

Tek Dozla Ölümcül İlaçlar

Doç Dr Özlem GÜNEYSEL

Dr Lütfi Kırdar Kartal EAH

Acil Tıp Kliniği

*"Tüm maddeler zehirdir, ilacı
zehirden ayıran dozudur"*



PARACELSUS

Paracelsus (1493-1541)

- Güvenli pozoloji, doğru reçeteleme;
- Doz aşımı;
- Tek doz güvenilirliği (?)

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ABSTRACTS

2011 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 29th Annual Report

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ABD, 2011, AAPCC*

Table 3A. Age and gender distribution of human exposures.

Age (y)	Male		Female		Unknown gender		Total		Cumulative total	
	N	% of age group total	N	% of age group total	N	% of age group total	N	% of total exposures	N	%
Children (<20)										
< 1	60,072	51.86	55,410	47.84	342	0.30	115,824	4.96	115,824	4.96
1	184,716	51.89	170,719	47.96	520	0.15	355,955	15.25	471,779	20.21
2	195,808	52.37	177,506	47.48	579	0.15	373,893	16.02	845,672	36.23
3	92,535	54.91	75,678	44.90	322	0.19	168,535	7.22	1,014,207	43.45
4	45,587	55.96	35,643	43.75	232	0.28	81,462	3.49	1,095,669	46.94
5	26,329	56.93	19,742	42.69	177	0.38	46,248	1.98	1,141,917	48.93
Unknown ≤5	1,304	46.37	1,169	41.57	339	12.06	2,812	0.12	1,144,729	49.05
Child 6–12	81,598	57.82	58,583	41.51	940	0.67	141,121	6.05	1,285,850	55.09
Teen 13–19	73,140	46.04	85,085	53.55	650	0.41	158,875	6.81	1,444,725	61.90
Unknown Child	1,700	38.11	1,680	37.66	1,081	24.23	4,461	0.19	1,449,186	62.09
Subtotal	762,789	52.64	681,215	47.01	5,182	0.36	1,449,186	62.09	1,449,186	62.09
Adults (≥20)										
20–29	95,021	46.96	107,125	52.94	220	0.11	202,366	8.67	1,651,552	70.76
30–39	66,143	43.15	87,048	56.79	101	0.07	153,292	6.57	1,804,844	77.33
40–49	57,958	41.66	81,069	58.28	80	0.06	139,107	5.96	1,943,951	83.29
50–59	47,482	40.16	70,702	59.79	58	0.05	118,242	5.07	2,062,193	88.35
60–69	28,642	37.86	46,984	62.10	30	0.04	75,656	3.24	2,137,849	91.60
70–79	16,111	35.55	29,195	64.42	17	0.04	45,323	1.94	2,183,172	93.54
80–89	9,632	33.60	19,016	66.34	18	0.06	28,666	1.23	2,211,838	94.77
≥90	1,678	29.06	4,093	70.89	3	0.05	5,774	0.25	2,217,612	95.01
Unknown adult	41,102	39.86	59,696	57.89	2,326	2.26	103,124	4.42	2,320,736	99.43
Subtotal	363,769	41.74	504,928	57.93	2,853	0.33	871,550	37.34	2,320,736	99.43
Other										
Unknown age	4,692	35.36	5,894	44.42	2,682	20.21	13,268	0.57	2,334,004	100.00
Total	1,131,250	48.47	1,192,037	51.07	10,717	0.46	2,334,004	100.00	2,334,004	100.00

Table 4. Distribution of age^a and gender for fatalities.^b

Age (y)	Male	Female	Unknown	Total (%)	Cumulative total (%)
< 1 year	3	1	0	4 (0.4%)	4 (0.4%)
1 year	1	1	0	2 (0.2%)	6 (0.5%)
2 years	4	4	0	8 (0.7%)	14 (1.2%)
3 years	1	0	0	1 (0.1%)	15 (1.3%)
4 years	1	2	0	3 (0.3%)	18 (1.6%)
5 years	2	0	0	2 (0.2%)	20 (1.7%)
Child 6–12 years	5	1	0	6 (0.5%)	26 (2.3%)
Teen 13–19 years	24	20	0	44 (3.8%)	70 (6.0%)
20–29 years	105	56	0	161 (13.9%)	231 (20.0%)
30–39 years	85	93	0	178 (15.4%)	409 (35.3%)
40–49 years	111	143	0	254 (21.9%)	663 (57.3%)
50–59 years	95	149	0	244 (21.1%)	907 (78.3%)
60–69 years	52	62	0	114 (9.8%)	1,021 (88.2%)
70–79 years	28	44	0	72 (6.2%)	1,093 (94.4%)
80–89 years	13	19	0	32 (2.8%)	1,125 (97.2%)
> = 90 years	6	12	0	18 (1.6%)	1,143 (98.7%)
Unknown adult	7	4	1	12 (1.0%)	1,155 (99.7%)
Unknown age	3	0	0	3 (0.3%)	1,158 (100.0%)
Total	546	611	1	1,158 (100.0%)	1,158 (100.0%)

^aAge includes cases with both actual and estimated ages as shown in Table 21.

