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Available online 6 August 2015

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http://dx.doi.org/10.1016/j.rec.2015.06.010

Use of Antihypertensive Drugs in Spain: National Trends From 2000 to 2012☆

Uso de medicamentos antihipertensivos en España: tendencias nacionales en el periodo 2000-2012

To the Editor,

Hypertension is a major global public health problem, mainly because of its contribution to the risk of cardiovascular events.[1,2] Epidemiological studies[2,3] have reported that hypertension control in Spain continues to be suboptimal and that, on occasions, targets (arterial blood pressure < 140/90 mmHg) are met in less than half of the hypertensive individuals under treatment.[2] A number of previous studies[4] have called attention to important changes in the patterns of use of antihypertensive drugs in recent decades.

Following the methodology described by the Observatory for the Use of Medicines of the Spanish Agency of Medicine and Medical Devices,[5] we examined the pattern of antihypertensive drug use in Spain from 2000 to 2012. We selected the treatment subgroups of the Anatomical Therapeutic Chemical Classification (ATC): antihypertensive agents (C02), diuretics (C03), beta-blockers (C07), calcium channel blockers (C08), and drugs that act on the renin-angiotensin system (C09), such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, and direct renin inhibitors (aliskiren). The analytical measure was the number of defined daily doses (DDD) dispensed per 1000 inhabitants per day (DID).[5] We used the consumption data provided by the Directorate-General of the Basic Service Portfolio of the Spanish Health and Pharmacy System, whose database compiles prescriptions for the medications covered by the Spanish Health System.

The patterns of use of antihypertensive drugs in Spain are shown in the Table (according to treatment subgroup and active ingredient). The use of antihypertensive medications in Spain increased from 2000 to 2012, and those most widely consumed were angiotensin receptor blockers and angiotensin-converting enzyme inhibitors. More specifically, the total used of antihypertensive drugs was 165.5 DID in the year 2000 and 299.0 DID in 2012. By group, angiotensin receptor blockers (18.2 DID and 93.8 DID in 2000 and 2012, respectively), angiotensin-converting enzyme inhibitors (62.2 DID and 86.4 DID, respectively), diuretics (32.8 DID and 44.8 DID, respectively), and calcium channel blockers (33.4 DID and 38.8 DID) were the most widely used antihypertensive drugs. Enalapril (42.7 DID), amlodipine (20.7 DID), furosemide (16.4 DID), ramipril (15.1 DID), valsartan (14.3 DID), and candesartan (12.5 DID) were the most widely used active ingredients in 2012.

The upward trends in use had been observed in an earlier study performed in Spain for the period from 1995 to 2001.[5] In the present report, the series was extended to cover 2000 to 2012, revealing continued growth, with an increase of 80.7%. This continued growth occurred even though there have been no important changes in the marketing of new antihypertensive medications with respect to the existing groups. It is important to mention the introduction of aliskiren in 2008, of imidapril in 2004, of olmesartan in 2004, and of eplerenone in 2005. The consumption of antihypertensive drugs has increased all over Europe,[6] and the growth in Spain is similar to the European average. Germany in central Europe, Finland among the Nordic countries, and Italy in the Mediterranean area were the countries with the widest use in absolute terms. The consumption of antihypertensive drugs in Spain is higher than in other countries such as France and Portugal, and lower than in the United Kingdom and the central European and Nordic countries, with the exception of Luxemburg and Iceland.[6]

Whether the increase in the intensity of antihypertensive therapy in Spain has contributed to improving blood pressure control is, at best, controversial. Although the results of the various studies may appear to disagree, the evidence suggests that, despite the increase in the consumption of antihypertensive drugs, blood pressure control in Spain continues to be inadequate. The growth observed could be related to the increase in the prevalence of treated hypertension and population aging.[1,2] One of the limitations of this study is that it does not enable us to determine whether the reason for the increment in medication use is the increase in the number of hypertensive patients being treated (including mild forms), the increase in the duration of the treatments, or both. In addition, estimation of drug use was based on the DDD, which is a unit of measure that does not necessarily coincide with the dose actually used in clinical practice. Moreover, true consumption of these drugs could be higher than that

☆ The opinions expressed in this report are the responsibility of the authors and, thus, do not necessarily reflect the point of view of the organisms in which they work.

