Estudio número 14

Terapias emergentes para el tratamiento de la hipoacusia neurosensorial.

Se realiza una revisión crítica de la literatura disponible tras una búsqueda en el registro de ensayos clínicos, y se evalúan los resultados documentados y los mecanismos de acción propuestos para las terapias emergentes usadas en el tratamiento de la hipoacusia neurosensorial.

Se identificaron 22 ensayos clínicos registrados en los Estados Unidos y se evaluaron seis moléculas con potencial terapéutico. De dichas 6 moléculas, 4 actuarían mitigando el estrés oxidativo que presumiblemente desemboca en la muerte de las células del neuroepitelio coclear. Una molécula busca manipular la cascada que lleva a la muerte celular y la última es una terapia de reemplazo celular, introduciendo con un virus un factor de transcripción que promueve la regeneración celular.

Quedan aún muchos pasos hasta que estas nuevas terapias lleguen al público en general, puesto que han de superar pruebas de eficacia y seguridad que suelen tardar años. Además, se van describiendo nuevos posibles mecanismos para el deterioro auditivo, como la pérdida de contactos sinápticos y la respuesta inmune, que supondrán en el futuro nuevas oportunidades de tratamiento para la hipoacusia.

Emerging Therapies for Sensorineural Hearing Loss.

Objective
To critically review and evaluate the proposed mechanisms and documented results of the therapeutics currently in active clinical drug trials for the treatment of sensorineural hearing loss.

Data sources
US National Institutes of Health (NIH) Clinical Trials registry, MEDLINE/PubMed.

Study selection & data extraction
A review of the NIH Clinical Trials registry identified candidate hearing loss therapies, and supporting publications were acquired from MEDLINE/PubMed. Proof-of-concept, therapeutic mechanisms, and clinical outcomes were critically appraised.

Data synthesis
Twenty-two active clinical drug trials registered in the United States were identified, and six potentially therapeutic molecules were reviewed. Of the six molecules reviewed, four comprised mechanisms pertaining to mitigating oxidative stress pathways that presumably lead to inner ear cell death. One remaining therapy sought to manipulate the cell death cascade, and the last remaining therapy was a novel cell replacement therapy approach to introduce a transcription factor that promotes hair cell regeneration.

Conclusion
A common theme in recent clinical trials registered in the United States appears to be the targeting of cell death pathways and influence of oxidant stressors on cochlear sensory neuroepithelium. In addition, a virus-delivered cell replacement therapy would be the first of its kind should it prove safe and efficacious. Significant challenges for bringing these bench-to-bedside therapies to market remain. It is never assured that results in non-human animal models translate to effective therapies in the setting of human biology. Moreover, as additional processes are described in association with hearing loss, such as an immune response and loss of synaptic contacts, additional pathways for targeting become available.

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