Neonatal cow milk sensitization in 143 case-reports: role of early exposure to cow’s milk formula

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Abstract. – Objective: Cow’s milk (CM) allergy (CMA) is a disease of infancy, usually appearing in the first months of life. Symptoms triggered by CM at first introduction are not completely defined. The evaluation of infants for possible CMA is one of the more common problems encountered by pediatricians. Purpose of this study was to investigate the prevalence of severe reaction to CM and clinical manifestation triggered by CM administration in the nurseries.

Materials and Methods: The series includes 143 prospectively studied CM-allergic babies.

Results: At the first introduction of CM, at the age of 1-8 months (median 4 months) all infants had immediate symptoms. The babies were probably sensitized during the first days of life. Particularly sensitizing appears to be the exposure to CM formulas in the neonatal nursery.

Discussion: Little doses of allergens are more sensitizing than larger ones. We provide clear evidence of the immunological effects of oral antigen administration during the neonatal period, and discuss the possible critical allergen transmission to the nursing baby via breast milk (BM).

Key Words: Cow’s milk allergy, Neonate, Neonatal nurseries, Severe reactions, CM sensitization, Breast milk.

Introduction

A major cause of sensitization to cow’s milk (CM) in genetically predisposed neonates is the inadvertent administration of CM in neonatal nurseries. Neonatal care should include 49-100% of such infants given supplements of CM or hydrolysate formulas (HFs) during the first 3-4 days of life1-5. Among these babies CM allergy (CMA) was more frequent6, until to 100% of infants, none of them had symptoms at the first CM administration7. Immediate reactions at the subsequent CM feeding bring into focus a delayed effect of the “hidden bottle”2. Høst et al3 documented that the 40-860 ml of CM received from 39 neonates during the first three days contained 0.4-7.4 g of β-lactoglobulin (β-LG). Feeding half of babies with a CM formula and half with HFs for 1-4 days and then with breast milk (BM), if necessary supplemented with HFs until the third month, total IgE titres were at the 5th day significantly related to the dose and frequency of supplements received (200-500 ml)7, maintaining significance until 12 months8, especially in at-risk babies.

In at-risk children, prospectively followed-up from birth during 18 months9 and re-evaluated at age 4-610, the cumulative prevalence of atopy was 18% in CM-fed or 33% in wholly BM-fed babies, in at-risk children the incidence was as high as 11 or 61%, respectively9. Newborns with 27-42 week gestational age and 2 SDs (standard deviation) below the mean normal weight at birth correspond to premature babies responding in a different manner to sensitization and onset of atopic manifestations. During the follow-up, the prevalence of atopy was nearly similar in both groups, yet skin prick tests (SPT) positive for CM significantly correlated with RAST only in CM-fed infants10. We have also studied four additional at risk infants who were exposed in the nursery to a first HF dose during their first days of life, and elicited acute allergic symptoms when fed again this HF at the end of an exclusive breastfeeding (data not shown).

Healthy newborns accidentally exposed to CM in a nursery develop a modest and transient antibody production (primary immune
response). Such initial responses are self-limit-
ed and gradually resolve due to development of
tolerance despite unremitting allergen ex-
positions. At the second encounter, CD4 clones
from non-atopic infants have a Th1 profile,
whereas in atopic infants provide help for IgE
synthesis (secondary immune response)\textsuperscript{11}.

Remarkably, there appears to be a consen-
sus that BM-feeding for at least 4-6 months
will delay, if not prevent allergy\textsuperscript{12-48}, although
a case of apparent sensitization via BM has
been reported\textsuperscript{48}.

**Materials and Methods**

We have prospectively studied 143 CM-al-
lergic babies, 79 males and 64 females aged 4-8
months (median 5 months) with IgE-mediated
CMA, who attended between June 1997 and
December 1999 the Allergy and Clinical
Immunology Division of Rome University “La
Sapienza” The diagnosis was based on SPTs,
all positive to CM, and oral food challenges
(OFCs) done in a hospital setting which were
positive to CM in 74 babies, to egg in one ba-
by, and to a HF in 50. In total, 125 out of 143
babies (87.4\%) were positive to OFCs.

