

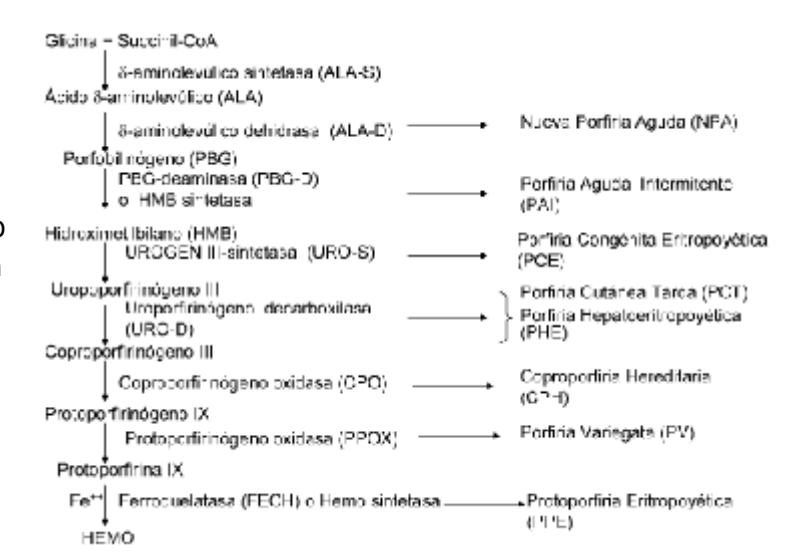
5-ALA

El ácido 5-aminolevulínico (5-ALA) es una pro-droga que causa **protoporfirinas** fluorescentes que se acumulan en los **gliomas** malignos.

La fluorescencia puede ser visualizada durante la cirugía por el uso de un microscopio modificado, que ayuda al cirujano a definir los márgenes del tumor. El tejido maligno provoca fluorescencia roja bajo iluminación con luz azul.

Con la ayuda de mapeo funcional hace que la resección sea viable en áreas elocuentes con tasas razonables de morbilidad tardía ¹⁾

Es un precursor de la síntesis del **grupo hemo**. Su administración exógena por vía oral puede inducir la acumulación de porfirinas fluorescentes (**protoporfirina IX**), en las células tumorales, de manera que cuando el tejido tumoral es iluminado con una luz violeta-azul (longitud de onda de entre 375 y 440 nm), se puede apreciar una fluorescencia roja resultado de la excitación de la protoporfirina IX acumulada. Esto permite la distinción intraoperatoria del tejido patológico, lo que facilita la resección tumoral y ayuda a conseguir mayores tasas de resección completa al detectar restos tumorales que, sin esta técnica, podrían pasar desapercibidos.



Se sugiere una asociación significativa, sin embargo, limitada, entre la ruptura de la **barrera hematoencefálica** y la porfirina inducida por el 5-ALA (Valdés y col., 2012).

Eficacia

La eficacia depende de la acumulación específica y la cantidad total de síntesis intracelular de protoporfirina IX (PpIX) en células tumorales

Stummer y col., publicaron sus resultados demostrando la utilidad del 5-ALA para mejorar el grado de la resección de gliomas cerebrales malignos (Stummer y col., 1998).

Añadido al mapeo intraoperatorio, conduce a una alta tasa de resecabilidad sin aumentar la tasa de morbilidad permanente (Schucht y col., 2012).

Desde entonces, la utilización de esta técnica está en franca difusión, habiéndose publicado artículos que hacen referencia a su utilidad en casos de lesiones distintas a los gliomas malignos.

Criterios de inclusión

Se pueden incluir todos los pacientes con sospecha de [glioma maligno](#) mediante TAC y/o Resonancia (Kamp y col., 2012).

En el estudio de Stummer y col., el 61% de los pacientes recibieron una resección total.

En ese estudio, los criterios de inclusión fueron

Tumor accesible a la resección completa (Stummer y col., 2006).

Histopatología confirmatoria de glioma maligno.

