*, confidence interval; *GIR*, glucose infusion rate

Los niveles máximos de CG y péptido C fueron los predictores significativos de HH prolongada.

En base a esos hallazgos sugieren que los puntos de corte deberían ser:

14 mg/kg/min para la CG máxima

0.9 ng/ml para el péptido C

Lo que resulta en:

Sensibilidad del 82%

Especificidad del 82%

Valor productivo positivo del 62%

Valor predictivo negativo del 93%

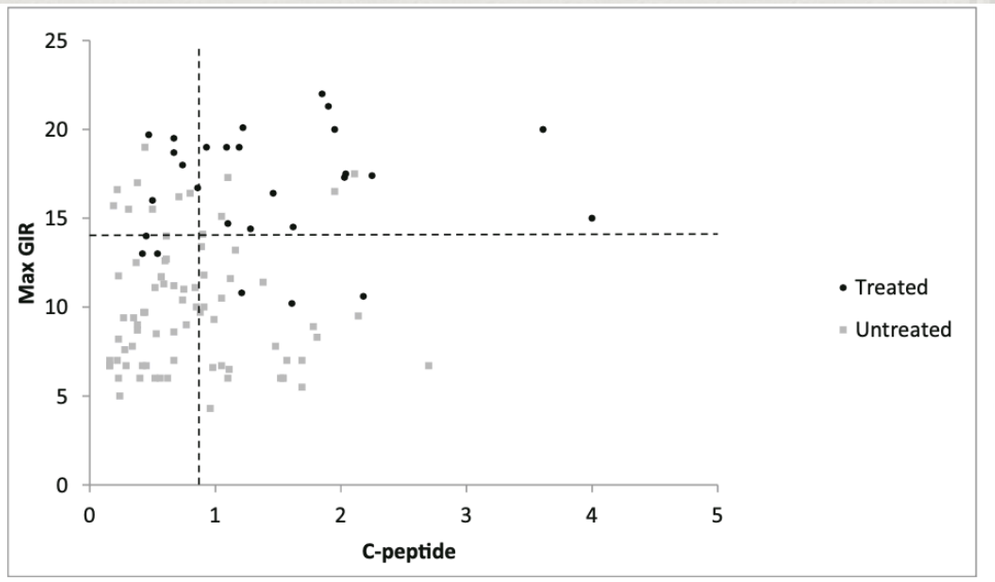

Fig. 1 A scattergram demonstrating the distribution of the treated (circles, $n = 28$) and untreated (squares, $n = 79$) groups according to C-peptide (X axis) and Max. GIR (Y axis). The dashed lines represent the proposed cutoff points to identify neonates with HH who may benefit from diazoxide treatment.

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- *Conclusiones:*
  - *Los niveles más altos de péptido C y la CG más altos pueden servir como herramientas clínicas para identificar a los recién nacidos con HH transitoria que pueden beneficiarse del tratamiento con diazóxido.*
  - *El inicio temprano del tratamiento puede reducir la duración de los líquidos intravenosos y la duración de la hospitalización, lo que resulta en una reducción del riesgo de infecciones y el costo de la hospitalización.*
  - *Además, nuestros hallazgos pueden sugerir que la incidencia de HH neonatal prolongada es mayor que las cifras actualmente aceptadas.*

European Journal of Pediatrics
https://doi.org/10.1007/s00431-019-03531-4

ORIGINAL ARTICLE

Ethical issues about the paradigm shift in the treatment of children with trisomy 18

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Received: 15 August 2019 / Revised: 8 November 2019 / Accepted: 12 November 2019

Abstract

Until recently, trisomy 18 was considered a disease incompatible with life, with a high percentage of electively terminated pregnancies. The usual behavior was denial of treatment. But some medical interventions have changed the survival of children. A search for articles published in the PubMed database on the latest medical decisions in newborns with trisomy 18 was done. Two main subjects were examined: (1) the chances of survival and (2) the perception of quality of life. Trisomy 18 is no longer considered a disease incompatible with life, and the discussion has shifted towards the type of treatment that is appropriate to initiate at birth. There are two medical attitudes towards these children: either palliative care or life-prolonging interventions. With medical intervention, the survival is as high as 23% at 5 years of age. Regarding the quality of life, all decision-makers emphasize the possibility of taking the child home. The physicians' perception is more pessimistic than that of the parents. Only a few children benefit from medical interventions.

Conclusion: There is a rethinking of treatment behavior in children with trisomy 18. The possible quality of life achieved should be further investigated. It seems inappropriate to simply dismiss medical interventions.

What is Known

• *Until recently, trisomy 18 was considered a disease incompatible with life. The most common behavior was abortion and denial of treatment.*

What is New

• *It is no longer considered a lethal disease. The type of medical intervention that is appropriate to perform is now being discussed. Selected children benefit from an interventionist approach.*

Algunos niños sobreviven más tiempo y con una mejor calidad de vida.

No hay experiencia clínica suficiente para determinar la mejor opción a seguir.

El objetivo de los enfoques intervencionistas siempre debe centrarse en la posible mejora de la calidad de vida. Para esto, es necesario evaluar cada caso particular, sin basar un enfoque o intervención particular exclusivamente en el diagnóstico de la trisomía 18 y, de manera concomitante, los pacientes deben ser seleccionados para quienes el beneficio de la intervención haya sido comprobado.

De esta manera, es más fácil garantizar que se realicen intervenciones efectivas y evitar intervenciones terapéuticas sin sentido.

Table 1 Survival range of newborns with trisomy 18 according to different medical

	With palliative approach[a] (%)	With an interventionist approach[b] (%)
First month	33–37.2 [1, 15]	83 [5]
1 year	3–13.4 [1, 5, 6, 8, 10, 15, 17, 33]	20–84 [5, 6, 8, 9, 18, 33]
5 years	12.3 [15]	23 [18]

[a] Palliative approach includes only palliative medical treatment (without palliative surgery)

[b] Interventionist approach: includes all active treatments

- *Conclusiones:*
  - *En la medicina perinatal, se ha replanteado las opciones de tratamiento en niños con trisomía 18.*
  - *La evaluación continua de las nuevas estrategias de tratamiento es importante para determinar la adecuación ética de los diferentes enfoques médicos para la afección.*
  - *Entre otros puntos clave, es importante evaluar sistemáticamente la posible calidad de vida lograda.*
  - *No parece apropiado negar simplemente un enfoque intervencionista basado únicamente en un diagnóstico de trisomía 18.*