Parents of each child gave details of their
allergic disease (if any) and their informed
consent. The babies were defined at risk of
atopy when at least one parent had or had
had diagnosed and treated atopic disease.

Data were statistically analyzed using the
Student t and the X\textsuperscript{2} tests.

**Results**

At the first introduction of CM, at the age
of 1-8 months (median 4 months) all infants
had immediate symptoms, as follows: ana-
phylactic shock (9 cases), urticaria-angioede-
ma (37 cases = 25.9\%), skin rash (13 cases =
9.1\%), diarrhea (25 cases = 17.5\%), vomiting
(19 cases = 13.3\%), respiratory manifesta-
tions (wheezing or rhinitis) (18 cases =
12.6\%), and worsening of atopic dermatitis
(AD) (59 cases = 41.2\%). Several children
had more than one allergic manifestation.

All children but twelve (82.8\%) had posi-
tive family history for atopy ($p = 0.0001$).

Only 10/143 infants (14.3\%) were fed CM
since birth; the other 133 were BM-fed for 3-
8 months (median 4.5 months). Two children
breastfed from birth were probably sensitized
to CM proteins present in BM since their
conditions improved when the nursing moth-
ers followed dietetic restrictions.

Analysing the clinical charts of the infants
and interviewing the parents, we learned that
135 (93\%) of the CM-allergic babies were fed
a CM formula in the neonatal nursery in the
first days of life ($p = 0.0001$).

**Discussion**

In this prospective study we learned that as
many as 133 newborns were fed CM in the
newborn nurseries, and this data tallies well
with previously alluded to studies. As a result
of OFCs, a larger proportion of babies
(41.2\%) had a worsening of AD symptoms,
however it is remarkable that 12.6\% present-
ed with respiratory manifestations.

As previously reported, there is a large con-
sensus that BM-feeding for at least 4-6 months
will delay, if not prevent allergy\textsuperscript{12-48}. A note of
cautions is their unmatched results owing to
methodological differences. Given that CM
and egg allergens are present in BM, it was al-
so thought that a maternal diet excluding the
above allergens may be important in atopy
prevention\textsuperscript{13,34,42}. A typical case was reported
by Lifschitz et al\textsuperscript{48}, an anaphylactic shock due
to CM protein hypersensitivity in a newborn
who was mistakenly fed BM that had been ex-
pressed before CM products were eliminated
from his mother’s diet, as it is correctly shown
in the title\textsuperscript{48}. More than 70 years ago Talbot\textsuperscript{49}
documented that AD in a fully breast-fed in-
fant could be related to chocolate ingested by
the mother, and that AD cleared up when the
nursing mother avoided the offending food, a
phenomenon recently confirmed\textsuperscript{3}.

However, IgE-mediated sensitization
through BM is rather rare: 0.042% \textsuperscript{50} or
0.28%\textsuperscript{3}. Therefore, inadvertent exposure to
CM appears to be far more important than the
very low CM amounts transmitted via BM\textsuperscript{51}. A
note regarding a study based on HFs for aller-
gy prevention\textsuperscript{17}: the frequency of BM-feeding
was high (98\%), and in 232 not randomized
such babies the incidence of CMA was 1.3%. The
study is far more important because new-
borns who received a CM formula in the nurs-
ery were not included into the program\textsuperscript{17}. We
have stressed the negative effects of the maternity wards. To avoid the possible risks it should be clearly stated that giving any formula in the first few days of life is strictly forbidden unless prescribed by a pediatrician or demanded by a mother who is unwilling or incapable to breastfeed her baby.

A new front was unexpectedly opened up by the significant report that a 22-week-old fetus responds to a great variety of oral and inhalant allergens including CM β-LG, and egg ovalbumin. That is why reducing intake of highly allergenic foods in the last trimester of pregnancy is mandated by a mother who is unwilling or incapable to breastfeed her baby.

In conclusion, as early as in 1935 Ratner recommended that isolated CM feedings be avoided during the newborn period.

References


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