^bIncludes cases with relative contribution to fatality of 1-Undoubtedly responsible, 2-Probably responsible, or 3-Contributory. This excludes reports with outcome of Death INDIRECT.

ABD

- Toplam başvuru: 2.334.004
- Ölüm : 1.158
- Oran : %0.05 (1/10.000)

Türkiye

Tablo 6: Vakaların Yaşa Göre Dağılımı, 2008

Yaş	Sayı	%
0 - 1	1.177	1,51
1	2.783	3,57
2	8.477	10,87
3	7.734	9,92
4	4.617	5,92
5 - 9	5.218	6,69
10 - 14	4.505	5,78
15 - 19	12.383	15,88
20 - 29	15.456	19,82
30 - 39	7.132	9,14
40 - 49	3.320	4,26
50 - 59	1.677	2,15
60 - 69	842	1,08
70 +	657	0,84
Bilinmeyen	2.010	2,58
Top la m	77.988	100,00

Türkiye

- Toplam başvuru: 77.988
- Ölüm : ?
- Oran : ?

En sık etkenler

Table 17B. Substance categories with the greatest rate of exposure increase (Top 25).

Substance (Major Generic Category)	Increase in exposures per year ^a		All substances in 2011
	Mean	95% CI ^a	
Analgesics	10,134	[12435, 7833]	322,016
Sedative/Hypnotics/Antipsychotics	7,959	[9083, 6835]	168,416
Cardiovascular Drugs	4,795	[5087, 4503]	102,766
Antihistamines	3,531	[4103, 2959]	94,159
Alcohols	2,129	[3163, 1095]	74,484
Vitamins	2,118	[2509, 1727]	70,195
Hormones and Hormone Antagonists	1,860	[2143, 1578]	60,234
Anticonvulsants	1,846	[2133, 1558]	49,607
Gastrointestinal Preparations	1,840	[2540, 1140]	50,414
Antidepressants	1,521	[2360, 682]	107,528
Other/Unknown Nondrug Substances	1,496	[2118, 873]	28,035
Cosmetics/Personal Care Products	1,312	[2694, -70]	218,269
Stimulants and Street Drugs	1,231	[2136, 326]	66,540
Topical Preparations	1,223	[2519, -72]	102,692
Muscle Relaxants	1,168	[1333, 1002]	28,857
Dietary Supplements/Herbals/Homeopathic	1,074	[1507, 641]	35,565
Anticholinergic Drugs	1,051	[1309, 792]	11,352
Miscellaneous Drugs	1,034	[1478, 590]	23,489
Antimicrobials	773	[1213, 333]	65,856
Unknown Drug	754	[861, 647]	21,184
Essential Oils	638	[695, 581]	10,906
Deodorizers	607	[842, 371]	24,255
Cleaning Substances (Household)	603	[2559, -1353]	192,771
Foreign Bodies/Toys/Miscellaneous	511	[1770, -749]	112,562
Anticoagulants	488	[521, 454]	8,315

^aIncrease and confidence intervals are based on least squares linear regression of the number of calls per year for 2000–2011.

