

SEQUELAE FROM MENINGOCOCCAL MENINGITIS IN CHILDREN

A critical analysis of dexamethasone therapy

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ABSTRACT - Objective: To evaluate the effectiveness of dexamethasone as an adjunctive therapy to antibiotics in children with meningococcal meningitis. **Method:** A total of 81 children diagnosed with meningococcal meningitis hospitalized in sequence were studied at the University Hospital of São Paulo University, with the objective of evaluating the presence of sequelae in four different groups of patients, following the administration of dexamethasone: Group I - 25 patients who received the first dose at least 10 minutes before the introduction of the antibiotic therapy; Group II - 19 patients who received the corticosteroid concomitantly; Group III - 14 patients for which the dexamethasone was administered after beginning the antibiotic scheme; Group IV - 23 patients that did not receive dexamethasone. The groups were evaluated for homogeneity through the prognostic indexes and clinical and laboratory characteristics, based on the records obtained at hospitalization. **Results:** Some degree of sequelae occurred in 16 (26.22%) of the survivors and 23 patients (28.39%) coursed with sequelae or died. The mean period of neurological attendance was 36.97 months and neurological alterations were detected in 16.17% of the patients. No significant difference was found between the four groups. There was also no statistical difference in the comparison of the neurological sequelae in the children from group IV with the children of groups I and II or even with groups I, II and III analyzed as a whole. The presence of hearing loss occurred in 11.11% of the patients, again there was no significant difference between the four groups. Psychological evaluation was performed using the WPSSI and WISC tests. A mild mental disability was detected in one patient from group I and another in group III. The overall analysis of the sequelae (neurological, auditory and intellectual level) also did not demonstrate any significant difference between the four groups. Comparing the children from groups I and II together and also groups I, II and III as a whole with the children in group IV also failed to detect a significant difference arising from the use or nonuse of the corticosteroid. **Conclusion:** Dexamethasone was not proven to be effective in decreasing the number of sequelae among patients with meningococcal meningitis.

KEY WORDS: sequelae, meningococcal meningitis, dexamethasone.

Seqüelas de meningite meningocócica em crianças: análise crítica da utilização da dexametasona

RESUMO - Objetivo: Avaliar a eficácia da dexametasona como uma terapia adjunta à antibioticoterapia em crianças com meningite meningocócica. **Método:** Foram avaliadas 81 crianças com diagnóstico de meningite meningocócica e hospitalizadas sequencialmente no Hospital Universitário da Universidade de São Paulo, com o objetivo de avaliar a presença de seqüelas em 4 diferentes grupos de pacientes, segundo a administração da dexametasona: Grupo I - 25 pacientes, que receberam a primeira dose pelo menos 10 minutos antes da introdução da antibioticoterapia; Grupo II - 19 pacientes que receberam o corticosteroide de modo concomitante à antibioticoterapia; Grupo III - 14 pacientes, nos quais a dexametasona foi administrada após o início do esquema antibiótico; Grupo IV - 23 pacientes que não receberam dexametasona. A avaliação das características clínicas e laboratoriais no momento da internação demonstrou que os 4 grupos poderiam ser considerados homogêneos. **Resultados:** Algum grau de seqüela ocorreu em 16 (26,22%) dos sobreviventes e 23 pacientes (28,39%) apresentaram seqüelas ou faleceram. O período médio de seguimento neurológico foi 36,97 meses e foram detectadas alterações neurológicas em 16,17% dos pacientes. Não se observaram diferenças significativas em relação a presença de seqüelas neurológicas entre os 4 grupos, não havendo também diferenças entre as crianças do grupo IV em relação ao agrupamento das crianças dos grupos I e II ou mesmo I, II e III. A presença de disacusia ocorreu em 11,11% dos pacientes, também não havendo diferenças entre os 4 grupos. A avaliação psicológica foi realizada através dos testes WPSSI and WISC. Foi detectada a presença de deficiência mental leve em um paciente do grupo I e em outro do grupo III. A avaliação global das seqüelas (neurológicas, auditivas e cognitivas) também não mostrou haver diferenças significativas entre os 4 grupos. A comparação conjunta das crianças dos grupos I e II e também dos grupos I, II e III com as do grupo IV, também não permitiu a verificação da presença de diferenças significativas em relação a utilização ou não do corticosteroide. **Conclusão:** A dexametasona não foi efetiva na redução de seqüelas em crianças com meningite meningocócica.