Table
Use of Antihypertensive Drugs in Spain According to Treatment Subgroup and Active Ingredient. Data Expressed as Defined Daily Doses per 1000 Inhabitants per Day

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Antihypertensive drugs (C02)													
Clonidine	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01
Doxazosin	4.27	5.15	6.08	7.10	7.74	7.98	8.19	8.42	8.54	8.87	8.88	8.64	9.05
Hydralazine	0.04	0.04	0.05	0.05	0.05	0.05	0.06	0.07	0.07	0.07	0.08	0.08	0.08
Methyldopa (racemic)	0.04	0.04	0.03	0.03	0.03	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Minoxidil	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	< 0.01	< 0.01
Moxonidine	0.22	0.25	0.25	0.29	0.32	0.33	0.35	0.38	0.40	0.43	0.42	0.39	0.38
Prazosin	0.07	0.06	0.05	0.05	0.04	0.03	0.03	0.02	0.02	0.02	0.02	0.01	0.01
Rauwolfia serpentina alkaloids[a]	0.07	0.05	0.04	0.02	0.01	0.01	< 0.01						
Reserpine and diuretics[b]	0.07	0.06	0.03	0.03	0.02	< 0.01							
Reserpine and diuretics, combinations with others[b]	0.14	0.12	0.10	0.08	0.07	0.05							
Total C02	4.95	5.77	6.65	7.66	8.30	8.50	8.67	8.92	9.06	9.43	9.43	9.16	9.56
Diuretics (C03)													
Bumetanide	0.02	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03	0.03
Chlorthalidone	5.17	5.12	5.01	5.02	5.21	5.20	5.23	5.19	5.11	5.10	4.89	4.61	4.82
Chlorthalidone/spironolactone	0.15	0.14	0.11	0.10	0.10	0.09	0.09	0.09	0.09	0.09	0.08	0.08	0.08
Eplerenone						< 0.01	0.03	0.08	0.23	0.31	0.36	0.48	0.62
Spironolactone	2.02	2.12	2.16	2.23	2.11	2.20	2.17	2.14	2.12	2.17	2.15	2.14	2.20
Furosemide	7.75	8.13	8.43	8.24	9.21	9.77	10.66	11.50	12.28	13.30	14.08	14.86	16.42
Furosemide-xanthinol/ triamterene	1.24	1.15	1.03	0.94	0.85	0.74	0.67	0.60	0.54	0.51	0.46	0.42	0.38
Hydrochlorothiazide	4.22	4.73	5.23	5.80	6.56	7.12	7.81	8.38	8.90	9.25	9.46	9.42	9.40
Hydrochlorothiazide/potassium sparing diuretics	3.97	3.83	3.63	3.49	3.34	3.16	3.01	2.84	2.63	2.53	2.33	2.16	2.06
Indapamide	4.65	4.75	4.80	5.03	5.10	4.95	4.89	4.71	4.52	4.43	4.12	3.79	3.77
Piretanide	0.03	0.03	0.02	0.02	0.02	0.01	0.01	0.01	0.01	0.01	0.01	0.01	< 0.01
Torasemide	2.47	3.07	3.72	4.34	4.72	4.82	4.93	4.93	4.97	5.16	5.05	4.79	4.72
Xipamide	0.74	0.66	0.59	0.53	0.47	0.41	0.37	0.33	0.30	0.28	0.25	0.22	0.20
Spironolactone/altizide	0.36	0.36	0.35	0.33	0.31	0.29	0.27	0.26	0.24	0.24	0.23	0.13	0.13
Mebutizide/ potassium sparing diuretics[c]	0.03												
Spironolactone/ bendroflumethiazide[d]	0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01		
Total C03	32.82	34.12	35.11	36.09	38.01	38.79	40.16	41.08	41.96	43.39	43.50	43.14	44.84
Beta blockers (C07)													
Acebutolol[a]	0.06	0.05	0.04	< 0.01	< 0.01	< 0.01	< 0.01						
Acebutolol/thiazide[a]	0.01	0.01	0.01	0.01	< 0.01	< 0.01	< 0.01						
Atenolol	6.38	6.64	6.78	6.84	7.38	7.33	7.64	7.65	7.48	7.51	7.32	7.10	7.22
Atenolol/bendroflumethiazide	0.05	0.04	0.04	0.04	0.03	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02
Atenolol/chlorthalidone	1.16	1.13	1.04	0.53	1.07	1.03	1.01	0.97	0.91	0.87	0.84	0.78	0.76
Atenolol/hydrochlorothiazide/ amiloride	0.06	0.06	0.06	0.05	0.05	0.05	0.04	0.04	0.04	0.04	0.04	0.04	0.04
Atenolol/hydralazine/ bendroflumethiazide[e]	< 0.01	< 0.01	< 0.01	< 0.01	0.01	0.01	0.01	0.01	0.01	0.01	0.01	< 0.01	
Bisoprolol	2.14	2.46	2.78	3.06	3.38	3.63	3.97	4.31	4.63	5.17	5.61	6.05	6.92
Bisoprolol/hydrochlorothiazide	0.39	0.46	0.51	0.57	0.64	0.67	0.70	0.71	0.71	0.75	0.73	0.70	0.71
Carteolol[f]	0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01			
Carvedilol	1.11	1.30	1.53	1.78	2.04	2.28	2.52	2.69	2.83	3.04	3.11	3.13	3.38
Celiprolol	0.09	0.08	0.07	0.06	0.06	0.05	0.05	0.04	0.04	0.04	0.04	0.03	0.03
Labetalol	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.03	0.03	0.03
Metoprolol	0.34	0.36	0.38	0.39	0.40	0.39	0.40	0.40	0.40	0.42	0.42	0.42	0.45
Metoprolol/felodipine	0.52	0.55	0.52	0.48	0.48	0.48	0.47	0.46	0.45	0.45	0.41	0.37	0.36
Metoprolol/thiazide[b]	0.01	0.01	< 0.01	< 0.01	< 0.01	< 0.01							
Nadolol	0.08	0.08	0.08	0.09	0.09	0.09	0.10	0.10	0.05	0.04	0.06	0.07	0.08
Nebivolol	0.43	0.75	1.00	1.20	1.29	1.32	1.46	1.70	2.03	2.52	2.70	2.71	2.83
Oxprenolol	0.05	0.04	0.04	0.03	0.03	0.02	0.02	0.02	0.02	0.02	0.02	0.02	0.01
Oxprenolol/chlorthalidone	0.08	0.07	0.06	0.06	0.05	0.04	0.04	0.03	0.03	0.03	0.02	0.01	0.01

