Cardiol Young 2007; 17: 185–188

ISSN 1047-9511
doi: 10.1017/S1047951107000224

Original Article

Influence of chronic intrauterine exposure to alcohol on structurally normal hearts

Thomas Krasemann,[1,2] Sandra Klingebiel[1]

[1]*Deptartment of Pediatric Cardiology, University Children's Hospital Muenster, Muenster, Germany;* [2]*Evelina Children's Hospital, St. Thomas Hospital, London, United Kingdom*

Abstract Abuse of alcohol during pregnancy is known to cause alcoholic embryopathy and congenital cardiac disease. We sought to establish if there were any cardiac abnormalities to be found in patients known to have alcoholic embryopathy, but with structurally normal hearts. We reviewed the electrocardiograms and echocardiographic data of 347 such patients without congenital cardiac disease. A shortened QT interval was found in half of the cases. The left ventricular diameter was small in one quarter of all patients, independent from age, gender, and the degree of alcoholic embryopathy. We conclude that intrauterine exposure to alcohol as a primary toxin can lead to minor cardiac abnormalities, even in the absence of structural congenital cardiac disease.

Keywords: Embryo; cardiac development; echocardiography; QT interval

It is known that chronic maternal intake of alcohol during pregnancy leads to the signs of alcoholic embryopathy in the newborn. Various clinical signs have been described, and led to a classification with different degrees of embryopathy, ranging from patients with minor affection, the so called "alcohol effects", to the most severely affected individuals considered to have the third degree of alcoholic embryopathy[1] (see Table 1). Up to one-third of the affected individuals have congenital cardiac disease.[2] This is not related to the amount of alcohol consumed during pregnancy.[2]

Adults can also develop alcoholic cardiomyopathy, with enlarged left ventricles and increased ventricular mass, due to chronic abuse of alcohol.[3] These findings are known to be partly reversible, with either abstinence or reduced daily alcoholic intake.[3] On the other hand, acute withdrawal of alcohol can cause alterations in the pattern of ventricular repolarization leading to sudden cardiac death.[4]

Until now, it has not been clear whether the cardiac function is altered in patients with alcoholic embryopathy but without congenital cardiac disease. These patients experience the effects of chronic alcoholic exposure during fetal life, and acute withdrawal at birth.

Methods

In a retrospective study of our comprehensive database spanning the 27 years from 1976 through 2003, we reviewed the electrocardiograms and echocardiographical data of all patients with the clinical signs of alcoholic embryopathy.

Patients were graded as having the first, second, or third degrees of alcoholic embryopathy,[1] or even lesser abnormalities, the so-called alcoholic effects[5] (see Table 1). We excluded all patients with congenital cardiac disease, apart from those with patency of the oval foramen.

All electrocardiograms and echocardiograms had been obtained for clinical reasons as part of the assessment or follow up for alcoholic embryopathy.

Correspondence to: Thomas Krasemann, MD, Evelina Children's Hospital, St. Thomas Hospital, Lambeth Palace Road, London SE1 7EH, United Kingdom. Tel: +44 20 7188 4562; Fax: +44 20 7188 4556; E-mail: Thomas.Krasemann@gstt.nhs.uk

Accepted for publication 31 May 2006

Table 1. Proposed modified[1] classification of alcoholic embryopathy based on a sum score ranking.

First degree	Greater than 40
Second degree	30–39
Third degree	10–29
Alcoholic effects	Less than 10

Physical symptom/sign	Incidence (%)	Score
Intrauterine growth retardation	89	4
Microcephaly	84	4
Gross motor delay	88	2–8
Hyperactivity disorder	70	4
Muscular hypotonia	59	2
Epicanthic folds	69	2
Ptosis	40	2
Blepharophimosis	11	2
Short nasal bridge	53	3
Nasolabial folds	71	1
Thin vermilion	62	1
Hypoplastic mandible	74	2
High arched palate	38	2
Cleft palate	7	4
Anomalous palmar creases	72	3
Clinodactyly V	54	2
Camptodactyly	17	2
Hypoplasia of the fingernails	13	1
Restricted supination	16	2
Hip subluxation	10	2
Congenital cardiac disease	29	4
Genital anomalies	47	2–4
Sacro-coccygeal dimple	46	1
Hernias	13	2
Urogenital system malformation	10	4

Echocardiographic measurements of left ventricular diastolic and systolic diameters were carried out in the short axis view, and fractional shortening was calculated. The left ventricular diameter was then corrected for body surface area.

