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Use of Drugs Prolonging QT Interval in Patients at the Time of Admission to Geriatric Department

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Abstract

The usage of drugs prolonging QT interval is common issue in old age. They were used by 67.5% of patients being admitted to geriatric department. Use of these drugs was associated with a higher 3-month mortality rate (36.6% versus 16.7%). This mortality rate was significantly higher in patients using 3 and more of these drugs. Patients, who did not survive 3 months used QT interval prolonging drugs significantly more often (83.3 % versus 67. 5%).The most frequently used group of drugs were diuretics used by 36% of patients. The most often used drug was furosemide, used by 32.5% of patients. The second most used group were antipsychotic drugs which were used by 24% of patients. The second most frequently used medicament was pantoprazole used by 22.5% patients. Antidepressants were used by 15.4% of patients. The most often used antidepressant was citalopram, which belongs to drugs with a high risk of QT interval prolongation. It was used by 6.1% of patients.

Keywords: Geriatric medicine; Pharmacology; Cardiology; QT interval

Introduction

A typical feature of care for older people is multi-morbidity with ensuing polypharmacy and using drugs with increased occurrence of adverse effects including drugs prolonging QT interval. There are many other causes of QT interval prolongation in old age like hypothyroidism, hyperkaliaemia and hypomagnesaemia, left ventricle hypertrophy, heart failure, hypertension, diabetes mellitus, and obesity, which can augment effect of drugs. Prolongation of QT interval is associated with increased risk of torsades de pointes, predisposing to ventricular fibrillation.

The Aim of Study

The aim of the study was to learn use of drugs prolonging QT interval in patients at the time of admission to geriatric department

Patients and Methods

The whole group comprised 228 patients (65 men and 163 women) with average age 82.4 years. (Table 1) 80.7% of the patients came from home, the rest were transferred from other departments. Use of QT prolonging medication [1] was recorded from the last treatment documentation before admission.

Corrected QT interval (QTc) was measured by ECG apparatus CMS 1200 G (Contec Medical Systems Co., Ltd.) in 192 patients. Patients were distributed to 3 categories according to QTc: 1 normal, resp. borderline (men <450 msec, women <470 msec), 2, prolonged (men >450 msec, women >470 msec) [2,3], with increased risk of complications (men, women= >500 msec [3]. 3-month survival was ascertained in 95 patients. Data were processed with standard statistical parametric and nonparametric tests (chi quadrate test, Student´s test, F test). The statistical significance was set on level p 0.05.

Results

67.5% of the patients used at least one drug prolonging QT interval (Table 2).

There was no significant difference between men and women.

Patients transferred from other departments used QTc prolonging drugs more often, but this difference was insignificant (Table 3).

Patients used 26 different drugs prolonging QTc interval (Table 4).

The most frequently used group of drugs were diuretics used by of 36% patients. The most often used drug was furosemide used by 32.5% of patients. The second most used group were antipsychotic drugs which were used by 24% of patients. The most often used antipsychotic drug was Tiapride. used by 10.4% of patients. The second most frequently used medicament was pantoprazole used by 22.5% patients. Antidepressants were used by 15.4% of patients. The most often used

	No		Yes		Together
	n	%	n	%	
men	18	37.7	47	72.3	65
women	56	34.4	107	65.6	163
together	74	32.5	154	67.5	228

Table 2: Use of drugs prolonging QT interval.

	no		yes		together
	N	%	N	%	
Home	64	34.8	120	65.2	184
Transferred from another department	10	22.7	34	77.8	44
together	74	32.5	154	67.5	228

$x^2=2.38<3.9$ >> measure of dependency V= 0.102

Table 3: Use of drugs prolonging QT interval in relation to stay before admission.

Sex	Admitted from home			Admitted from other departments			Together	
	N	average age	%	N	average age	%	N	average age
men	51	81.5	78.5	14	80.8	21.5	65	81.4
women	133	82.7	81.6	30	83.2	18.3	163	82.8
together	184	82.4	80.7	44	82.4	19.3	228	82.4

Table 1: Composition of patients group.

antidepressant was citalopram. which belongs to drugs with high risk of QT interval prolongation. It was used by 6.1% of patients. The other drugs with a high potential of QT interval prolongation included amiodarone (5.6%). quinolones (5.6%) and escitalopram (4.8%). Patients. who did not survive 3 months used QTc interval prolonging drugs significantly more often (83.3 % versus 67.5% (Table 5).

QTc interval was significantly longer in deceased patients (Table 7).

This difference was significant in age groups 65-74 and 85 plus (Table 8).

Mortality rate rose with severity of QTc prolongation. This increase was significant in patients with QTc longer than 550 msec (Table 9).

There was no relation between number of drugs and length of QTC interval (Table 10).

Patients using 3 and more drugs had a significantly higher 3-month mortality rate (Tables 11 and 12).