Table *(Continued)*
Use of Antihypertensive Drugs in Spain According to Treatment Subgroup and Active Ingredient. Data Expressed as Defined Daily Doses per 1000 Inhabitants per Day

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Propranolol	0.62	0.62	0.62	0.63	0.63	0.62	0.64	0.65	0.68	0.74	0.74	0.74	0.79
Propranolol/other antihypertensive drugs[f]	0.06	0.05	0.05	0.04	< 0.01	< 0.01	< 0.01	< 0.01	< 0.01	0.00			
Sotalol	0.17	0.17	0.17	0.17	0.17	0.17	0.16	0.16	0.16	0.18	0.17	0.14	0.15
Nebivolol/ hydrochlorothiazide											0.05	0.24	0.33
Total C07	13.84	14.97	15.81	16.06	17.82	18.24	19.27	20.00	20.50	21.85	22.31	22.59	24.10
Calcium channel blockers (C08)													
Amlodipine	11.95	13.06	13.97	14.71	15.21	15.62	16.23	16.95	17.78	18.69	18.79	19.09	20.76
Barnidipine		< 0.01	0.23	0.40	0.69	0.78	0.84	0.96	1.33	1.43	1.38	1.34	0.95
Diltiazem	4.85	4.77	4.70	4.64	4.55	4.42	4.35	4.28	4.18	4.18	4.00	3.76	3.72
Felodipine	0.88	0.74	0.64	0.55	0.47	0.40	0.33	0.28	0.25	0.23	0.20	0.18	0.17
Lacidipine	1.57	1.37	1.18	1.03	0.90	0.78	0.69	0.62	0.55	0.50	0.44	0.38	0.36
Lercanidipine	1.06	1.40	1.58	1.67	1.84	2.24	2.67	3.03	3.22	3.36	3.27	3.13	3.24
Manidipine				0.13	0.81	1.23	1.66	2.21	2.80	3.33	3.59	3.57	3.89
Nicardipine	1.16	1.04	0.96	0.90	0.84	0.75	0.67	0.59	0.53	0.49	0.44	0.39	0.36
Nifedipine	6.83	6.33	5.97	5.63	5.25	4.91	4.68	4.45	4.22	4.04	3.73	3.44	3.34
Nimodipine	1.02	0.93	0.83	0.72	0.61	0.51	0.45	0.39	0.34	0.30	0.26	0.22	0.20
Nisoldipine	0.25	0.19	0.16	0.13	0.11	0.09	0.07	0.06	0.05	0.05	0.04	0.03	0.03
Nitrendipine	0.68	0.57	0.49	0.43	0.38	0.33	0.30	0.27	0.25	0.23	0.20	0.18	0.17
Verapamil	3.19	3.04	2.89	2.75	2.59	2.42	2.30	2.18	2.05	2.00	1.85	1.70	1.61
Total C08	33.45	33.43	33.61	33.67	34.23	34.46	35.24	36.29	37.55	38.82	38.20	37.42	38.79
Agents acting on the renin-angiotensin system (C09)													
ACE inhibitors and associations													
Benazepril	0.50	0.41	0.35	0.30	0.25	0.21	0.18	0.16	0.15	0.15	0.13	0.11	0.10
Benazepril/hydrochlorothiazide									< 0.01	< 0.01	< 0.01	< 0.01	< 0.01
Captopril	7.98	7.53	6.93	6.09	5.69	4.77	4.63	4.08	3.52	3.16	2.70	2.29	2.11
Captopril/hydrochlorothiazide	1.76	1.63	1.47	1.30	1.24	1.11	1.00	0.90	0.80	0.73	0.64	0.57	0.52