El uso no aprobado en pacientes pediátricos parece ser más útil en los gliomas recurrentes de alto grado. La acumulación de fluorescencia en otras entidades tumorales cerebrales pediátricos no es predecible y se debe evaluar en futuros estudios clínicos antes de ser integrado en los protocolos de tratamiento actuales ²⁾

[Cuestionario para pacientes pediátricos](#)

Administración

La dosis estándar preoperatoria es de 1.500 mg Gliolan (Medac, Alemania) disuelto en 50 ml de agua estéril 2-4 horas antes de la cirugía (un vial de Gliolan contiene 1.500 mg).

La dosis recomendada es de 20 mg / kg.

A los pacientes se les realiza una RM cerebral dentro de las primeras 72 horas postoperatorias, para determinar su estado de resección postoperatoria.

Evaluación postoperatoria

La evaluación de las imágenes postoperatorias se basan en secuencias T1 (FLAIR) sin y con contraste.

Si existe duda sobre el significado de un elemento se considera tumor residual.

Categorías de resección

Resección total

Resección subtotal (menos del 5% de tumor residual)

Tumor residual.

Seguridad

El estudio de Stummer y col., con posterior análisis del mismo conjunto de datos, demostró que las resecciones guiadas por fluorescencia son generalmente seguras (Stummer y col., 2006), pero tienen un riesgo ligeramente más alto de deterioro neurológico temporal - sobre todo en los pacientes con

déficit neurológico pre-existente, que no han respondido a los esteroides (Stummer y col., 2011).

Toxicidad

En la serie de Cortnum y Laursen, no hubo efectos secundarios tóxicos (Cortnum y Laursen, 2012).

Tumores intramedulares

El uso de la fluorescencia para la resección de tumores intramedulares ha sido comunicada previamente por otros autores. Arai et al. publicaron 3 casos de ependimomas intramedulares en los que la fluorescencia intraoperatoria del tejido tumoral fue de utilidad para conseguir la resección completa de las lesiones. Shimuzu et al. consiguen una resección completa de un ependimoma intramedular cervical gracias al uso de esta técnica (Bernal-García et al. 2010).

Método

Se ha creado un sistema de ablación por láser que puede proporcionar un análisis de alta precisión para la resección que con una mejora adicional, puede ser utilizado (Liao y col., 2012).

Gliomas malignos

El ácido 5-aminolevulínico (5-ALA) ha ganado importancia como un agente fotodinámico intraoperatorio de diagnóstico para la extirpación de los gliomas malignos.

Condujo a un aumento significativo en la incidencia de la resección completa (65% frente a 36%), la mejora de la supervivencia sin progresión en 6 meses (41% frente a 21%), y menos reintervenciones, así como el retraso en la aparición de deterioro neurológico (Colditz y col., 2012).

El significado de la fluorescencia de la pared ventricular durante el procedimiento, es aún desconocido.

La RM preoperatoria predice si existe apertura ventricular con la fluorescencia 5-ALA, según la localización tumoral, pero no predice, si la pared del ventrículo va a ser fluorescente o no. La fluorescencia de la pared del ventrículo no es un predictor de complicaciones o de supervivencia.

La localización del tumor periventricular es un factor independiente de mal pronóstico (Tejada-Solís y col., 2012).

Meningiomas

La aplicación de esta técnica para la resección de los meningiomas apenas ha sido explorado, en un total de 32 (97%) , la 5-ALA-fluorescencia inducida del tumor fue confirmado en un total de 31 (94%) pacientes. La fluorescencia no se correlacionaron con los hallazgos histológicos (n = 30 de OMS I-II, n = 1 de OMS grado III) o con edema cerebral preoperatorio y la administración de esteroides. No se observaron efectos adversos atribuibles a 5-ALA, concluyendo que es una herramienta intraoperatoria útil y prometedora para la visualización de meningioma (Coluccia 2010).

Permite una clara delimitación de tejido tumoral intraoperatorio de la duramadre adyacente, no afectada. A nivel microscópico, existe una correlación muy cerca de la fluorescencia de tumor, pero algunas células tumorales no presentan fluorescencia (Whitson et al. 2011).

Hemangioblastoma

Es un método útil para discernir si las células tumorales presentes en la pared del quiste peritumoral de un hemangioblastoma (Utsuki y col., 2011).

Ependimoma intramedular

Es útil para detectar los márgenes del tumor.

Cuando se combina con la monitorización electrofisiológica, puede ayudar a lograr la resección del tumor con seguridad máxima (Inoue y col., 2012).

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