PALAVRAS-CHAVE: seqüelas, meningite meningocócica, dexametasona.

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Several therapeutic studies have discussed the role of corticosteroid as a factor responsible for the lower incidence of neurological or auditory disturbances among patients with bacterial meningitis¹⁻⁸. Analysis of these studies enables the conclusion that this occurs in meningitis caused by *Haemophilus influenzae* and possibly also due to *Streptococcus pneumoniae*, in children aged over 6 weeks^{2,4,5,9,10}. However, in relation to meningitis caused by *Neisseria meningitidis*, the few studies in the literature have not demonstrated any benefits arising from the use of corticosteroid and this has been the most frequent causal agent among the author's patients and responsible for an epidemic outbreak in São Paulo which began in February 1988, when its incidence crossed the confidence limits of the control diagram and where it has remained to date, with a mean of about 5-8 cases/100,000 inhabitants/year¹¹⁻¹³.

With the objective of evaluating the role of dexamethasone therapy in the treatment of the meningococcal meningitis, we studied children with this diagnosis, interned sequentially at the University Hospital of the University of São Paulo (HU-USP), from December 1987 to July 1994, in order to analyze the sequelae.

METHOD

Patients

All children were over six weeks of age and hospitalized at HU-USP with a diagnosis of meningococcal meningitis. This diagnosis was only established in those cases in which there was isolation of the bacterium in the cerebrospinal fluid (CSF), or in the blood, and in this last circumstance, only if there were more than 20 leukocytes/mm³ in the CSF. All the patients were treated with conventional antibiotic therapy, for a minimum period of seven days. Antibiotics were always administered intravenously, namely ampicillin, 400 mg/kg/day, divided into four daily doses and/or chloramphenicol, 100 mg/kg/day, four times a day, or; ceftriaxone, 100 mg/kg/day, in two doses a day (associated to the ampicillin for those under three months of age), or crystalline penicillin, 400,000 units/kg/day in four to six administrations.

Regarding the use of corticosteroid and the moment of its introduction, as an adjunctive therapy for bacterial meningitis, four different options were studied: Group I - Patients that received dexamethasone at least 10 minutes before the introduction of intravenous antibiotic therapy; Group II - Children that received dexamethasone concomitant with the start of the antibiotic scheme; Group III - Patients that received dexamethasone after beginning the antibiotic therapy; Group IV - Patients that did not receive dexamethasone as an adjunctive therapy.

The dexamethasone was administered at a dose of 0.6mg/kg/day, every 6 hours, for 4 days.

The children admitted after July 1989, received dexamethasone concomitant to or close to the first dose of the intravenous antibiotic therapy, a procedure at that time justified by the studies of Lebel et al.¹ and Mustafa et al.¹⁴. However, during the course of the study, the corticosteroid was introduced at least 10 minutes before the first antibiotic dose, based on new findings concerning the physiopathol-

ogy of the lesion as showed by Waagner et al.¹⁵, Odio et al.¹⁶ and Schaad et al.⁷.

The study started, in a prospective form, in July 1989. In order to create a control group, with patients who were not submitted to corticotherapy, patients hospitalized between December 1987 and June 1989 with the same diagnosis at HU-USP were also studied.

Evaluation of the homogeneity between the four groups, was performed in relation to the following three clinical scores of gravity: Herson and Todd¹⁶, Turini et al.¹⁷ and Tesoro and Selbst¹⁸. These evaluate, at the moment of the diagnosis, the disease duration, presence of petechiae, hemodynamic instability, level of conscience, meningeal signs and epileptic crises. The four groups were also compared in relation to their age, sex, race, nutritional state and to the previous occurrence of hospitalization due to fever, vomiting and convulsion. Blood cell count, hemoglobin, platelets, CSF leucocyte count, protein and glucose at admission were also analysed.