Cilazapril	1.95	1.64	1.34	1.12	0.94	0.77	0.65	0.55	0.46	0.41	0.34	0.28	0.24
Cilazapril/hydrochlorothiazide	0.45	0.41	0.36	0.32	0.28	0.25	0.22	0.20	0.17	0.16	0.14	0.12	0.11
Enalapril	26.39	28.25	29.25	29.81	32.15	31.48	35.13	35.80	37.67	38.72	39.14	39.61	42.73
Enalapril/hydrochlorothiazide	4.59	4.81	4.94	5.19	5.80	6.18	7.25	8.00	8.67	9.33	9.82	10.30	11.64
Enalapril/calcium channel blockers			0.1	0.47	0.8	0.89	0.89	0.96	1.70	1.80	2.52	2.84	2.99
Spirapril[g]	0.22	0.22	0.24	0.26	0.25	0.23	0.19	0.15	0.12	0.06	< 0.01	< 0.01	< 0.01
Fosinopril	1.78	1.66	1.54	1.46	1.26	1.07	0.94	0.82	0.72	0.64	0.56	0.48	0.45
Fosinopril/hydrochlorothiazide	0.47	0.50	0.51	0.53	0.49	0.44	0.40	0.38	0.34	0.33	0.30	0.26	0.26
Imidapril					< 0.01	0.06	0.15	0.22	0.27	0.48	0.63	0.77	1.16
Lisinopril	4.52	4.50	4.32	4.01	3.78	3.54	3.47	3.40	3.39	3.50	3.57	3.64	3.94
Lisinopril/hydrochlorothiazide	1.62	1.64	1.56	1.50	1.42	1.33	1.33	1.32	1.32	1.37	1.41	1.46	1.62
Perindopril	0.57	0.58	0.62	0.71	0.81	0.82	0.76	0.71	0.66	0.57	0.52	0.48	0.48
Perindopril/indapamide				0.01	0.18	0.33	0.48	0.54	0.60	0.70	0.69	0.66	0.66
Quinapril	4.11	3.93	3.76	3.60	3.13	2.61	2.23	1.93	1.67	1.49	1.29	1.11	1.01
Quinapril/ hydrochlorothiazide	1.08	1.01	0.94	0.89	0.80	0.69	0.62	0.55	0.48	0.44	0.39	0.34	0.30
Ramipril	2.87	3.24	4.32	5.61	7.31	8.33	9.12	9.72	10.58	11.84	12.58	13.16	15.15
Ramipril/felodipine							0.03	0.05	0.04	0.04	0.03	0.03	0.04
Ramipril/hydrochlorothiazide									< 0.01	0.04	0.10	0.18	0.30
Trandolapril	0.50	0.44	0.38	0.35	0.31	0.26	0.24	0.21	0.18	0.15	0.13	0.11	0.09
Trandolapril/verapamil	0.83	0.99	0.97	0.94	0.93	0.89	0.83	0.80	0.76	0.74	0.66	0.57	0.52
Total ACE inhibitors and associations	62.20	63.38	63.90	64.48	67.81	66.27	70.74	71.43	74.29	76.84	78.29	79.37	86.42
ARB and associations													
Candesartan	4.59	5.47	5.79	6.03	7.10	6.28	8.26	10.01	11.39	12.77	12.80	12.55	12.52
Candesartan/ hydrochlorothiazide		0.54	0.94	1.15	1.28	2.51	2.59	2.63	2.68	2.83	3.16	3.54	3.73
Eprosartan		0.68	1.62	2.07	2.60	2.50	2.26	2.16	2.16	2.20	2.02	1.73	1.57
Eprosartan/hydrochlorothiazide						0.13	0.52	0.62	1.47	1.73	1.71	1.57	1.57
Irbesartan	3.01	3.64	4.36	5.31	5.88	5.99	6.22	6.35	6.41	6.62	6.54	6.13	6.04