En sık etkenler

EK – 4: EN FAZLA ZEHİRLENME NEDENİ OLAN İLK 50 İLAÇ

SIRA	ATC KOD	GRUP AÇIKLAMASI	VAKA	YÜZDE
1	R02BA01	Paracetamol	5.801	6,78
2	R05X00x	Diğer kombine ÜSYE ilaçları	3.706	4,33
3	N06AA09	Amitriptiline	3.485	4,07
4	N06AB06	Sertraline	2.113	2,47
5	N02BA01	Flurbiprofen	1.754	2,05
6	N02BA02	Naproxen	1.536	1,80
7	N02BA04	Acetylsalicylic acid (analjezik & antipiretik)	1.489	1,74
8	N02BA05	Diclofenac	1.452	1,70
9	N06AB10	Escitalopram	1.386	1,62
10	J01CR02	Beta laktamaz inh. içeren penisillin kombinasyonları	1.247	1,46
11	N05BB01	Hydroxyzine	1.133	1,32
12	N02BA02	Metamizole sodium	1.123	1,31
13	N05BA12	Alprazolam	1.111	1,30
14	N02BA01	İbuprofen	1.044	1,22
15	A02BC03	Lansoprazole	1.022	1,19
16	N06AB04	Citalopram	991	1,16
17	N05AH04	Quetiapine	966	1,13
18	N06AB05	Paroxetine	925	1,08
19	N05AX08	Risperidone	915	1,07
20	N02BA01	Thiocolchicoside	797	0,93
21	N02BA01	Butylscopolamine ve analjezikler	795	0,93
22	N03BX30	Fenylramidol	772	0,90
23	A03FA01	Metoclopramide	765	0,89
24	N05AH03	Olanzapine	738	0,86
25	N03AG01	Valproic acid	728	0,85

Veri Güvenilirliği

ABD >> Türkiye

Table 21. Listing of fatal nonpharmaceutical and pharmaceutical exposures.

Annual Report ID	Age	Substances	Substance Rank	Cause Rank	Chronicity	Route	Reason	RCF	Analyte	Blood Concentration @ Time
54ai	48 y F	ethanol	1	1	U	Ingst+ Inhal	Int-A	2	ethanol	0.04% (wt/Vol) In Whole Blood @ Autopsy
		ethanol	1	1					ethanol	0.05% (wt/Vol) In Vitreous @ Autopsy
		freon	2	2						
55ai	48 y F	ethanol	1	1	U	Ingst	Int-A	2	ethanol	0.34% (wt/Vol) In Whole Blood @ Autopsy
		ethanol	1	1					ethanol	0.35% (wt/Vol) In Vitreous @ Autopsy
		temazepam	2	2					temazepam	1.7 mcg/mL In Whole Blood @ Autopsy
56ai	48 y F	ethanol	1	1	U	Ingst	Int-A	2	ethanol	0.39% (wt/Vol) In Whole Blood @ Autopsy
		ethanol	1	1					ethanol	0.4% (wt/Vol) In Vitreous @ Autopsy
57ai	48 y F	ethanol	1	1	U	Ingst	Int-A	2	ethanol	0.48% (wt/Vol) In Whole Blood @ Autopsy
		ethanol	1	1					ethanol	0.5% (wt/Vol) In Vitreous @ Autopsy
58pi	48 y M	ethanol (non-beverage)	1	1	U	Ingst	Unk	3	ethanol	120 mg/mL In Blood (unspecified) @ 1 h (pe)
59pai	49 y M	ethanol	1	1	A	Ingst+ Unk	Int-U	1		
		heroin	2	2					morphine (free)	200 mcg/L In Blood (unspecified) @ Autopsy
60ai	49 y M	ethanol	1	1	U	Ingst+ Unk	Int-A	2	ethanol	0.27% (wt/Vol) In Whole Blood @ Autopsy
		ethanol	1	1					ethanol	0.31% (wt/Vol) In Vitreous @ Autopsy
		morphine	2	2					morphine (free)	0.26 mcg/mL In Whole Blood @ Autopsy
61pai	50 y M	ethanol	1	1	A	Ingst	Int-A	1		
		mirtazapine	2	2						
62ai	50 y M				U	Ingst	Int-A	2		

Drug	No. of fatalities
Iron supplements	32
Antidepressants	
desipramine	6
imipramine	2
amitriptyline	2
trazadone	2
amoxapine	1
Total	13
Methadone	6
Nifedipine	5
Diphenhydramine/phenylpropanolamine	4
Aspirin	3
Morphine	3
Methyl salicylate (winter green)	3
Codeine	2
Anticonvulsants	

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Zehirlenme Nedenleri

- Hatalı kullanım,
- Dozlama yanlışları,
- Zamanlamanın unutulması (Erken alma),

En sık Öldüren

DEMİR (!)

