

嬰兒乳粉與母乳中 β -內醯胺抗生素及重金屬之調查

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摘 要

本研究係調查嬰兒乳粉及母乳中 β -內醯胺抗生素(β -lactam antibiotics)及重金屬之污染情形。抗生素之檢測係採用生物分析法(bioassay)-*Bacillus stearothermophilus* disc method;而重金屬則以原子吸收光譜儀(atomic absorption spectrophotometer)予以測定。調查結果顯示嬰兒乳粉中並無抗生素之檢出。而母乳中則有抗生素之殘留,在接受抗生素(ampicillin及supercillin)治療之22位產婦中,在分娩後第3、第7及第14天,抗生素之檢出率分別為84.6%、22.7%及9.1%,抗生素之濃度則介於0.014-0.686 IU/ml之間。此結果顯示婦女育兒哺乳期間之用藥,需特別留心,以減少母乳中抗生素之污染,確保嬰兒的健康。至於重金屬方面,嬰兒乳粉中鉛、鎘、汞及砷的平均含量分別為 0.008 ± 0.019 ppm、 0.005 ± 0.007 ppm、 0.006 ± 0.008 ppm及 2.155 ± 3.380 ppb,此結果顯示受調查之嬰兒乳粉重金屬的污染在正常範圍內。而母乳中鉛、鎘、汞及砷的平均含量分別為 0.027 ± 0.029 ppm、 0.003 ± 0.003 ppm、 0.001 ± 0.004 ppm及 0.656 ± 2.346 ppb,此顯示受調查的產婦其母乳中重金屬含量均在正常範圍之內。

前 言

就國內生活環境而言,母乳或嬰兒乳粉為多數新生嬰兒唯一營養來源。然而由於人為因素或環境劣化,母乳或嬰兒乳粉或許有污染之虞,以致於影響嬰兒的健康。常見的污染物質包括藥物、重金屬、農藥及工業污染物等^(1,2)。母乳中抗生素的殘留,與孕婦體質以及藥物之施用狀況有關,藥物殘留程度則與母體藥物代謝能力、藥物理化性質以及投藥方式有關⁽²⁾。因此,一旦產婦接受抗生素之治療,母乳就有殘留之可能,至今已有多種抗生素在母乳中被檢出之報告⁽²⁾。抗生素對於嬰兒的傷害有致死休克(lethal shock)、出疹反應(anaphylatic reaction)及其他臨床性過敏疾病⁽³⁻⁵⁾。此外,也會破壞正常腸道菌叢之平衡,或者產生抗藥性不良反應。而過量抗生素對於嬰兒尚可能有拒絕餵食(refusal of nurse)、昏睡(sleepiness)、嘔吐(vomiting)以及出血性貧血(hemolytic anemia)等副作用⁽⁶⁻⁸⁾。因此,對於嬰兒乳粉及母乳中抗生素之殘留應加以重視。目前抗生素常用之分析方法為生物分析法(bioassay)中

濾紙平皿法(disc plate method),此法係採用*Bacillus subtilis*菌株⁽⁹⁾。而本研究則採用*Bacillus stearothermophilus*為測試菌株,此因該菌在抗生素分析上,具有藥物感受性(susceptibility)較強,靈敏度較佳,時間較短及不易有雜菌污染等優點⁽¹⁰⁾。母乳中重金屬的殘留,多因環境因素經由食物鏈污染所致。調查中顯示其污染程度與環境地理因素、孕婦的生活習慣及年齡有關⁽²⁾。母乳中殘留的重金屬,以汞、鎘及鉛為多見,大都因工業污染而來,而許多食物中也有微量存在^(2,11)。一般牛乳中鉛、鎘、汞及砷的含量分別為0.02-0.04 ppm,0.02-0.37 ppm,0.001-0.006 ppm及0.03-0.06 ppm^(2,11),而乳粉中鉛及鎘的含量為0.125-0.56 ppm⁽¹²⁾及0.02-0.31 ppm⁽²⁾。至於母乳中鉛、鎘、汞及砷的含量平均為0.021 ppm⁽¹³⁾、0.019 ppm⁽¹¹⁾、0.006 ppm⁽¹⁴⁾及3.74 ppb⁽²⁾。母乳及乳粉中重金屬的分析方法有電化學分析法⁽¹⁵⁾(electrochemical method)、中子活化分析法⁽¹⁶⁾(neutron activation method)及原子吸收光譜儀分析法⁽¹⁷⁻¹⁹⁾(atomic absorption spectrometry, AAS)。一般重金屬的檢測多採用AAS法,而AAS法又包括石墨爐原子吸收光譜儀