Procedures

Whenever possible, the children were submitted to initial neurological evaluation, within the first 24 hours after hospitalization and at regular intervals. With the objective of evaluating the neurological, psychological and auditory sequelae, they were followed-up in outpatient consultations.

The neurological evaluation was always performed by the same neurologist and those children under four years of age, besides the neurological exam, were also assessed using the growth scale of Gesell and Amatruda¹⁹, thus enabling the Quotient of Development (QD) to be established.

Learning difficulties was investigated among the patients older than six years of age. A teacher's report usually pointed the difficulties observed; parents observations on concentration disturbances and the children's exercise books were analyzed. Behavioral disorder was defined as any change in the child's usual conduct, characterized by aggressiveness, excessive crying or attention deficit. Epileptic crises were considered as sequelae when they occurred after hospital discharge.

Evaluation of auditory acuity was performed in 63 out-patients, using behavioral or tonal audiometry, immitance measurements and brainstem evoked responses, with determination of the hearing threshold. Behavioral audiometry was performed in non-collaborative patients or those under two years of age, according to the methodology of Northern and Downs²⁰. The results of hearing evaluations were classified, according to Davis²¹ as - normal: 0 to 25 dB; mild hearing loss: 26 to 40 dB; moderate hearing loss: 41 to 70 dB; severe hearing loss: 71 to 90 dB and profound hearing loss: above 91 dB. The audiologists were not informed which patients received or not corticosteroid therapy. The psychological evaluation was performed at least three months after hospital discharge, with the objective of evaluating the Intelligence Quotient (IQ). The patients aged between three years and 11 months to six years and seven months at the moment of the evaluation, were submitted to psychological evaluation, using the Wechsler Preschool and Primary Scale of Intelligence (WPPSI), while those over six years and seven months old, were assessed by the Wechsler Intelligence Scale for Children (WISC). These tests were not appropriate for one of the patients who presented major retardation in the neuropsychomotor development

and serious bilateral hearing deficit, consequently this patient was also submitted to the Stanford-Binet Intelligence Scale Tests. The criteria of the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)²² were used classifying the gravity of the mental impairment, based on the evaluation of IQ, as follows: deficiency - IQ from 55 to 69; moderate deficiency - IQ between 40 and 55; severe deficiency - IQ of 25 to 40; and profound deficiency - IQ below 25. Again the psychologists responsible for the cognitive assessment were not informed which patients had been administered corticosteroid.

According to the relatively small number of sequelae in each individual section (neurological, auditory and intellectual), and to achieve a better comparison of the therapeutic groups, regarding the use of dexamethasone, a modified criterion of Sell et al.²³ was used and patients were grouped in four categories according to their long term course as follows: a. without sequelae: IQ > 70; without significant neurological or auditory alterations; without epileptic crises or serious behavioral disturbances. b. slight sequelae: slight alteration in hearing or speech, or; behavioral problems (with IQ > 70) or; learning difficulty. c. moderate sequelae: IQ between 50 and 69, or; epileptic crises requiring medication, or; moderate auditory deficit, or; motor deficit, or; partial alterations in vision. d. severe sequelae: IQ < 50, or patient totally dependent. The patients with preexistent conditions, such as epileptic crises and congenital anomalies associated to developmental impairments were excluded from this analysis.

The patients included in the study were classified according to the criteria of the Brazilian Association of Market Research (five socioeconomic classes) and also in relation to the level of maternal education.

Statistical analysis was accomplished using the Statistical Packages for Social Sciences software (SPSSPC+, -5.0) and LOTUS 123 and FOX-PRO-2.0 database software. For comparison of the categorical variables, the non-corrected chi-square test was used for the contingency tables with Yates correction whenever the expected frequencies were less than five, or when the chi square was only slightly significant. In the test for difference between groups with continuous variables and scores, the Kruskal-Wallis test was applied. For all tests, the significance level was set at $p = 0.05$ for rejection of the null hypothesis.