- Şekere benzer görünüm,
- Gebelik dönemi kullanım sonrası evde bulunma,
- Zararsız (yararlı !) olduğunun düşünülmesi;



Table 1. Medicinal preparations that can be fatal for a 10kg toddler upon ingestion of a one dose unit

Drug	Minimal potential fatal dose (mg/kg)	Maximal dose unit available (mg unless otherwise stated)	No. of tablets that can cause fatality
Tricyclic antidepressants			
amitriptyline	15	100	1–2
imipramine	15	150	1
desipramine	15	75	1–2
Antipsychotics			
loxapine	30–70	50	1–2
thioridazine	15	200	1
chlorpromazine	25	200	1–2
Antimalarials			
chloroquine	20	500	1
hydroxychloroquine	20	200	1
quinine	80	650	1–2
Anti-arrhythmics			
quinidine	15	324	1
disopyramide	15	150	1
procainamide	70	1000	1
flecainide	25	150	1–2
Calcium channel blockers			
nifedipine	15	90	1–2
verapamil	15	360	1
diltiazem	15	360	1
Camphor	100	1 g/5mL	1 tsp
Methyl salicylate	200	1.4 g/mL	<1 tsp
Theophylline	8.4	500	1
Narcotics			
codeine	7–14	60	1–2
hydrocodone	1.5	60 mg/5mL	<1 tsp
methadone	1–2	40	1
morphine		200	1
Oral hypoglycemics			
chlorpropamide	5	25	1
glibenclamide	0.1	2.5	1
glipizide	0.1	5	1
Podophyllin 25%	15–20	1.25 g/5mL	1mL

tsp = teaspoon.

Gerçekten öldürüyor mu?

Table II. Acute drug ingestion fatalities in infants and toddlers ≤ 2 years of age in the US from 1990 to 2000

Drug	No. of fatalities
Iron supplements	32
Antidepressants	
desipramine	6
imipramine	2
amitriptyline	2
trazadone	2
amoxapine	1
Total	13
Methadone	6
Nifedipine	5
Diphenhydramine/phenylpropanolamine	4
Aspirin	3
Morphine	3
Methyl salicylate (winter green)	3
Codeine	2
Anticonvulsants	
carbamazepine	1
valproic acid	0
Total	1
Benzonatate	1
Acetaminophen (paracetamol)	1
Diphenoxylate	1
Dextropropoxyphene	1
Promethazine	1
Clonidine	1
Benazepril	1
Clonazepam	1
Clozapine	1
Hydrocodone	1
Flecainide	1
Glipizide	1

TCA

Table 1. Case Reports of Tricyclic Antidepressant Severe Effects in Children

TCA	mg/kg	Dose	Weight	Age	Effect	Disposition	Study
Amitriptyline	17.5	1050 mg	≈ 60 kg	14 yr	Seizures	Recovery	Walsh, 1986 (61)
Amitriptyline	*5 (25)	50 mg (250)**	Unknown	9 m	Unresponsive	Fatal	Litovitz et al., 1993 (46)
Amitriptyline	?	?	Unknown	2 mo	Unresponsive	Fatal	Perrot, 1988 (62)
Amitriptyline	?	?	Unknown	5 yr	Unresponsive	Fatal	Litovitz et al., 1989 (42)
Amitriptyline	?	"Adult Dose"	Unknown	2 mo	Unresponsive	Fatal	Litovitz et al., 2001 (54)
Desipramine	*6.67	100 mg	Unknown	3 yr	Seizures/dysrhythmias	Recovery	Jue, 1976 (60)
Desipramine	30	?	Unknown	19 mo	Seizures/dysrhythmias	Recovery	DeCastro et al., 1980 (58)
Desipramine	*50	500 mg	Unknown	15 mo	Respiratory failure	Fatal	Litovitz et al., 1989 (42)
Desipramine	*>50	600–800 mg	Unknown	20 mo	Seizures/dysrhythmias	Fatal	Litovitz et al., 1990 (43)
Desipramine	*>50	500–600 mg	Unknown	10 mo	Cardiac dysrhythmias	Fatal	Litovitz et al., 1991 (44)
Desipramine	*>80	1000–1250 mg	Unknown	2 yr	Apneic/unresponsive	Fatal	Litovitz et al., 1999 (52)
Imipramine	15	?	Unknown	6 yr	Sudden death	Fatal	Saraf et al., 1974 (59)
Imipramine	>15	?	Unknown	27 mo	Seizures/dysrhythmias	Fatal	Walsh, 1986 (61)
Imipramine	30	?	Unknown	18 mo	Seizures/dysrhythmias	Fatal	DeCastro et al., 1980 (58)
Imipramine	32.1	450 mg	14 kg	4 yr	Cardiac dysrhythmias	Fatal	Cronin et al., 1979 (57)

* Estimated weight-based dose based on average weights: 1 yr = 10 kg; 2 yr = 12 kg; 3 yr = 15 kg; 4 yr = 17 kg; 5 yr = 20 kg; 6 yr = 23 kg.

