

Relationship Between Intra-Operative Hyperthermia, Post-Operative Fever and Local Infectious Complications in Children Undergoing Cochlear Implant Surgery

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Ribak Z and Tailakh MA. These authors have contributed equally to this study.

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1. Abstract

1.1. Objective: To examine the relationship between Intra-operative hyperthermia (IOH) and post-operative fever (POF) and local complications in children undergoing Cochlear Implantation (CI) surgery.

1.2. Study Design: Retrospective cohort study.

1.3. Setting: Tertiary care University Hospital.

1.4. Participants: The study includes all pediatric CI surgery procedures conducted in one hospital between 2007 and 2017. A total of 213 CI procedures were performed on 191 children (ages 9 months to 17 years; mean 3.54 years).

1.5. Main Outcome and Measure: Clinical data including demographics, type of surgery (unilateral, bilateral), presence of IOH and POF, and local infectious complications within one month after surgery.

1.6. Results: Ten patients (4.9%) developed IOH, of which two

developed POF. Of the remaining non-IOH cases (95.1%), 29 children (14.3%) developed POF. IOH correlated with cases of bilateral CI (80% bilateral CI versus 20% unilateral CI; $p = 0.002$). IOH also correlated with the duration of operation (289 min versus 189 min, respectively; $p = 0.025$). Local complications were recorded in 30 patients: 2 that developed POF in the IOH group, and 28 (14.3%) in the non-IOH group. No correlation was observed between the occurrence of either IOH or POF, and the occurrence of local complications.

1.7. Conclusions: IOH and POF are not uncommon in children that undergo CI surgery, however, in the present study cohort, both conditions are not associated with the development of local infectious complications. Additionally, IOH does not appear to predict the development of POF.

2. Key points:

- Post-operative fever and intra-operative hyperthermia are commonly encountered in all surgical disciplines

- The role of both entities in children undergoing cochlear implant is unclear
- Its relationship and the effect on local complications is presently unknown
- Here, IOH and POF are found to be not unusual in children undergoing CI surgery.
- Both IOH and POF seem to be benign conditions that do not influence the development of local infectious complications

3. Introduction

Cochlear implantation (CI) is a surgical procedure that allows for the rehabilitation of hearing in patients with severe sensorineural hearing loss. It is well-defined and particularly. Nonetheless, there are numerous surgical complications that may include CSF leaks, wound infection and facial paralysis [1-3].

Intra-operative hyperthermia (IOH) is a well described pediatric phenomenon which has recently been noted in children undergoing CI [4]. Although the etiology of IOH remains unclear, it is suggested to follow a genetic predisposition. However, in the case of CI surgery, it is thought to be due to the unbalance of thermoregulation by hypothalamic disruption [4-5].

Post-operative fever (POF) is another common complication following surgical procedures [7-8]. Although POF rarely indicates an infection, it does quite frequently lead to very costly fever workups. We have previously described early POF following pediatric CI surgery (up to 72 hours after surgery) with an incidence of 19.2% that was unrelated to local infections or any long-term complications [9].

In this present study, we examine the relationship between IOH and POF in children who underwent CI surgery, and their relation to post-operative local infectious complications.

4. Materials and Methods

Retrospective cohort study

4.1. Ethical Considerations

The Institutional Ethics Committee approved the study.

4.2. Participants

All cases consisted of children younger than 18 years who underwent CI surgery at the Soroka Medical Center between the years of 2007 and 2017 were included in this study. The data collected included: age, sex, type of surgery (unilateral, bilateral), event of intra-operative hyperthermia, post-operative fever, and the occurrence of local infectious complications. Body temperature was taken at the beginning of each operation, during the operation and at the end of the operation. For each patient, data included both intravenous agents and the length of operation.

4.3. Intra-Operative Hyperthermia and Post-Operative Fever

IOH during CI surgery and POF within the first 72 hours following CI surgery, were defined as an elevation in body core temperature of 38°C or above, regardless of site of measurement (i.e., rectum or nasopharynx). Same-side post-operative local infectious complications were defined as any local swelling, redness, abscess, acute otitis media, acute mastoiditis or acute meningitis within one month following surgery.