The data were compared to normal values as reported in the literature.[6,7] To compare the differences of proportions, we calculated confidence intervals at 95% for samples of the Binomial distribution. We used the approximation of S. Wallenstein, in combination with the Yates correction for continuity.

Results

From our comprehensive database, we identified 499 patients with the clinical signs of alcoholic embryopathy, of whom 347 patients, 185 being male and 162 female, did not have congenital cardiac disease. They were aged from one month to 16 years. Of these patients, 468 electrocardiograms, 262 from males and 206 from females, and 261 echocardiograms, 123 from males and 129 from females, could be analysed retrospectively. The distribution into the different degrees of alcoholic embryopathy is shown in Tables 2 and 3.

Table 2. Electrocardiograms in patients with alcohol embryopathy.

Degree of alcohol embryopathy	Number
Alcoholic effects	156
First degree embryopathy	172
Second degree embryopathy	81
Third degree embryopathy	59

Table 3. Echocardiograms in patients with alcohol embryopathy.

Degree of alcohol embryopathy	Number
Alcoholic effects	114
First degree embryopathy	100
Second degree embryopathy	32
Third degree embryopathy	15

The analysis of the electrocardiograms revealed a shortened QRS-duration in 44% of all patients, independant of the degree of alcoholic embryopathy, age, and gender. Corrected QT-duration using Bazett's formula was shorter than age-related normal values in 52% of the males, and 55% of the affected females, independant of age and the degree of alcoholic embryopathy. The median QTc-duration of our patients with alcoholic embryopathy compared to normal values is depicted in Figure 1. Heart rate was below the normal range in 4% of the male and 8% of the female patients, and above the normal range in 13% of the male and 11% of the female patients. There were no significant differences of QRS-duration, corrected QT-interval and heart rate between the genders, or between those having different degrees of embryopathy. Only the male patients with third degree of embryopathy had a significantly shorter corrected QT-interval than the male individuals with only alcoholic effects.

The left ventricular diastolic diameter measured echocardiographically in M-mode was smaller, when compared to normal values, in 24% of the male and in 37% of the female patients. This was independant from the degree of embryopathy. The left ventricular diastolic diameters of our patients compared to normal values are shown in Figure 2.

The left ventricular systolic diameter was smaller in 18% of the male and 21% of the female patients, independant from age and degree of embryopathy. Fractional shortening was reduced in 8% of male patients, and increased in 13%. In female patients fractional shortening was reduced in 9% and increased in 14%. There were no differences between the sexes or the degree of alcoholic embryopathy.

https://doi.org/10.1017/S1047951107000224 Published online by Cambridge University Press

