International Centre for Allied Health Evidence

University of South Australia

International Centre for Allied Health Evidence

iCAHE

A member of the Sansom Institute

*i*CAHE JC Critical Appraisal Summary

Journal Club Details

Journal Club location	**Womens and Children's**
JC Facilitator	**Lisa Callahan**
JC Discipline	**Audiology**

Question

Can early treatment of congenital CMV reduce the likelihood or severity of hearing loss in newborns?

Review Question/PICO/PACO

P – Infants, children, newborns, neonates
I – Early diagnosis and treatment of congenital CMV
C – Later diagnosis and treatment of congenital CMV
O – Presence/severity of hearing loss

Article/Paper

Kimberlin DW, Lin CY, Sánchez PJ, Demmler GJ, Dankner W, Shelton M, Jacobs RF, Vaudry W, Pass RF, Kiell JM, Soong SJ. Effect of ganciclovir therapy on hearing in symptomatic congenital cytomegalovirus disease involving the central nervous system: a randomized, controlled trial. The Journal of pediatrics. 2003 Jul 31;143(1):16-25.

Please note: due to copyright regulations CAHE is unable to supply a copy of the critically appraised paper/article. If you are an employee of the South Australian government you can obtain a copy of articles from the DOHSA librarian.

Article Methodology:

Click here to access critical appraisal tool

International Centre for Allied Health Evidence (iCAHE)

CONTACTS
www.unisa.edu.au/cahe
iCAHE@unisa.edu.au
Telephone: +61 8 830 22099
Fax: +61 8 830 22853

University of South Australia
GPO Box 2471
Adelaide SA 5001
Australia

CRICOS Provider Number 00121B

University of South Australia

International Centre for Allied Health Evidence
iCAHE

A member of the Sansom Institute

Ques No.	Yes	Can't Tell	No	Comments
1	✓			**Did the trial address a clearly focused issue?** Effect of Ganciclovir Therapy on hearing in Symptomatic Congenital Cytomegalovirus disease involving the central nervous system: A randomized controlled trial.
2	✓			**Was the assignment of patients to treatments randomised?** Neonates with symptomatic CMV disease involving the central nervous system were randomly assigned to receive 6 weeks of intravenous ganciclovir versus no treatment. The primary end point was improved brainstem-evoked response (BSER) between baseline and 6-month follow-up (or, for patients with normal baseline hearing, normal BSER at both time points).
3	✓			**Were all of the patients who entered the trial properly accounted for at its conclusion?** A total of 42 patients meeting all entry criteria were available for assessment of hearing change in the best ear at 6 months. Of these, 25 received ganciclovir and 17 received no treatment. For the biological total ear hearing evaluation, there were 85 ears with both baseline and 6-month BSER assessments, with 49 ears from ganciclovir recipients and 36 ears from control patients. Out of the total patients that met inclusion criteria nine died during the course of the study: 3 were in the ganciclovir group and 6 were in the control group (P = .31). No death was related to complications of study drug. Causes of death for the 3 ganciclovir recipients included complications of CMV, necrotizing enterocolitis, and cardiopulmonary arrest. **Is it worth continuing?** Yes
4			✓	**Were patients, health workers and study personnel 'blind' to treatment?** It is not reported whether patients, health workers and study personnel were 'blind' to the treatment.
5	✓			**Were the groups similar at the start of the trial?** Neonates with symptomatic (clinically apparent disease in the newborn period) congenital CMV disease involving the CNS were eligible for enrolment into this trial. All study subjects had confirmed isolation of CMV from a urine specimen obtained before study enrolment and within the first month of life,15 and all had evidence of CNS disease, such as (1) microcephaly; (2) intracranial calcifications; (3) abnormal cerebrospinal fluid (CSF) for age; (4) chorioretinitis; and/or (5) hearing deficits. Infants ≤1 month of age, ≥32 weeks' gestation, and weighing ≥1200 g at birth were eligible for study participation. Patients were ineligible for the study if death was imminent, if they received other antiviral agents or immune globulin, had creatinine >1.5 mg/dL, were HIVinfected, or had hydranencephaly.

International Centre for Allied Health Evidence (iCAHE)

CONTACTS
www.unisa.edu.au/cahe
iCAHE@unisa.edu.au
Telephone: +61 8 830 22099
Fax: +61 8 830 22853

University of South Australia
GPO Box 2471
Adelaide SA 5001
Australia

CRICOS Provider Number 00121B

University of South Australia

International Centre for Allied Health Evidence iCAHE

A member of the Sansom Institute

6		✓		**Aside from the experimental intervention, were the groups treated equally?** Patients randomly assigned to receive ganciclovir therapy had laboratory assessments for drug toxicity (complete blood counts, alanine aminotransferase [ALT], bilirubin, uric acid, creatinine) performed at study entry and on days 3, 5, 7, 10, 14, 17, 21, 28, 35, and 42. Patients randomly assigned to no therapy had laboratory assessments obtained weekly. Toxicity assessments were quantified with the use of the NIAID Division of AIDS Toxicity Tables, 1994.
7				**What are the results? How large was the treatment effect?** From 1991 to 1999, 100 patients were enrolled. Of these, 42 patients had both a baseline and 6-month follow-up BSER audiometric examination and thus were evaluable for the primary end point. Twenty-one (84%) of 25 ganciclovir recipients had improved hearing or maintained normal hearing between baseline and 6 months versus 10 (59%) of 17 control patients (P = .06). None (0%) of 25 ganciclovir recipients had worsening in hearing between baseline and 6 months versus 7 (41%) of 17 control patients (P < .01). A total of 43 patients had a BSER at both baseline and at 1 year or beyond. Five (21%) of 24 ganciclovir recipients had worsening of hearing between baseline and $1 year versus 13 (68%) of 19 control patients (P < .01). A total of 89 patients had absolute neutrophil counts determined during the course of the study; 29 (63%) of 46 ganciclovir-treated patients had grade 3 or 4 neutropenia during treatment versus 9 (21%) of 43 control patients (P < .01).
8				**How precise was the estimate of the treatment effect?** P values and 95% confidence intervals
9	Journal Club to discuss			**Can the results be applied to the local population?** **CONTEXT ASSESSMENT (please refer to attached document)** – *Infrastructure* – *Available workforce (? Need for substitute workforce?)* – *Patient characteristics* – *Training and upskilling, accreditation, recognition* – *Ready access to information sources* – *Legislative, financial & systems support* – *Health service system, referral processes and decision-makers* – *Communication* – *Best ways of presenting information to different end-users* – *Availability of relevant equipment* – *Cultural acceptability of recommendations* – *Others*
10				**Were all important outcomes considered?**

11		**Are the benefits worth the harms and costs?**
12		**What do the study findings mean to practice (i.e. clinical practice, systems or processes)?**
13		**What are your next steps?** ***ADOPT, CONTEXTUALISE, ADAPT*** **And then (e.g. evaluate clinical practice against evidence-based recommendations; organise the next four journal club meetings around this topic to build the evidence base; organize training for staff, etc.)**
14		**What is required to implement these next steps?**

International Centre for Allied Health Evidence (*i*CAHE)

CONTACTS
www.unisa.edu.au/cahe
iCAHE@unisa.edu.au
Telephone: +61 8 830 22099
Fax: +61 8 830 22853

University of South Australia
GPO Box 2471
Adelaide SA 5001
Australia

CRICOS Provider Number 00121B

University of South Australia

International Centre for Allied Health Evidence *i*CAHE

A member of the Sansom Institute