All patients received intra-operative IV antibiotic prophylaxis (amoxicillin-clavulanic acid, 25 mg/kg) followed by two more doses within the first 24 hours after surgery.

4.4. Statistical Analyses

Patient characteristics and results are reported as means \pm standard deviations for normally distributed quantitative data or as medians and interquartile ranges for non-normally distributed data. Nominal and categorical variables are expressed as numbers (percentages). The primary outcomes were post-operative complications (yes/no) and POF (yes/no). A Chi-square test was used for dichotomous variables and a Student's t-test was used for continuous variables. Multivariate binary logistic regression was used to evaluate any independent association between patient characteristics and the development of complications or POF as a dichotomous variable.

All statistical analyses were performed using IBM SPSS Statistics, version 25. Results were considered statistically significant at $p < 0.05$.

5. Results

5.1. Demographics

Between the years 2007 and 2017, 191 patients aged 9 months to 17 years (mean 3.54 years), underwent 213 procedures, accounting for 260 cochlear implants at Soroka Medical Center. Of these, 69 procedures (32%) were simultaneous bilateral cochlear implants. Etiology was y hereditary in 80%; 2 of the patients were operated on for post-meningitis deafness; 4 of the procedures were for inner-ear congenital malformations (2 for incomplete partition type and 2 with an enlarged vestibular aqueduct). Of all the procedures, 88 were performed on males (41%) and 125 on females (59%). 100 procedures were performed on Bedouin Arab patients (63%) and 72 on non-Bedouin, mainly Jewish, patients (34%). Demographic and clinical characteristics of the patients are summarized in (Table 1).

5.2. Patients with IOH Versus Patients Without IOH

Out of 213 procedures, 10 patients developed IOH. The remaining patients belong to the non-intra-operative hyperthermia (NIOH) group. There were no significant differences observed between the groups in regard to age, gender, ethnicity, number of CI surgeries (one versus more than one), or the cause of deafness (Table 1).

Table 1: Patient characteristics and group comparisons

Characteristics:		IOH (n = 10)	NIOH (n = 203)	P Value:
Age	Months (median, SD)	23.5 ± 12.63	26.0 ± 40.98	0.26
Gender	Male	5 (50%)	83 (40.9%)	0.56
	Female	5 (50%)	120 (59.1%)	
Ethnicity	Arab	6 (60%)	129 (63.5%)	0.81
	Jewish	4 (40%)	68 (33.5%)	
	Other	0 (0%)	6 (3%)	
Type of surgery	Unilateral	2 (20%)	142 (70%)	<0.01
	Bilateral	8 (80%)	61 (30%)	
Etiology of deafness	Heredity	8 (80%)	163 (80.3%)	0.59
	Acquired	1 (10%)	8 (3.9%)	
	Unknown	1 (10%)	32 (15.8%)	
POF	Yes	2 (20%)	29 (14.3%)	0.64
Post-operative complications*	Yes	2 (20%)	28 (14.3%)	0.64
Anesthesia length** Median (IQR)		289 (252-354.75)	189 (159-286)	0.025
Temp. (°C) Median (IQR)	During operation	36.9 (36.4-37.4)	36.1 (35.6-36.43)	<0.001
	Peak	38.3 (38-38.6)	36.9 (36.3-37.2)	<0.001
	Beginning of operation	35.9 (35.6-36.2)	35.8 (35.3-36.3)	0.64
	End of operation	38.3 (37.8-38.5)	36.7 (36.1-37.2)	<0.001
Number ICU of admissions		1 (14%)	1 (1%)	0.01

IOH, intra-operative hyperthermia; NIOH, non-intra-operative hyperthermia. *Seven patients in the NIOH group did not have data regarding complications. **Intra-operative parameters: n = 7 in the IOH group and n = 101 in the NIOH group.