RESULTS

A total of 81 patients with a diagnosis of meningococcal meningitis was analyzed, of these 40 (49.38%) were male and 41 (50.62%) females. The patients' age varied from two to 150 months, with a mean of 44.17 and median of 33 months. The patients' distribution in the groups was as follows: Group I - 25 children; Group II - 19 children; Group III - 14 children, and Group IV - 23 children.

There was a prevalence of children aged under 48 months (59.25%), but there was no significant difference in the distribution by age group in the four therapeutic groups. Homogeneity was also verified in the four therapeutic groups in relation to the level of severity of symptoms assessed by the three clinical scores of gravity (Table 1), level of mothers' education and their distribution according to socioeconomic class.

The four groups of patients were homogeneous in terms

of the findings from the blood count (hemoglobin and leukocytes) and in the CSF (cells, glucose and protein) (Table 2).

There were seven deaths (8.64%), all of which occurred in the first 24 hours of hospitalization and were related to a picture of septicemia, with cardiovascular and coagulation disturbances. Five children presented a normal neurological exam at hospital discharge, but failed to return for reevaluation by the neurologist and consequently were not included in the analysis of the sequelae. Hearing evaluation was not performed in another six children. The IQ tests were not performed in three patients, besides the children that did not return for any consultation and in those one under three years and 11 months of age.

The presence of some form of sequel was detected in 16 patients corresponding to 26.22% of the 61 patients that completed the neurological, psychometric and auditory evaluations. Of the 81 children included initially, at least 28.39% coursed with sequelae or died.

The neurological follow up was completed by 69 patients, with a mean out-patient attendance of 36.97 months (median, 34.50 months). One patient was excluded from the analyses, a patient with delayed development identified prior to the onset of meningeal infection. The alterations detected are summarized in Table 3. Due to the small number of neurological sequelae it was not possible to identify significant differences between the four therapeutic groups. Furthermore, no statistical differences were found between the age at the moment of diagnosis or a given serologic group and the presence of sequelae.

The presence of hearing impairment related to the four therapeutic groups is shown in Table 4. Auditory evaluation was performed in 63 children, with a mean audiological follow-up of 33.57 months (mean, 29 months); one patient, with a profound hearing loss in the left ear was excluded from the analysis as this problem was already present before hospitalization to treat the meningitis. The statistical analysis did not demonstrate a significant difference between the incidence of dysacusia and any therapeutic group.

IQ tests were performed in 44 patients. The presence of mental deficiency was found in only two patients, one belonging to group I and the other to group III.

Table 5 analyzes the presence of all researched sequelae (neurological, mental and auditory impairment) in the patients studied. From the 74 survivors, 61 children were evaluated in the three areas and the presence of some type of alteration was detected in 16 children (26.22%).

The statistical analyses did not show any significant differences between the four therapeutic groups; the same occurred when comparing the evaluation of groups I and II together (18.18% with sequelae) with those of group IV (31.25% with sequelae). The presence of sequelae in all the patients that received dexamethasone (groups I, II and III) was 24.44%, which was again similar to the patients of the con-

Table 1. Clinical characteristics at admission of 81 patients with meningococcal meningitis, according to therapeutic group.