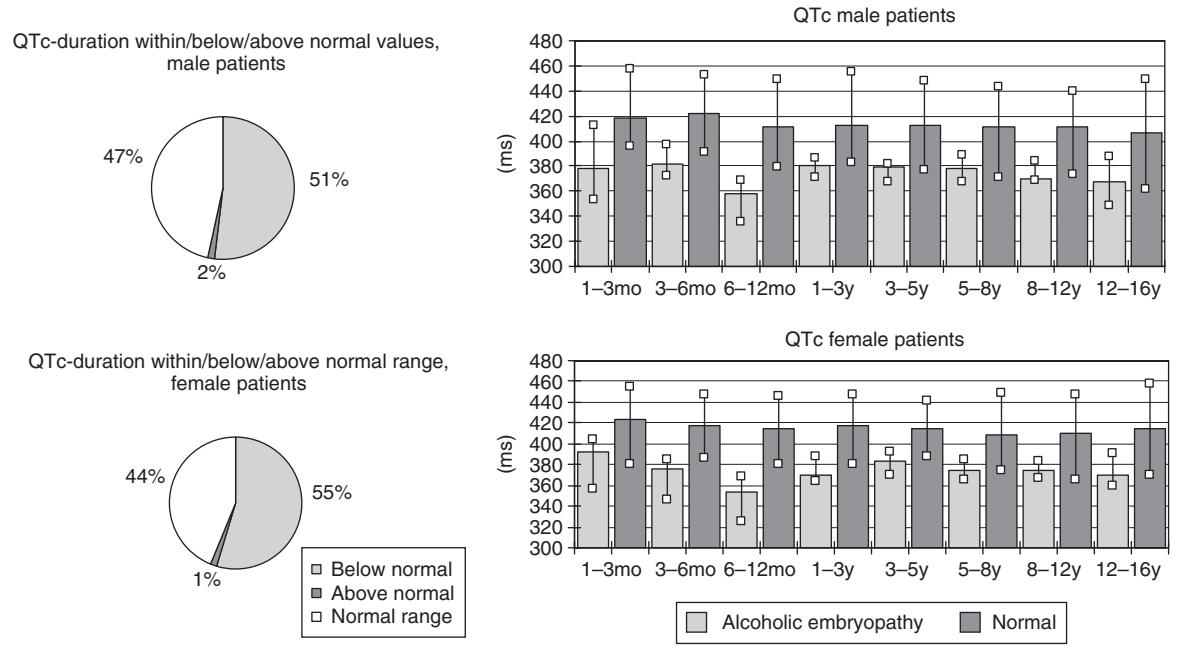

Figure 1.
QT duration in children with alcoholic embryopathy compared to normal values, related to age according to {6}.

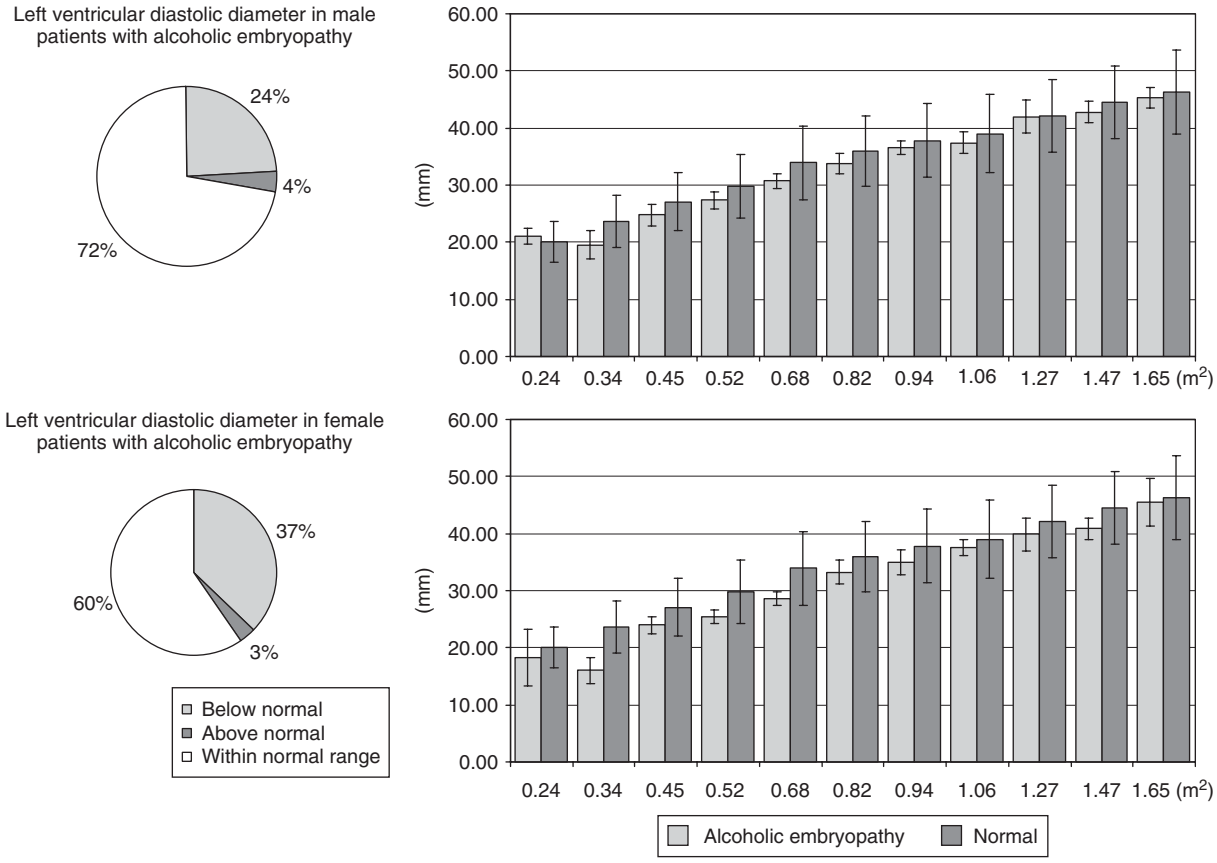

Figure 2.
Left ventricular diastolic diameter in children with alcoholic embryopathy compared to normal values, related to body surface area according to {7}.

https://doi.org/10.1017/S1047951107000224 Published online by Cambridge University Press

Discussion

Our study shows that echocardiographic and electrocardiographic measurements often show slightly altered values in patients with alcoholic embryopathy without congenital cardiac disease, independent of gender, age, and degree of alcoholic embryopathy.

