We are Missing the Neurocognitive Consequences of Chemotherapy-Induced Hearing Loss in Pediatric Brain Tumor Survivors

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Background

Current treatment for pediatric brain tumors has resulted in increased survival rates, such that we are now positioned to consider the quality of survivorship[1,2]. A common treatment regimen includes surgery, radiation, and chemotherapy – specifically, platinum-based drugs[3]. Use of platinum-based chemotherapy is associated with ototoxicity. Roughly 60% of pediatric brain tumor survivors treated with platinum-based drugs sustain hearing loss[2,4]. This hearing loss, which can persist and worsen over time[5] can also negatively impact academics and overall quality of life in these developing children[6]. This systematic review summarizes current research on the cognitive effects of chemotherapy-induced hearing loss, both during and after treatment[6].

Objectives

This systematic review examined the effects of chemotherapy-induced hearing loss on cognitive function in pediatric brain tumor survivors.

Methods

Data Sources: Searches of 4 databases (PubMed, Emcare, PsycINFO, CINAHL) with no date or language restrictions identified 37 unique results. Search terms included pediatric, brain neoplasm/tumor, chemotherapy, and an extensive list of terms related to cognitive and language deficits.
Study Selection: Included studies: (1) described cognitive or language dysfunction in children undergoing (or who had undergone) platinum-based chemotherapy for a brain tumor (2) provided objective measurements of cognition and/or language, and (3) were published in peer-reviewed journals. Studies were not excluded if the patients received radiation or surgery.
Data Extraction: Data were extracted according to Cochrane recommendations including characteristics of participants, outcomes, and studies. Quality assessment of all 3 eligible studies was performed using an adapted PEDro scale plus a treatment assessor criterion. Screening, data extraction, and quality assessment reliability was performed.

PRISMA flow Diagram of Records

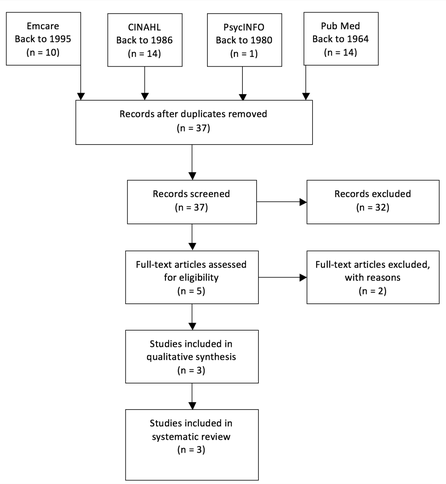

Table 1. Participant Characteristics

Authors, Year	Hearing	Group n	Gender	SNHL n	Age of HL diagnosis (years)	Cancer Diagnosis	Cancer Dx: Age (years)	Platinum-Based Chemotherapy
Heitzer et al., 2020	NH	19	M: n = 13 F: n = 6	No = 19	Average: N/R Range: N/R	Medulloblastoma, primitive neuroectodermal tumor, or pineoblastoma	Average: 7.4 Range: 2.2-15.4	Cisplatin
	SNHL	17	M: n = 15 F: n = 2	Yes = 17	Average: N/R Range: N/R	Medulloblastoma, primitive neuroectodermal tumor, or pineoblastoma	Average: 6.9 Range: 2.2-12.3	Cisplatin
Olivier et al., 2019	NH	196	M: n = 117 F: n = 79	No = 196	Average: 9.55 Range: N/R	Medulloblastoma, primitive neuroectodermal tumors, atypical teratoid or rhabdoid tumors, or pineoblastomas	Mean age at diagnosis: 9.15 Range: N/R	Platinum-Based Treatment (i.e., cyclophosophamide, cisplatin, vincristine, amifostine
	SNHL	64	M: n = 42 F: n = 22	Yes = 64	Average: 7.92 Range: N/R	Medulloblastoma, primitive neuroectodermal tumors, atypical teratoid or rhabdoid tumors, or pineoblastomas	Mean age at diagnosis: 9.15 Range: N/R	Platinum-Based Treatment (i.e., cyclophosophamide, cisplatin, vincristine, amifostine
Orgel et al., 2016	NH & SNHL	58	M: n = 36 F: n = 22	Yes = 32 No = 26	Average: 9.2 Range: N/R	Medulloblastoma Other CNS tumors	Mean age at diagnosis: 6.7 Range: N/R	Cisplatin and carboplatin

Abbreviations: NH = Normal Hearing; SNHL = Sensorineural Hearing Loss; M = Male, F = Female; N/R = Not Reported; CNS = Central Nervous System

Table 2. Cognitive & Language Assessments

Study	Measurement Time Point	Measurement Instrument	Neurocognitive Outcome	Statistical Analyses	
				Regression	Raw
Orgel et al., 2016	Average 4.6 years after diagnosis	Wechsler Scales of Intelligence	Wechsler FSIQ Verbal comprehension Working memory Processing speed Perceptual reasoning	p = 0.038 p = 0.082 p = 0.003 p = 0.126 p = 0.003	N/R
Heitzer et al., 2020	6.7 years after craniospinal irradiation	Wechsler Scales of Intelligence	Wechsler FSIQ Verbal comprehension Working memory Processing speed Perceptual reasoning	p = 0.019 p = 0.107 p = 0.225 p = 0.138 p = 0.016	p = 0.008 p = 0.031 p = 0.62 p = 0.57 p = 0.94
Olivier et al., 2019	1 year, 3 years, and 5 years after diagnosis	Woodcock-Johnson Third Edition, Tests of Achievement and Cognition	Passage comprehension Working memory Processing speed Sound awareness Phonemic awareness Word attack Letter-word identification Reading fluency	p = 0.0069 p = < 0.001 p = 0.0135 p = N/R p = < 0.001 p = 0.0305 p = N/R p = N/R	p = 0.356 p = N/R p = 0.9765 p = 0.0017 p = 0.2358 p = 0.4879 p = 0.5249 p = 0.6706

Significant differences between NH group and SNHL group

Abbreviations: FSIQ = Full Scale Intelligence Quotient;; N/R = Not Reported

Conclusions

1. There is a paucity of data describing how sensorineural hearing loss caused by platinum-based chemotherapy affects the lives and cognitive skills of developing children. The studies that have been completed so far have shown that chemotherapy-induced hearing loss has a negative effect on cognition in pediatric brain tumor survivors.
2. Previous research has shown that platinum-based chemotherapy poorly effects the development of cognitive skills in pediatric brain tumor survivors, but more research is needed on the consequences that may be specific to chemotherapy-induced hearing loss.
3. The studies included in this systematic review indicate that a larger focus must be placed on providing baseline cognitive assessments for children prescribed chemotherapy for brain tumors. For many participants, baseline cognitive measures were not available. The inclusion of baseline assessments in cognitive research is necessary.
4. Further assessments should be completed during and after treatment so that timely intervention may be provided if a cognitive deficit begins to appear.
5. Referrals for these assessments should become standard, interdisciplinary procedures when prescribing platinum-based chemotherapy to children diagnosed with pediatric brain tumors.

Future Directions

1. Implement cognitive baseline and follow-up assessments to detect the effects of chemotherapy over time.
2. Conduct collaborative research including care givers, audiologists, oncologists, speech-language pathologists, educators, psychologists, social workers, and other professionals involved in assessments and referrals for hearing loss and cognition in children diagnosed with a pediatric brain tumor.
3. Increase the sample size and group similarity of the study in order to provide an accurate representation of cognitive deficits.

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