| | Dexamethasone | | | | Total (n=81) |
|---------------------------------|-----------------------|------------------------|------------------------|-------------------------|-----------------|
| | Before I (n=25) | During II (n=19) | After III (n=14) | Control IV (n=23) | |
| Fever | 24 (96.00%) | 18 (94.74%) | 14 (100%) | 22 (95.65%) | 78 (96.30%) |
| Meningeal signs | 20 (80.00%) | 16 (84.21%) | 12 (85.71%) | 20 (86.96%) | 68 (83.95%) |
| Duration of disease: > 3 days | 1 (4.00%) | 3 (15.79%) | 2 (14.29%) | 1 (4.35%) | 7 (8.64%) |
| < 1 day | 0 (0%) | 0 (0%) | 0 (0%) | 1 (4.35%) | 1 (1.23%) |
| Seizures | 5 (20.00%) | 2 (10.53%) | 3 (21.43%) | 4 (17.39%) | 14 (17.28%) |
| Motor disturbances | 0 (0%) | 3 (15.79%) | 2 (14.29%) | 1 (4.35%) | 6 (7.41%) |
| Prostration | 13 (52.00%) | 13 (68.42%) | 8 (57.14%) | 11 (47.83%) | 45 (55.56%) |
| Coma | 0 (0%) | 1 (5.26%) | 0 (0%) | 1 (4.35%) | 2 (2.47%) |
| Hemodynamic instability | 3 (12.00%) | 4 (21.05%) | 0 (0%) | 8 (34.78%) | 15 (18.52%) |
| Cutaneous signs | 18 (72.00%) | 9 (47.37%) | 5 (35.71%) | 17 (73.91%) | 49 (60.49%) |
| Herson and Todd gravity score | | | | | |
| Mean | 1.84 | 2.08 | 2.43 | 2.37 | 2.15 |
| Median | 2.00 | 1.75 | 2.25 | 2.00 | 2.00 |
| Standard deviation | 1.31 | 1.78 | 1.30 | 1.54 | 1.48 |
| Turini gravity score | | | | | |
| Mean | 1.60 | 1.28 | 1.86 | 1.65 | 1.59 |
| Median | 1.00 | 1.00 | 2.00 | 1.00 | 1.00 |
| Standard deviation | 1.04 | 1.07 | 0.77 | 1.03 | 1.00 |
| Tesoro and Selbst gravity score | | | | | |
| Mean | 1.32 | 1.28 | 1.00 | 1.52 | 1.31 |
| Median | 1.00 | 1.00 | 1.00 | 1.00 | 1.00 |
| Standard deviation | 1.03 | 0.89 | 0.78 | 1.27 | 1.04 |

control group (group IV), with 31.25% presenting sequelae.

The evaluation of only the most intense sequelae, more easily attributed to the meningitis and classified according to the method of Sell et al.²³ as moderate (there were no cases of serious sequelae in this population), occurring in 15% of the patients in group I, 15.38% of the children in group II, 25% of the patients in group III and 12.50% of those in group IV, also did not demonstrate any significant differences between the groups. Analyzing the children that received dexamethasone concomitantly, before or close to the beginning of the

antibiotic therapy (groups I and II), of which 18.51% presented moderate sequelae and groups I, II and III (23.52% with moderate sequelae) also failed to detect any significant differences from those patients that did not receive dexamethasone.

DISCUSSION

Despite the experimental demonstration of the therapeutic action of dexamethasone in bacterial meningitis, clinical expe-

Table 2. Laboratorial characteristics of the 81 patients, at their admission and according to the therapeutic group.

| | Dexamethasone | | | | Total (n=81) |
|--------------------------------|-----------------------|------------------------|------------------------|-------------------------|-----------------|
| | Before I (n=25) | During II (n=19) | After III (n=14) | Control IV (n=23) | |
| <i>I - Hemogram Hb (g%)</i> | | | | | |
| Mean | 10.8 | 9.6 | 10.3 | 10.3 | 10.3 |
| Median | 11.0 | 10.1 | 10.3 | 10.2 | 10.4 |
| Standard deviation | 2.2 | 2.7 | 0.9 | 1.4 | 2.0 |
| Leukocytes (/mm ³) | | | | | |
| Mean | 15392.0 | 16508.2 | 11850.0 | 14921.7 | 14867.6 |
| Median | 13600.0 | 13700.0 | 8300.0 | 15000.0 | 13700.0 |
| Standard deviation | 7657.9 | 8832.8 | 7959.0 | 6795.0 | 7742.0 |
| <i>II - CSF</i> | | | | | |
| Leukocytes (/mm ³) | | | | | |
| Mean | 6925.3 | 5620.3 | 9653.5 | 3100.8 | 6041.1 |
| Median | 3820.0 | 4181.0 | 2463.5 | 866.5 | 2503.0 |
| Standard deviation | 11731.4 | 6417.4 | 17968.2 | 6359.1 | 10958.2 |
| Protein (mg/dl) | | | | | |
| Mean | 239.5 | 412.6 | 265.0 | 167.8 | 262.3 |
| Median | 198.0 | 180.0 | 259.0 | 53.0 | 199.0 |
| Standard deviation | 152.0 | 822.2 | 146.1 | 185.8 | 416.6 |
| Glucose (mg/dl) | | | | | |
| Mean | 30.0 | 26.7 | 20.4 | 45.5 | 32.0 |
| Median | 25.0 | 16.0 | 7.5 | 54.0 | 21.0 |
| Standard deviation | 27.2 | 31.3 | 25.1 | 32.4 | 30.3 |