5.3. IOH Versus Length of Surgery

144 patients underwent unilateral CI, while 69 patients underwent bilateral CI. There was no observed difference in regard to the etiologies of deafness between patients undergoing a unilateral or bilateral procedure. In the bilateral CI group, IOH was observed in 8 patients (80%) and was only seen in 2 patients in the unilateral CI group (20%) ($p < 0.05$, Table 1).

5.4. IOH versus POF

POF was discovered following 31 procedures. Of these, 2 were from the 10-patient IOH group, however, no causative infections were identified and no antibiotic treatment was initiated in these patients. Neither of these 2 patients suffered from early post-operative complications. The remaining patients with POF (29 patients) were placed in the NIOH group (14.3%). In 4 patients a clear etiology for POF was found (pharyngitis, gastroenteritis, periorbital cellulitis or dysentery). 5 of the 29 patients showed post-operative complications including, swelling (3 patients), otitis media (1 patient), and acute bacterial meningitis (1 patient). Multivariate analysis showed that developing IOH during CI surgery is not associated with the occurrence of POF ($p = 0.923$; (Table 2)).

Table 2: Multivariate analysis, potential risk factors for POF

Characteristic:	Odds Ratio	95% CI	P Value
Age in months	0.99	0.97-1.00	0.13
Gender (males)	2.22	1.00-4.92	0.05
Ethnicity (Arab Beduin)	1.54	0.62-3.80	0.35
Bilateral procedure	1.25	0.52-3.00	0.62
Etiology (hereditary)	1.09	0.11-10.74	0.93
Intra-operative hyperthermia	1.08	0.19-5.95	0.92

5.5. Post-Operative Local Complications

There was no significant difference in post-operative complications between the IOH and NIOH groups. Specifically, post-operative inflammatory complications were observed in 2 patients from the IOH group (1 with local swelling and 1 with acute otitis media) and in 28 patients from the NIOH group (14.3%; 13 with swelling, 8 with otitis media, 4 with local infection, 2 with meningitis, and 1 with otitis externa). Multivariate analysis showed that IOH is not associated with post-operative complications ($p = 0.89$, (Table 3)).

Table 3: Multivariate analysis of potential risk factors for post-operative complication in CI surgery

Characteristic:	Odds Ratio	95% CI	P Value
Age in months	0.99	0.98-1.01	0.79
Gender (males)	1.46	0.65-3.27	0.35
Ethnicity (Arab Beduin)	1.16	0.48-2.79	0.74
Bilateral procedure	1.57	0.64-3.82	0.32
Etiology (hereditary)	1.29	0.14-12.03	0.82
Intra-operative hyperthermia	1.11	0.20-5.97	0.89
Post-operative fever	1.42	0.51-3.97	0.49

5.6. Intra-Operative Parameters

Intra-operative data (i.e., duration of operation, minute-by-minute temperature recordings, intravenous agents employed, intra-operation complications and ICU admission) was available for 108 patients (Table 1). According to this data, the duration of anesthesia was significantly longer in the IOH group when compared to the NIOH group (289 min and 189 min, respectively). 1 of the patients from the IOH group was admitted to the ICU with suspected malignant hyperthermia and his operation was stopped after 182 minutes.

There was no significant difference in patient's temperature at the

beginning of the operations between the IOH and NIOH groups (35.9°C and 35.8°C, respectively; $p = 0.639$); however, statistical significance was observed for temperature at the end of the operation between these groups (38.3°C IOH and 36.7°C NIOH; $p < 0.001$). The peak temperature measured in the IOH group was 38.3°C, while the peak temperature measured in the NIOH group was 36.9°C ($p < 0.001$).

A positive and significant correlation is seen between body temperature and duration of surgery ($p < 0.05$), as well as between peak temperature during the operation and the duration of the operation ($p < 0.001$) (Figure 1). 2 patients were admitted to the ICU: 1 due to suspected malignant hyperthermia (IOH group) and the other due to low oxygen saturation during the operation (NIOH group).