分析法⁽¹⁷⁾(graphite furnace AAS, GFAAS)、冷蒸氣原子吸收光譜儀分析法⁽¹⁸⁾(cold vapor AAS, CVAAS)及氫化物生成原子吸收光譜儀分析法⁽¹⁹⁾(hydride generation AAS, HGAAS)。由於母乳或嬰兒乳粉中鉛、鎘、汞及砷之含量甚低,同時理化性質不一,故必須考慮可能因樣品之消化前處理方式、藥品純度、容器材質或測定時儀器設定條件等因素,造成分析上的偏差。由於母乳中重金屬與抗生素對嬰兒會造成不良影響^(3-8,20),又因工作關係,許多婦女以乳粉取代母乳餵食嬰兒,故嬰兒乳粉之衛生安全應加以重視。本研究即針對部份國產及進口嬰兒乳粉及母乳中重金屬和 β -內醯胺抗生素(β -lactam antibiotics)之殘留現狀加以探討,以為參考。所謂 β -內醯胺抗生素指具有beta ring結構之抗生素ampicillin及supercillin都是beta-lactam antibiotics。由於此類抗生素廣泛應用於臨床產科,避免感染,是故本研究選擇此類抗生素為調查對象。關於母乳中上述二種物質污染之國內報告並不多。

材料與方法

一、嬰兒乳粉之來源

自民國77年8月起每季自市場隨機採購不同批號之國產3種品牌(A、B與C)以及進口3種品牌(D、E及F)之嬰兒乳粉各2罐,彼等出廠日期均在有效期限內。樣品於室溫下保存,於保存期間內完成樣品分析。

二、母乳之來源

自77年9月起由新竹國軍813醫院,進行母乳之採集,計40人。每位產婦採集3次,採集時間分別為分娩後第3天、第7天及第14天。每次約採取30-150 ml母乳。採集後,於冷凍狀態下保存。由於其中僅22人接受 β -內醯胺抗生素(ampicillin及supercillin)之處理,故抗生素之調查僅以此22人為對象。

三、抗生素之分析

採用 *Bacillus stearothermophilus* disc method⁽²¹⁻²³⁾。樣品前處理方法為母乳解凍後,80°C加熱5分鐘,破壞原有母乳中天然抗菌物質,加熱後立即以冰浴冷卻備用,而嬰兒乳粉則依標示固形分之含量,以無菌水稀釋還原後冷藏備用。製備培養用平板時,則取 *Bacillus stearothermophilus* 孢子懸浮液(Thermospore Suspension PM, Difco 1801-52-6, Detroit, MI)1 ml加入100 ml之 Bacto Antibiotic

Medium 4 (Difco 0263-01-4) 或 Bacto PM Indicator Agar (Difco 1800-15-3)中混合均勻,於9 cm平板中加入6 ml含有孢子之培養基,此培養基須於5日內用完。分析時,取直徑6 mm濾紙(disc)(Schleicher & Schuell Inc., Keene, NH),以微量吸管吸取20 μ l樣品液於濾紙上,俟其風乾後置於上述平板中培養(55°C, 3小時)。以游標尺測量抑菌環大小,每一平板中並且置放已知濃度之青黴素G (penicillin G, Sigma PEN-NA, St. Louis, MO),其濃度分別為0.01、0.025、0.05及0.1 IU/ml以定量樣品液中抗生素含量。若樣品中疑有青黴素存在時,則以青黴素酵素(penicillinase)處理該樣品加以確認之⁽²⁴⁾。本調查方法之disc method係針對beta-lactam antibiotics,由於此法為官方的方法,可用於定量。樣品之80°C加熱5分鐘的前處理,不會造成beta-lactam antibiotics之破壞。樣品中若有其他的抗生素之存在,可藉由penicillinase處理加以判斷。產婦經beta-lactam antibiotics處理,其母乳中有該類抗生素之機會較高;而嬰兒奶粉之原料乳中,也以beta-lactam antibiotics的殘留為較多見。調查中自然地也以beta-lactam antibiotics為主,但是疑有其他抗生素之存在,所以配合利用penicillinase處理,輔助判斷是否有其他抗生素之存在。當樣品之disc四周產生抑菌環時,表示其中有抑菌物質之存在。然後再經penicillinase處理,假如依然存有抑菌環,則表示此抑菌物質不是beta-lactam antibiotics;反之,無抑菌環之存在,則表示此抑菌物質是beta-lactam antibiotics。