rience in human beings has presented limited results. In spite of the beneficial results reported by some studies in childhood meningitis due to *S. pneumoniae* and mainly *H. influenzae*^{1,2,4,5,9}, there are still no conclusive answers in relation to the action of corticosteroid in decreasing the degree of sequelae in meningitis caused by *N. meningitidis*⁹.

The main limitation of the present study lies in the fact that a randomized and blind distribution was not effected. Nevertheless, the patients analyzed came from the same area of the city of São Paulo, with a similar distribution among the different therapeutic groups in relation to several parameters, such as nutritional state, age group, socioeconomic class and level of maternal education. Analysis of the laboratory and clinical parameters, including indexes for the prognosis of gravity, at the moment of hospitalization also demonstrated a homogeneity between the various therapeutics groups. Thus, the sample of patients was an appropriate population for evaluating the therapeutic effectiveness of dexamethasone.

Out of the 74 survivors, it was possible to evaluate 69 children (93.24%) as out-patients for a mean period of 36.97 months after hospital discharge (median = 34.50 months); 63

patients (85.13%) underwent an audiological assessment for a mean time of 33.57 months (median = 29 months) and 66 children (89.18%) were appraised using the IQ tests (WPPSI and WISC) or QD test (Gesell and Amatruda).

At the end of the research, some degree of alteration was detected in relation to motor deficit, epileptic seizures, delayed neuropsychomotor development, behavioral disturbance, learning disturbance, language disorder, mental or hearing impairments in 16 of the 61 (26.22%) children that were submitted to the complete evaluation, including the audiological, psychological and neurological tests. Hence, considering the total sample of 81 patients, 24 (29.62%) coursed with some of the above mentioned disturbances or died.

Hearing loss was confirmed in seven patients (11.29%) of the 62 patients assessed. This incidence is in agreement with the findings of other studies, in relation to meningococcal meningitis treated conventionally without the use of corticosteroid²⁴⁻²⁶.

In the present study, hearing loss was most frequent in group III, in which four patients (36.36%) presented dysacusia. On

Table 3. Presence of neurological sequelae, according to therapeutic group.

| | Dexamethasone | | | | Total (n=68) |
|-----------------------|-----------------------|------------------------|------------------------|-------------------------|-----------------|
| | Before I (n=23) | During II (n=14) | After III (n=14) | Control IV (n=17) | |
| Neurological sequelae | | | | | |
| Motor disabilities | 0 (0%) | 1 (7.14%) | 0 (0%) | 1 (5.88%) | 2 (2.94%) |
| Epileptic seizures | 0 (0%) | 0 (0%) | 0 (0%) | 1 (5.88%) | 1 (1.47%) |
| Behavioral problems | 1 (4.35%) | 1 (7.14%) | 1 (7.14%) | 1 (5.88%) | 5 (7.35%) |
| Learning disabilities | 1 (4.35%) | 1 (7.14%) | 0 (0%) | 2 (11.76%) | 4 (5.88%) |
| Developmental delay | 1 (4.35%) | 2 (14.29%) | 1 (7.14%) | 1 (5.88%) | 5 (7.35%) |
| Language disorders | 1 (4.54%) | 1 (8.33%) | 1 (11.11%) | 2 (11.76%) | 5 (7.81%) |
| Duration of follow-up | | | | | |
| Mean | 24.83 | 36.57 | 33.71 | 56.41 | 36.97 |
| Median | 20.00 | 39.50 | 34.00 | 70.00 | 34.50 |
| Standard deviation | 18.78 | 15.77 | 22.00 | 26.06 | 23.85 |

comparing the incidence of cases of hearing alteration among the children from group III with those of group I: 4.76%, group II: 14.29%, and group IV: no case, no statistically significant difference was detected at the 5% confidence limit.