Table *(Continued)*
Use of Antihypertensive Drugs in Spain According to Treatment Subgroup and Active Ingredient. Data Expressed as Defined Daily Doses per 1000 Inhabitants per Day

	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	2012
Irbesartan/hydrochlorothiazide	0.55	1.25	1.79	2.35	2.97	3.19	3.50	3.97	4.28	4.71	4.77	4.55	4.54
Losartan	1.99	2.11	2.40	2.78	3.38	4.28	5.09	5.78	6.20	6.65	6.89	7.10	8.05
Losartan/hydrochlorothiazide	1.09	1.55	2.14	2.63	3.04	3.25	3.43	3.64	3.73	3.85	3.89	4.02	4.55
Olmesartan					0.69	2.65	3.87	3.01	5.23	5.98	6.25	6.42	6.82
Olmesartan/amlodipine										0.26	1.70	2.39	2.65
Olmesartan/amlodipine/ hydrochlorothiazide												0.14	1.08
Olmesartan/ hydrochlorothiazide								0.10	0.52	0.96	1.30	1.92	2.68
Telmisartan	2.77	3.88	4.80	4.74	4.62	4.56	4.81	5.34	5.93	6.59	6.82	7.00	7.39
Telmisartan/amlodipine												0.14	0.34
Telmisartan/hydrochlorothiazide						0.45	0.62	1.15	2.40	2.98	3.43	3.72	4.07
Valsartan	3.39	4.86	6.88	8.73	9.98	9.85	9.81	10.23	12.15	14.60	14.74	14.08	14.34
Valsartan/amlodipine									0.41	1.80	2.46	2.53	2.48
Valsartan/amlodipine/ hydrochlorothiazide											0.09	0.84	1.28
Valsartan/hydrochlorothiazide	0.83	1.19	1.61	2.17	2.88	4.08	5.45	6.57	7.35	7.79	8.07	7.85	8.07
Total ARB and associations	18.22	25.16	32.32	37.96	44.42	49.72	56.44	61.56	72.33	82.32	86.64	88.20	93.76
Renin inhibitors													
Aliskiren									0.05	0.83	1.39	1.92	1.26
Aliskiren/hydrochlorothiazide											0.17	0.41	0.32
Total renin inhibitors									0.05	0.83	1.55	2.32	1.57
Total C09	80.40	88.50	96.20	102.50	112.20	116.00	127.20	133.00	147.40	160.70	167.10	170.40	181.70
Total antihypertensive drugs	**165.50**	**176.80**	**187.40**	**196.00**	**210.60**	**216.00**	**230.50**	**239.30**	**256.50**	**274.20**	**280.60**	**282.70**	**299.00**