In studies using rats, alcohol given during pregnancy is a primary toxin for the developing organism, consistently leading to reduced cardiac mass and depressed function, even when the affected animals reached adulthood.[8] In such rats microstructural changes of the myocytes were found after exposure to alcohol during pregnancy.[9,10] Other experimental studies using chick embryos showed that the degree of myocytic damage is dependant on the genetic background.[11]

It might be suspected that the reduced left ventricular diameter is related to retardation of growth, which is common in those with alcoholic embryopathy.[5] We related the left ventricular diameter to the body surface area, thus ruling out these effects.

Interestingly, shortened QRS- and QTc-durations are very common in patients with alcoholic embryopathy with structurally normal hearts, as are smaller left ventricular diameters. The electrocardiographic changes might be caused by a smaller ventricle, but this is speculative. On the other hand, this is comparable to the findings of the studies in rats.[8]

There are no signs of alcoholic cardiomyopathy as seen in adult alcoholics.[3] Other than in alcoholic embryopathy, the changes in these adults occur after the heart has developed, due to the secondary toxicity of alcohol. In these individuals, cardiac function improved after withdrawal of the toxin.[3]

In our patients the diminished left ventricular diameter and shortened QT duration are constantly seen in all age groups after intrauterine exposure to alcohol. There was no evidence of secondary long term effects due to withdrawal after birth. Only one newborn developed disturbances of rhythm immediately after birth, which probably were related to withdrawal.[12] The effects of primary and secondary alcoholic toxicity seemed be combined in this patient.

Of course, our study has its limitations: We compared our data to a historical group from the literature, not to data acquired in our institution. On the other hand, this is a retrospective study, with data collected from 1976 until 2003. The data was obtained in the same way as described in the literature.[7]

We conclude that intrauterine exposure to alcohol as a primary toxin can lead to minor cardiac abnormalities, even in the absence of structural congenital cardiac disease.

Dedication

We dedicate this manuscript to Hermann Loser, who collected most of the data, and died too early.

References

1. Loser H, Pfefferkorn JR, Themann H. Alkohol in der Schwangerschaft und kindliche Herzschaeden. Klin Padiatr 1992; 204: 335–339.
2. Nicolas JM, Fernandez-Sola J, Estruch R, et al. The effect of controlled drinking in alcoholic cardiomyopathy. Ann Intern Med 2002; 136: 192–200.
3. Day CP, James OFW, Butler TJ, Campbell RWF. QT prolongation and sudden cardiac death in patients with alcoholic liver disease. Lancet 1993; 341: 1423–1428.
4. Majewski F. Untersuchungen zur Alkoholembryopathie. Fortschr Med 1978; 96: 2207–2213.
5. Abel EL. Prenatal effects of alcohol. Drug Alcohol Depend 1984; 14: 1–10.
6. Rijnbeek PR, Witsenburg M, Schrama E, Hess J, Kors JA. New normal limits for the pediatric electrocardiogram. Eur Heart J 2001; 22: 702–711.
7. Henry WL, Ware J, Gardin JM, Hepner SI, McKay J, Weiner M. Echocardiographic measurements in normal subjects: growth related changes that occur between infancy and childhood. Circulation 1978; 57: 278–285.
8. Ren J, Wold LE, Natavio M, Ren BH, Hannigan JH, Brown RA. Influence of prenatal alcohol exposure on myocardial contractile function in adult rat hearts: role of intracellular calcium and apoptosis. Alcohol Alcohol 2002; 37: 30–37.
9. Fuseler JW. Maternal ethanol consumption induces transient compensatory hyperplasia of developing cardiac tissue in the neonatal rat. Alcohol Alcohol 1993; 28: 657–666.
10. Syslak PH, Nathaniel EJ, Novak C, Burton L. Fetal alcohol effects on the postnatal development of the rat myocardium: an ultrastructural and morphometric analysis. Exp Mol Pathol 1994: 60: 158–172.
11. Cavieres MF, Smith SM. Genetic and developmental modulation of cardiac deficits in prebatal alcohol exposure. Alcohol Clin Exp Res 2000; 24: 102–109.
12. Krasemann T. QT-prolongation in the newborn and maternal alcoholism. Cardiol Young 2004; 14: 565–566.