** In this case, the child's mother reported giving the child half a 100 mg tablet, but postmortem found 253 mg amitriptyline in the child's stomach.

Ölüme Neden Olan Mekanizmalar

TABLE 1

Medications toxic to children in small quantities and associated major effects

Drug	Major toxic effects
β-Blockers	Hypotension, bradycardia
Calcium channel blockers	Hypotension, bradycardia
Camphor	Seizures
Clonidine	Central nervous system and respiratory depression; hypotension, bradycardia
Diphenoxylate/atropine (Lomotil)	Central nervous system and respiratory depression; anticholinergic effects
Tricyclic antidepressants	Cardiac arrhythmias, seizures, anticholinergic effects
Sulfonylureas	Hypoglycemia
Benzocaine	Methemoglobinemia, seizures
Lindane	Seizures
Methyl salicylate	Seizures, central nervous system depression, metabolic acidosis
Quinidine	Cardiac toxicity, seizures, visual, and auditory disturbances
Quinine	Cardiac arrhythmias, seizures, visual, and auditory disturbances

J Emerg Nurs 2003;29:290-3.

Hangi Miktarlar ?

Medicinal preparations that can be fatal for a 10kg toddler upon ingestion of a one dose unit

Drug	Minimal potential fatal dose (mg/kg)	Maximal dose unit available (mg unless otherwise stated)	No. of tablets that can cause fatality
Antimalarials			
Camphor	100	1 g/5mL	1 tsp
Methyl salicylate	200	1.4 g/mL	<1 tsp
Theophylline	8.4	500	1
Narcotics			
codeine	7–14	60	1–2
hydrocodone	1.5	60 mg/5mL	<1 tsp
methadone	1–2	40	1
morphine		200	1
Oral hypoglycemics			
chlorpropamide	5	25	1
glibenclamide	0.1	2.5	1
glipizide	0.1	5	1
Podophyllin 25%	15–20	1.25 g/5mL	1mL

Madde Alımı (İlaç Dışı)

Table 1 Clinical features, toxicology and postmortem findings

<i>Case no.</i>	<i>Age (years)</i>	<i>Clinical data</i>	<i>Toxicology (blood concentrations)</i>	<i>Pathology</i>
1	21	Collapsed at rave. Agitation, unconscious, 44°C, cardiac arrest	MDMA (4.2 mg/l) Amphetamine (1.4 mg/l)	Heart—contraction band necrosis Liver—focal necrosis Brain—focal haemorrhage, neuronal degeneration
2	20	Collapsed at disco. Thirst, convulsions, 36°C, ↑BP, low Na ⁺ , unconscious. Water intoxication	MDMA (0.04 mg/l)	Heart—widespread foci of necrosis Liver—foci of necrosis Brain—gross oedema, focal haemorrhage. Pituitary necrosis
3	24	Collapsed and died at disco. ? Temperature	MDEA (0.187 mg/l) Amphetamine (0.453 mg/l)	Heart—focal necrosis Liver—focal necrosis
4	21	Found dead in bed after party. No symptoms	MDMA (2.1 mg/l) MDEA (3.5 mg/l) MDA (8.5 mg/l) Amphetamine (0.256 mg/l)	Heart—normal Liver—focal necrosis Brain—focal haemorrhage Inhalation of vomit
5	20	Found unconscious in bed. Rigidity, 39.5°C, ↑LFTs, cerebral hypoxia. Survived four days	MDMA (0.09 mg/l) MDA (0.13 mg/l)	Heart—widespread foci of necrosis Liver—extensive necrosis Brain—hypoxic changes, DIC Lung—pulmonary infarcts
6	25	Sudden collapse in street. Previously well, witnessed collapse. Brought in dead	MDMA (trace in urine) MDA (trace in urine)	Heart—widespread foci of necrosis Liver—focal necrosis
7	23	Progressive jaundice and liver failure. All investigations negative. Admitted heavy ecstasy use, even after onset of jaundice	Admitted regular ecstasy use	Heart—normal Liver—massive hepatic necrosis Brain—normal

LFTs = liver function tests.

Öneriler...

1. Korunma;
2. Potansiyel toksik ajanların, farklı uyarılarla etiketlenme;
3. ZDM bilgilendirmelerinin detaylandırılma;
4. Reçeteleme sırasında yeterli uyarı₂₃

AMİRİM DOKTOR
ÖLÜRKEN KATİLİNİ
YAZMIŞ AMA
OKUYAMIYORUZ!



g/05