ACE, angiotensin-converting enzyme; ARB, angiotensin receptor blockers.
Footnotes concerning the approval of some of the above agents:
[a] Overturned in 2006.
[b] Overturned in 2005.
[c] Overturned in 2000.
[d] Overturned in 2010.
[e] Overturned in 2011.
[f] Overturned in 2009.
[g] Overturned in 2012.
Note: The values represented in the table have been rounded to two decimals.

reflected here since prescriptions issued by private physicians were excluded.

With the recent publication of new clinical practice guidelines recommending less ambitious or more flexible targets for arterial blood pressure levels, the patterns of use could change, resulting in better rates of blood pressure control in the years to come.

Acknowledgments

We wish to thank the Directorate-General of the Basic Service Portfolio of the Spanish Health and Pharmacy System for providing us with the information on the consumption of medications used in the present report.

FUNDING

Virginia Greciano was the recipient of a grant for training in the Spanish Agency of Medicine and Medical Devices during the course of the present study.

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Available online 8 August 2015

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Acute Myocardial Infarction in a Neonate Caused by a Coronary Thrombosis: a Considerable Diagnostic and Therapeutic Challenge

Infarto agudo de miocardio en un neonato causado por trombosis coronaria: un gran reto diagnóstico y terapéutico

To the Editor,

Although neonatal acute myocardial infarction secondary to coronary thrombosis is extremely rare, it has high mortality (about 90%)[1] and its early diagnosis requires a high level of clinical suspicion. Of the few cases described in the literature, most are of unknown origin.[2] Reported risk factors include prothrombotic conditions, myocarditis, prematurity, neonatal asphyxia, Kawasaki disease, and placement of an umbilical venous catheter.[1–4] Various therapeutic strategies are available, such as surgical thrombectomy,[5] systemic or local thrombolytic treatment (although controversial in neonates, there have been some successful results),[2,4] and use of an extracorporeal membrane oxygenator as hemodynamic support.[2–6]

The present scientific letter concerns a male neonate, with no relevant obstetric history except for maternal gastroenteritis at 12 days before birth, who was born at 37 + 5 weeks gestation via emergency cesarean section due to pathological cardiotocography (DIP II). His Apgar score was 6/9. At birth, he required positive pressure ventilation for 3 min due to poor respiratory effort. He was admitted to the neonatal intensive care unit under clinical management and continuous monitoring. There, a marked progressive clinical worsening was seen, with a poor general status and mixed acidosis that required intubation, mechanical ventilation, and refractory intensive inotropic support. For the latter, he was administered stress doses of hydrocortisone. Echocardiography was performed to rule out cardiogenic shock as a differential diagnosis, revealing severe ventricular dysfunction with ejection fraction $< 15\%$, with minimal motion of the lateral wall but with preserved right ventricular function. Both coronary arteries were adequately visualized, but no visualization was possible of left coronary artery flow. In addition, a 12-lead electrocardiogram showed deep Q waves in DI, aVL, and V_5-V_6 (Figure 1).