Discussion

Use of drugs prolonging QT interval increases risk of torsades des pointes development with possible progression to ventricular fibrillation. The study NHANES III (The Third National Health and Nutrition Examination Survey) found out that use of drugs with potential to prolong QT interval in last month double risk of QT prolongation [4]. QT interval can be prolonged by many drugs which use older people often. These medicaments were used by 67.5 % of patients. Use of drugs is influenced by type of population. Drugs prolonging QT interval were prescribed to 18% of emergency department patients. 1.6% of them used more than one of these medicaments. Prescription rate of these drugs has increased from 10.4% to 22.2% in period 1995 to 2009 [5].

	N	%		N	%
Quinolones	13	5.6	Quetiapine	17	7.4
Fluconazole	4	1.7	Risperidone	1	0.4
Hydrochlorothiazide	4	1.7	Sulpiride	1	0.4
Furosemide	75	32.5	Promethazine	4	1.7
Indapamide	5	2.6	Aripiprazole	3	1.3
Amiodarone	13	5.6	Olanzapine	4	1.7
Isradipine	1	0.4	Tiapride	24	10.4
Pantoprazole	52	22.5	Hydroxyzine	4	1.7
Famodipine	4	1.7	Trazodone	4	1.7
Tamsolusin	1	0.4	Sertraline	1	0.4
Mirabegron	1	04	Vefalaxín	2	0.9
Donepezil	1	0.4	Citalopram	14	6.1
Haloperidol	4	1.7	Escitalopram	11	4.8

Notice: Drugs with high risk of QT interval prolongation (High-risk-QT-drug CredibleMed

Table 4: Use of drugs prolonging QT interval.

	no using		Using QT prolonging drugs		together
	n	%	n	%	
Decreased	5	16.7	30	83.3	35
Surviving	25	32.5	52	67.5	77
Ttogether	30	26.8	82	73.2	112

Table 5: Comparison of QT interval prolonging medicaments use in relation to 3-month surviving QTc was longer in patients using QTc interval prolonging drug. but this difference was significant only in women (Table 6).

	MEN							
	used			did not use			together	
	N	Average QTc	sd	N	Average QTc	SD	N	Average QTc
normal-borderline	1	440.0	0.0	5	435.8	10.9	6	436.5
prolonged	6	464.8	8.6	12	467.5	13.8	18	466.6
High risk of complications	6	557.3	22.0	22	570.0	60.0	28	567.3
together	13	505.6	50.9	39	521.3	72.6	52	517.3
	WOMEN							
normal - borderline	26	436.5	37.6	36	440.5	19.2	62	438.8
prolonged	9	485.0	8.5	14	484.9	8.9	23	485.0
High risk of complications	15	562.9	45.8	40	592.0	56.0	55	584.1
together	50	483.2	66.5	90	514.7	80.9	140	503.5

Women/together-t-test: tvyp=2.00 > ttab=0.99 ==> significant p0.05

Table 6: Distribution of QTc interval.

	N	mean	SD	P 0.05
deceased	29	538.0*	84.9	tcalc=3.03>ttab=1.98
surviving	66	488.7	72.6	
together	95	503.7	79.8	*significant

Table 7: Comparison of QTc interval duration in deceased and surviving patients.

Age group	Deceased			Surviving			tcalc for p0.05
	N	average	s2	N	average	s2	
65-74	5	501.4	2 507.4	7	439.3	807.6	2.48>2.28
75-84	13	537.6	6 857.8	35	500.3	5 434.9	1.46<2.011
85 plus	11	555.0	8 877.6	24	486.1	5 402.7	2.21>2.42
Together	29	538.0	7 214.5	66	488.7	5 265.8	

Table 8: Comparison of QTc interval duration in deceased versus surviving in different age groups.

Category of QT interval prolongation	Deceased		Surviving		N (100%)
	N	%	N	%	
Normal-borderline men under 450 msec women under 470 msec	7	20.0	28	80.0	35
Prolonged (less than 500 msec)	4	22.2	14	77.8	18
Increased risk (more than 500 msec)	5	29.4	12	70.6	17
Very high risk (>550 msec)	13*	52.0	12	48.0	25
Together	29	30.5	66	69.5	95

Table 9: Comparison of 3-month mortality rate in relation to severity of QTc prolongation group.

	Died			Survived			N (100 %)
	N	average	SD	N	average	SD	
Did not use	5	531.8	58.2	20	466.8	70.4	25
used	24	539.3	89.5	46	498.2	71.4	70
1 drug	11	554.3	105.8	27	499.4	76.3	38
2 drugs	5	541.4	88.5	16	504.0	66.6	21
3 and more	8	517.3	54.1	3	457.0	25.5	11
Together	29	538.0	84.9	66	488.7	72.6	95

Table 10: Relation between number of drugs and length of QTc.