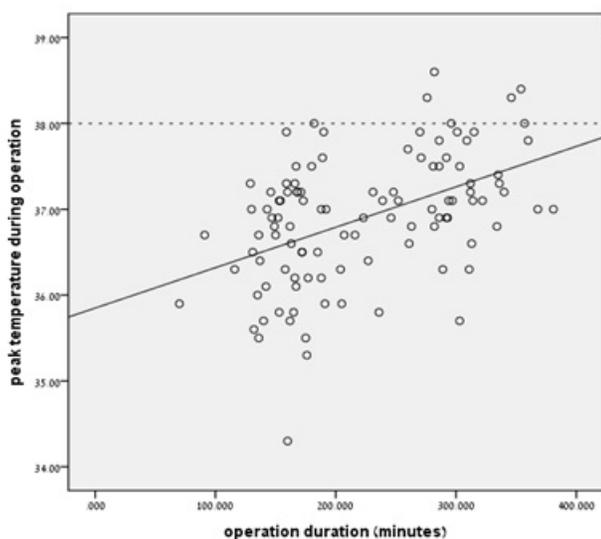


Figure 1: Peak temperature and duration of operation. Dashed line, hyperthermia defined as 38°C or above; solid line, linear regression. Temperature (°C). Data from 108 CI surgical procedures.

Intravenous agents used during the operation included Propofol, Perfalgan, Neostigmine, Atropine, Midazolam, Emerone, Tracium and Morphine; no differences were evident in the use of these agents between the IOH and NIOH groups.

6. Discussion

The focus of this study was to examine the relation between IOH and POF in children undergoing CI surgery, and to explore their association with common local complications. Schwartz A et al. [4] has previously described IOH in the pediatric population and has concluded that patients undergoing CI surgery are susceptible to IOH, particularly without an identified cause. However, a higher incidence of IOH in CI surgeries was observed when compared to anatomically similar surgeries, such as mastoid or ophthalmic surgeries. A significant difference in the length of anesthesia between

IOH and NIOH groups was also seen.

In the present study, IOH appears to be a benign phenomenon. Multivariate analysis shows that IOH does not predispose the patient to POF or to other post-operative inflammatory complications.

The overall incidence of IOH during CI in the present study is 4.7%. This is lower than the incidence of 10% that was previously reported by Schwartz A et al. Thus, the complication of IOH during CI has become less frequent in recent years. However, very interestingly there has recently been a larger fraction of bilateral implants which is the same patient group that initially had higher rates of IOH. While a bilateral procedure is longer in duration, thus exposing the patient to prolonged anesthesia, intravenous anesthesia has been replacing inhaled anesthesia in the past several years [4].

According to the present study, IOH is not associated with the occurrence of POF. In fact, POF is not unusual in CI surgery. Its incidence has been shown to be 19.2% [9], while the incidence of POF in the present study was found to be 14.5% and continues to represent a benign entity with no major clinical significance. Although there is minimal clinical significance to POF, this finding still remains a large financial burden as the POF-related work up remains high.

The post-surgical complication rate in the present study was similar to the rate found in the literature [1]. However, while many studies examined complications following CI surgeries, the present study focused specifically on inflammatory complications, with the rationale of a possible common axis connecting IOH, POF and infectious complications.

The present study has several limitations. As a retrospective study, data on complications that had occurred following patient discharge may be lacking. In addition, sample size in the intra-operative analysis is relatively small: out of 190 patient records, only 108 had sufficient data across all study parameters. Therefore, a robust conclusion regarding a putative correlation between length of anesthesia time and hyperthermic events could not be made. A larger study with a more detailed documentation of each parameter per patient is required in order to identify how factors such as anesthesia, room temperature and heating methods, can affect hyperthermic events in CI surgery.

Taken together, based on the presently studied cohort, IOH and POF are independent of one another. They are also not uncommon in children undergoing CI surgery. Indeed, here, IOH does not predict the development of POF. Furthermore, hyperthermic events do not seem to influence the development of any local complications.

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