四、重金屬之分析

計有40位產婦之母乳樣品。鉛與鎘之測定係採用高壓消化前處理方式⁽²⁵⁾,再經石墨爐(graphite furnace, Perkin-Elmer HGA-400, Norwalk, CT)之乾燥、灰化及原子化加熱處理後,以原子吸收光譜儀(atomic absorption spectrophotometer, Perkin-Elmer 603)予以測定⁽²⁶⁾。為避免基質干擾,測定時添加 $\text{NH}_4\text{H}_2\text{PO}_4$ 當做基質修飾劑(matrix modifier)。在分析汞時,其樣品前處理與鉛、鎘略同,唯添加2.5 ml硝酸與0.5 ml硫酸以及20-30 mg V_2O_5 替代3 ml硝酸⁽¹⁸⁾,再經冷蒸氣生成技術處理(cold vapor generation technique, Perkin-Elmer MHS-10)後,以原子吸收光譜儀予以測定⁽²⁸⁾。而砷之分析,其樣品前處理係採用濕式消化方式,再以氫化物生成法處理後,以原子吸收光譜儀予以測定⁽¹⁹⁾。為確定分析的可靠性,均採用標準參考物質(reference materials)-BCR No. 151 milk powder

Table 1. Residual antibiotics in human milk samples and drug treatment after parturition

Age (years)	Duration of Hospitalization (days)	Drugs Used*	Antibiotic Residue (IU/ml) at Days after Parturition		
			3	7	14
28	5	Sup	0.124	N.D.**	N.D.
29	5	Amp	0.152	N.D.	N.D.
25	7	Sup	0.034	N.D.	N.D.
27	4	Amp	0.016	N.D.	N.D.
24	8	Sup	0.686	0.164	N.D.
32	5	Amp	0.062	N.D.	N.D.
34	6	Amp	0.122	N.D.	N.D.
34	6	Sup	0.172	N.D.	N.D.
30	4	Sup	0.412	0.146	0.124
23	4	Amp	0.062	N.D.	N.D.
24	5	Sup	N.D.	N.D.	N.D.
26	4	Sup	N.D.	N.D.	N.D.
31	8	Amp	0.074	0.022	N.D.
30	6	Sup	0.524	N.D.	N.D.
29	4	Sup	0.064	N.D.	N.D.
27	4	Sup	0.014	N.D.	N.D.
32	6	Sup	0.032	N.D.	N.D.
30	6	Sup	0.624	0.022	0.042
26	6	Sup	0.034	0.018	N.D.
25	4	Amp	0.072	N.D.	N.D.
27	4	Sup	0.162	N.D.	N.D.
30	4	Sup	N.D.	N.D.	N.D.

* Capsules of 500 mg of ampicillin (Amp) or supercillin (Sup) were taken orally by the women at 6-hr intervals.

** N. D. =not detected

(Community Bureau of Reference, Commission of the European Communities)當做重金屬測定之參考標準品。

結果與討論

一、嬰兒乳粉及母乳中抗生素之調查

這次調查六種國產與進口嬰兒乳粉中並無抗生素檢出；然而22位受調查之產婦母乳中卻有抗生素之檢出(表一)，產後第3天、第7天及第14天，母乳中有β-內醯胺抗生素之檢出，其檢出率分別為84.6%、22.7%及9.1%，而殘留含量分別介於0.014-0.686 IU/ml、0.018-0.164 IU/ml及0.042-0.124 IU/ml之間。雖然其檢出殘留量不高，但有些敏感患者對於0.003 IU/ml之抗生素即發生過敏反應⁽³⁻⁴⁾，而過量之抗生素對於嬰兒尚可能有其他副作用⁽⁶⁻⁸⁾，如導致破壞正常腸道菌叢之平衡等。此次調

查結果顯示產婦在生產及育兒哺乳期間由於抗生素的使用，會造成母乳中藥物之殘留而不利於嬰兒的健康。母乳中抗生素殘留程度與母體藥物代謝能力、藥物理化性質以及投藥方式有關，一般分娩婦女之抗生素停藥期長短，將視感染程度而異，通常在產後3-5天即停藥。表一顯示不同婦女的母乳中抗生素之殘留情形，供為參考說明，母乳中抗生素殘留與母體藥物代謝能力、藥物理化性質以及投藥方式有關，因此，一旦產婦接受抗生素之治療，母乳就有殘留之可能，故分娩婦女之抗生素的使用，必須非常謹慎。

二、嬰兒乳粉及母乳中重金屬之調查

嬰兒乳粉中重金屬的污染情形列在表二，顯示進口及國產嬰兒乳粉中鉛、鎘、砷及汞平均含量並無明顯差異，其中進口嬰兒乳粉E品牌之砷含量偏高，其因不明，可能與其生產之背景環境條件有關。由於砷之測定屬於極微量的分析，就檢測之敏感度