Analyzing all the sequelae as a whole (neurological, auditory and cognitive), as shown in Table 5, also did not allow the characterization of any effect from the dexamethasone in the therapeutics for meningococcal meningitis in these patients.

These data demonstrate the absence of benefit from the corticosteroid in terms of decreasing the sequelae, suggesting that with regard to meningococcal meningitis adjunctive therapy with dexamethasone is not so effective as the results of the research by Lebel et al.¹, Odio et al.⁵ demonstrated in relation to *H. influenzae*.

Consequently, based on this study and also the absence of proven benefits from the use of corticosteroid in meningococcal meningitis in other researches, we suggest that dexamethasone should be removed from the therapeutics of patients with meningitis, when this causal agent is identified. We consider that the pathophysiology of meningitis caused by *N. meningitidis* is similar to that due to *S. pneumoniae* and *H. influenzae*, however with a much greater rapidity in triggering the chain reaction that eventually causes lesions of the nervous system. Thus, even with precocious therapeutic there is no longer sufficient time available for the action of dexamethasone in the sense of reducing the liberation of cytokines

and their consequences, such as: the expression of adhesion glycoproteins between the polymorphonuclear and endothelial cells; the action of phospholipase A2 and nitric oxide synthase, among others^{27,28}. This must be the same reason that explains the lesser effect of corticosteroid in the clinical trials (even in meningitis caused by *S. pneumoniae* and *H. influenzae*)^{1,2,5}, in relation to studies and experiments with animal models, in which there is greater control of the onset of the infection and administration of dexamethasone²⁹⁻³².

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Table 4. Presence of auditory sequelae, according to therapeutic group.

| | Dexamethasone | | | Control IV (n=16) | Total (n=62) |
|-----------------------|-----------------------|------------------------|------------------------|-------------------------|-----------------|
| | Before I (n=21) | During II (n=14) | After III (n=11) | | |
| Auditory evaluation | | | | | |
| Hearing loss | 1 (4.76%) | 2 (14.29%) | 4 (36.36%) | 0 (0%) | 7 (11.29%) |
| Mild | 0 (0%) | 0 (0.00%) | 1 (25.00%) | 0 (0%) | 1 (14.29%) |
| Moderate | 0 (0%) | 1 (50.00%) | 0 (0%) | 0 (0%) | 1 (14.29%) |
| Severe/profound | 1 (100%) | 1 (50.00%) | 3 (75.00%) | 0 (0%) | 5 (71.43%) |
| Duration of follow-up | | | | | |
| Mean | 22.00 | 30.21 | 33.09 | 51.31 | 33.57 |
| Median | 17.50 | 32.50 | 29.00 | 68.00 | 29.00 |
| Standard deviation | 18.75 | 17.69 | 23.33 | 28.75 | 24.65 |

Hearing loss: mild 26 to 40 dB, moderate 41 to 70 dB, severe 71 to 90 dB, profound above 91 dB.

Table 5. Presence of sequelae, according to the modified scale of Sell, according to therapeutic group.

| | Dexamethasone | | | Control IV (n=16) | Total (n=61) |
|---------------|-----------------------|------------------------|------------------------|-------------------------|-----------------|
| | Before I (n=20) | During II (n=13) | After III (n=12) | | |
| Normal | 17 (85.00%) | 10 (76.92%) | 7 (58.33%) | 11 (68.75%) | 45 (73.77%) |
| Sequelae Mild | 0 (0%) | 1 (7.69%) | 2 (16.67%) | 3 (18.75%) | 6 (9.84%) |
| Moderate | 3 (15.00%) | 2 (15.38%) | 3 (25.00%) | 2 (12.50%) | 10 (16.39%) |

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