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EPID-04. CAUSES AND LONG-TERM COURSE OF OTOTOXICITY IN PEDIATRIC MEDULLOBLASTOMA AND EPENDYMOMA PATIENTS – CUMULATIVE PLATINUM AND COCHLEAR IRRADIATION DOSE MATTER

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BACKGROUND: Ototoxicity is a well-known side effect of treatment with platinum-containing chemotherapy and radiotherapy (RT). Nevertheless, precise dose-effect relationships are still lacking. METHODS: Patients from the HIT2000 trial receiving first-line treatment for medulloblastoma (MB) or ependymoma (EPN) who were alive at last follow-up and had at least one audiogram prior to and after administration of chemotherapy with cisplatinum and radiotherapy were included into this study. Treatment details (incl. cochlear irradiation dose [CID]) and audiological outcome were analyzed. The ototoxicity was graded using the HIT scoring. RESULTS: Courses of 101 patients were analyzed. Median audiology follow-up was 6 years [range: 1.0–18.1 years]. Ototoxicity grade ≥1 was documented for n=66 patients (65.4%). For n=27 this resulted in treatment modification. Univariable analyses revealed different proportions of ototoxicity (grade ≥1) regarding histology (CMB: 50/65, LCAMB: 3/3, DMB/MBEN: 8/12, EPN: 5/21; p<0.001), tumor location (supratentorial: 3/9, infratentorial: 63/92; p<0.001), metastatic status at diagnosis (M0: 46/77, M+: 20/24; p=0.003), radiation field (CSI: 59/75, local RT: 6/21, no RT: 1/5; p<0.001), CID (continuous variable, p=0.001) and cumulative cisplatinum dose (continuous variable, p<0.001). Certainly, disease specific parameters (histology/staging) were related to treatment intensity (cisplatinum/irradiation dose). Multivariable analyses confirmed the impact of cumulative cisplatinum dose (p=0.01) and CID (p=0.04). ROC-analyses allowed the definition of cut-offs for high risk of ototoxicity grade ≥1 (cisplatinum: 70mg/m^2 BSA, CID: 37.5 Gy) and ototoxicity risk estimation, when applying doses above the respective cut-offs (cisplatinum dose increase by 1mg/m^2 BSA results in 4% higher risk for ototoxicity grade ≥1; CID dose increase by 1 Gy results in 4.6% higher risk for ototoxicity grade ≥1). CONCLUSIONS: Ototoxicity affects a majority of children receiving adjuvant treatment for MB and EPN. To avoid disabilities and negative effect on quality of live, dosage of cisplatinum and radiotherapy should be scrutinized and reduced whenever possible.