With the diagnosis of cardiogenic shock due to acute left ventricular dysfunction, treatment was begun with prostaglandins to maintain systemic cardiac output through the arterial conduit. The differential diagnosis included myocarditis (due to the maternal history of gastroenteritis), coronary thrombosis, and an anomalous origin of the left coronary artery in the pulmonary artery (although it was unlikely because symptoms do not usually begin until pulmonary resistance decreases). Treatment was started with intravenous gamma-globulins and acyclovir, and it was decided to perform cardiac catheterization. Due to the patient's considerable hemodynamic instability, catheterization was delayed until the fourth day of life, but revealed a filling defect of 1 m in diameter in the left coronary artery, compatible with a thrombosis or dissection of the left main coronary artery (Figure 2, Video of the supplementary material), confirming the diagnosis of acute myocardial infarction due to thrombosis of the left coronary artery. Initial treatment was to consist of intravenous heparin and systemic r-TPA (recombinant tissue plasminogen activator) or acetylsalicylic acid but, due to the shock-induced coagulopathy, the considerable risk of brain bleeding, and the late diagnosis, treatment was begun with intravenous heparin alone for 7 days, at a dosage of 1.5 mg/kg body weight every 12 hours. The first percutaneous treatment considered was placement of an intracoronary stent, but this approach was rejected due to the risk-benefit of stent implantation in a neonate. Another possibility was intracoronary administration of r-TPA, but recovery of myocardial viability was considered unlikely due to the delayed diagnosis. In the following days, reopening of the coronary artery was seen on ultrasound, but with minimal recovery of ventricular function (30% ejection fraction). Serological and polymerase chain reaction studies of the blood for the presence of virus were negative, as were thrombophilic studies. The patient remained in the neonatology unit for 94 days due to his considerable hemodynamic lability in response to minimally invasive procedures and intercurrent processes. He was eventually discharged with diuretic

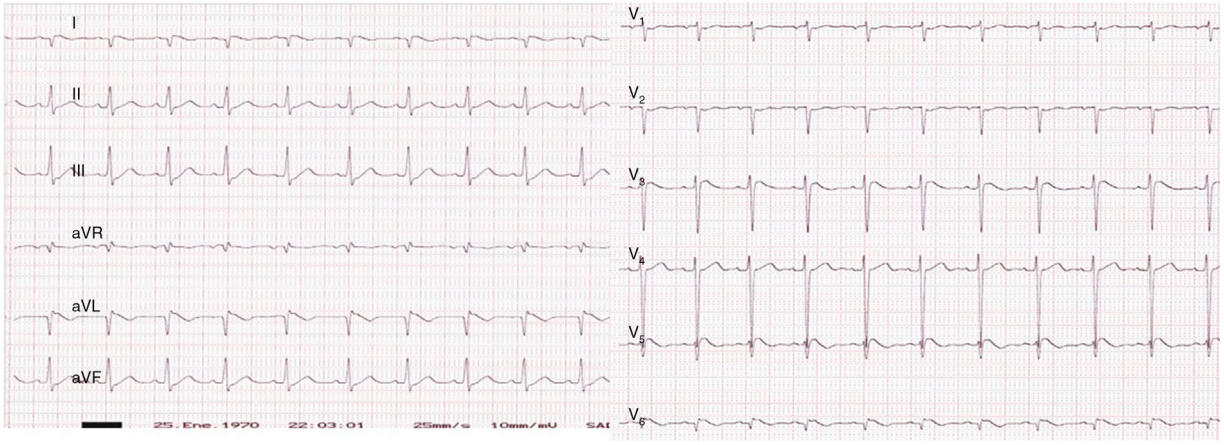

Figure 1. Electrocardiogram showing deep Q waves in DI, aVL, and V_5-V_6.