Our data are closest to findings of German authors who found out that aforementioned drugs were used by 58.7% of patients hospitalized at geriatric department [6] 23.7% of our patients used more than one drug prolonging QT interval. which is in concordance with the aforementioned German study (22.1%) The array of drugs prolonging QTc interval consisted of 26 medicaments. Table 12 shows comparison of different medicaments prolonging QTc with the aforementioned German study [6].

German authors revealed use of another drugs prolonging QT interval (Mirtazapine. Melperone. Domperidone. Xipamide. Amitryptiline. Formoterol. Pipameron. Amantadine) which were not used by our patients. More frequent use of quinolones and diuretics in our study can be explained by more acute character of our department. The German study included also patients from rehabilitation units. Patients at our department had multiple chronic conditions and they were hospitalized for acute problems e.g. infection. heart failure. Our patients used antidepressants less frequently than German patients (15.4% versus 23.2%). The most frequently used antidepressants (citalopram and escitalopram) have high potential to prolong QT interval. Their use was less frequent than in the aforementioned German study (21.1% resp. 10.9%)

Usage of drugs prolonging QTc was associated with higher 3-month mortality. Deceased patient used these drugs significantly more frequently (83.3 % versus 69.7%). 30 (36.6%) of 82 patients who used medicaments prolonging QT interval died. Only 5 (16.7%) of 30 patients who did not use these drugs did so. QTc interval was significantly longer in patients using drugs prolonging this interval. QTc was significantly longer in patients who passed. This difference was significant in women and in age groups 65-74 and 82 plus years. Higher mortality in patients using QTc prolonging drugs was also observed by Dutch authors who found an almost trebling in the risk of sudden death in patients using these medicaments [2]. Relation of QTc interval prolongation was also revealed by Israeli authors who found out that deceased patients had prolonged QTc intervals more frequently (9.6% versus 6%) [7].

A more detailed comparison is no possible because we did not analyses cause of death.

Additive effects of contemporary use of more drugs prolonging QTc on QTc duration was not confirmed. which is in agreement with Dutch authors [8].

We observed that the use of 3 and more of these drugs was associated with increased mortality rate.

53.9% of our patients had a QTc longer than 470 msec. 43.7% of the patients had this interval longer than 500 msec. what is significantly more than it was revealed by other authors. Prolonged QTC interval was observed in 25 % residents of a nursing home. Only 15% of them had a QTc longer than 500 msec [9]. QTc interval was prolonged in 32% of patients in geriatric department [7].

Higher prevalence of QTc interval prolongation in our department can be explained by more serious condition of our patients as it is evidenced by their higher mortality rate (30.6% versus 6%) than in Israeli study) [7].

Due to limited number of patients in our study it was not possible to analyse potential of different drugs to prolong QTc. From a practical point of view. it is important that citalopram which belongs to drugs with a high potential to prolong QTc [10] was used by 6.1 % of patients which is much less than it was in the German study (15%) [6]. Usage of other higher risk drugs was comparable with data from the aforementioned study except for more frequent use of quinolones in our patients (5.6% versus 1.3%) and more frequent use of escitalopram in German study (8.2% versus 4.8%)

Conclusions

- Use of drugs prolonging QTc interval is frequent issue in patients treated in geriatric departments

- Use of drugs prolonging QTc interval is associated with higher 3month mortality rate

- The 3-month mortality rate is higher in patient using 3 and more drugs prolonging QTc interval

Acknowledgements

	Died		Survived		N (100%)
	N	%	N	%	
0	5	25	20	75	25
1	15	34.1	29	65.9	44
2	6	25.0	18	75.0	24
3 and more	9	64.3	5	35.7	14
Together	35	31.3	77	68.8	112

Table 11: Relation of drug number and 3-month surviving.

	Our study	Schächtle et al. [6]		Our study
Quinolones	5.6	1.3 (levofloxacin)	Quetiapine	7.4
Fluconazole	1.7		Risperidone	0.4
Hydrochlorothiazide	1.7	5.2 (+1.4 s Ramiprilom)	Sulpiride	0.4
Furosemide	32.5	9.2	Promethazine	1.7
Indapamide	2.6		Aripiprazole	1.3
Amiodarone	5.6	4.6	Olanzapine	1.7
Isradipine	0.4		Tiapride	10.4
Pantoprazole	22.5		Hydroxyzine	1.7
Famodipine	1.7		Trazodone	1.7
Tamsolusíne	0.4		Sertraline	0.4
Mirabegron	04		Vefalaxíne	0.9
Donepezil	0.4		Citalopram	6.1
Haloperidol	1.7	2.1	Escitalopram	4.8

Notice: Drugs with higher potential to prolong QT interval (High-risk-QT-drug CredibleMed)

Table 12: Comparison of use of different drugs prolonging QT in German and our study.

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