Table 2. Heavy metal contents of domestic and imported infant milk powders

Brands	Pb (ppm)	Cd (ppm)	Hg (ppm)	As (ppb)
Domestically-produced milk powders				
A	0.017	0.001	N.D.	1.769
B	0.008	0.006	0.010	1.234
C	0.005	0.001	0.005	1.736
Mean*	0.010	0.003	0.005	1.580
Imported milk powders				
D	0.005	0.002	0.010	0.880
E	0.004	0.012	0.007	7.089
F	0.006	0.003	0.003	0.227
Mean**	0.005	0.006	0.006	2.729
Mean of all brands	0.008	0.005	0.006	0.155

* Sample size (n=42)

** Sample size (n=36)

而言,在ppb範圍內比較7.089,2.729及0.227三個數值,彼等可視為相近而無顯著差異。進口奶粉E之砷含量在正常範圍(30-60 ppb)。此結果與過去報告^(2,12)比較,其含量均在正常範圍內。此結果比李等人(1983)報導進口嬰兒乳粉中鉛含量為0.21-1.27 ppm為低⁽²⁹⁾,亦較曾氏(1985)報告嬰兒乳粉中鉛平均含量0.883 ppm(0.261-1.979 ppm)低⁽³⁰⁾。由40位產婦母乳中所做重金屬之調查結果,顯示鉛、鎘、汞及砷平均含量分別為0.027 ppm(0-0.056 ppm)、0.003 ppm(0-0.006 ppm)、0.001 ppm(0-0.005 ppm)及0.656 ppb(0-3.002 ppb)(表二)。其中砷含量差異較大,此可能與其生活環境、產婦之生活習慣以及年齡有關⁽²⁾。此調查結果與歐美地區母乳中鉛、鎘、汞及砷平均含量為0.021 ppm⁽¹³⁾、0.019 ppm⁽¹¹⁾、0.006 ppm⁽¹⁴⁾及3.74ppb⁽²⁾之報告比較,顯示受測產婦母乳中重金屬並無偏高之現象。

結 論

本研究調查六種國產與進口嬰兒乳粉,發現並無 β -內醯胺抗生素之檢出。又鉛、鎘、汞及砷四種重金屬含量均在正常範圍內。而母乳中卻有 β -內醯胺之抗生素殘留檢出,在22位受測產婦中,產後第3天86.4%(19/22)母乳中有 β -內醯胺抗生素殘留(0.014-0.686 IU/ml),產後第7天,22.7%(5/22)母乳中有此類抗生素檢出(0.018-0.164 IU/ml)。而產後第14天,仍有9.1%(2/22)母乳中尚有抗生素殘留(0.042-0.124 IU/ml)。而40

位產婦之母乳中重金屬含量均在正常範圍內。此初步調查結果顯示孕婦於生產及育兒哺乳期間,抗生素之使用需特別留意。

誌 謝

本研究由財團法人純青嬰幼兒營養研究基金會提供經費及協調,國軍813醫院陳霞護理長及同事等多人之協助,以及參與調查之產婦們之充分配合與合作,謹誌謝忱。

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Survey of β -Lactam Antibiotics and Heavy Metals in Infant Milk Powder and Human Milk

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ABSTRACT

The contents of β -lactam antibiotics (ampicillin and supercillin) and heavy metals in human milk and infant milk powders were surveyed in this study. The bioassay-*Bacillus stearothermophilus* disc method was used for the detection of the antibiotics, while heavy metals were determined by atomic absorption spectrophotometry. Results showed that there was no detectable antibiotics in infant milk powders, but residues of β -lactam antibiotics were commonly found in human milk samples. For 22 women studied, 84.6%, 22.7% and 9.1% of their breast milk samples were found to contain β -lactam antibiotics (ranging from 0.014-0.686 IU/ml) on the third, seventh and fourteenth day, respective-

ly, after parturition with drug intake or injection. Therefore, more precaution should be exercised when ingesting antibiotics during the period of conception and nursing. The average concentration of lead, cadmium, mercury and arsenic in infant milk powders was found to be 0.008 ± 0.019 ppm, 0.005 ± 0.007 ppm, 0.006 ± 0.008 ppm and 2.155 ± 3.380 ppb, respectively. Whereas the average concentration of these heavy metals in human milk samples was 0.027 ± 0.029 ppm, 0.003 ± 0.003 ppm, 0.001 ± 0.004 ppm and 0.656 ± 2.346 ppb. It was concluded that the contents of heavy metals in infant milk powders and human milk samples were in the normal range.

Key words : Breast milk, Milk powder, Heavy metals, β -lactam antibiotics.