Evaluation of needs for therapeutic monitoring of digoxin in a tertiary hospital

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Key words: *rationality; defined daily dose; therapeutic drug monitoring; digoxin.*

Summary. *Objectives. To collect the data about the consumption of digoxin, evaluate the tendencies towards usage of this drug during 2004–2007, and to find departments, which cover the main part of digoxin consumption in a tertiary hospital. To evaluate the intensity of serum digoxin concentration measurements during 2005–2007.*

Material and methods. Our study was carried out in a tertiary hospital with 2600 beds and 63 departments. Consumption of digoxin is expressed in defined daily doses per 100 occupied beds daily during 2004–2007. All serum concentration measurements in 2005–2007 were evaluated.

Results. The main consumers of digoxin in 2007 were the Units of Endocrinology, Pulmonology and Immunology, Cardiology II, Neurosurgical Reanimation and Intensive Care, Neurology, Eye Disorders I, Intensive Care Unit of Cardiology; they consumed 51.05% of total digoxin. In total, 58 digoxin measurements were performed in 2005, 89 in 2006, and 64 in 2007. The intensity of serum concentration measurements for digoxin is 1/147 (one measurement for 147 defined daily doses) in 2005, 1/89 in 2006, and 1/107 in 2007. These results show that intensity of serum digoxin concentration measurements is low.

Conclusions. Twenty-two out of the 63 departments cover 90% of digoxin consumption per year. The changes in digoxin consumption were not statistically significantly different in 2004–2007. There was a tendency towards an increase in serum digoxin concentration measurements during the 3-year period. Digoxin concentration outside therapeutic ranges was established in about half of all cases in 2005–2006, but there was an increase in normal serum concentration in 2007.

Introduction

Digoxin has been used to treat heart failure for more than 200 years. It is no longer the first-choice drug, but still it is used in some clinical situation, namely for treatment of patients with congestive heart failure and atrial fibrillation (1, 2). There are many problems encountered in trying to choose an effective dose for a drug such as digoxin. It is difficult because of such components as narrow therapeutic index, difficulty to define therapeutic endpoints, patients' variability, and varying effects of pathological states and drugs on digoxin disposition (3).

The use of digoxin must be adjusted to each patient individually according to patients' age, weight, and renal function (4). Dosing must be controlled according to not only clinical effect, but to digoxin level monitoring as well. In suspected toxicity or ineffectiveness, digoxin plasma concentration should be measured. Potassium levels and kidney function parameters are also needed to be controlled (5, 6).

Irrational use of narrow therapeutic index drug – digoxin – is a big problem of the health system, but the tendencies of using and monitoring this drug are still unknown in Lithuania.

We tried to evaluate the monitoring level of digoxin in a tertiary hospital in case to determine it is rational or not.

The objectives of our study were to collect the data about the consumption of digoxin, to evaluate the tendencies of usage of this drug during 2004–2007, to find the main consumers of digoxin, and to evaluate the intensity of serum digoxin concentration measurements during 2005–2007.

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Materials and methods

This was a retrospective observational study carried out in a tertiary hospital with 63 clinical departments and 2600 beds. Data on digoxin usage and the beds occupied in the different units per year were obtained from computer system of the Hospital and Pharmacy for 2004–2007. All measurements of serum digoxin concentration were performed by routine laboratory tests, and data were received from the database of the Laboratory of Clinical Chemistry and Hematology.

The defined daily dose (DDD) methodology was used to express the consumption of digoxin. The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. DDDs provide a fixed unit of measurement independent of price and formulation enabling the researcher to assess trends in drug consumption and to perform comparisons between population groups. The WHO bases it on the number of packs of all drugs used, the number of dose units in each pack and DDD values allocated. The DDD for digoxin is 0.25 mg. Consumption in hospitals is expressed in the DDDs per every 100 occupied beds daily (OBD) (7, 8).

In our calculations, we included data of packs issued to inpatients only. We adapted an Excel spreadsheet, which facilitated to convert packs into DDDs. Further DDD analysis was performed to express consumption per every 100 OBD for a single unit in clinical departments. Mean value of DDD/100 OBD was estimated for every year, and mean values were compared among all four years.

The main consumers, consuming 90% of all digoxin per year, were determined. Ninety percent of drug usage (DU 90%) in the main departments was presented as DDD/100 OBD for descriptive purposes for all four years.

We collected data about the intensity of digoxin monitoring – number of serum concentration measurements performed for digoxin in 2005–2007. Evaluation of all serum concentration measurements was performed as well. Digoxin concentration was considered "normal," when it was between 1–2.6 nmol/L, "too high" – when it was higher than 2.6 nmol/L, and "too low" – when it was lower than 1 nmol/L (2).

Data were processed with SPSS 16.0 using descriptive and comparative statistics for nonparametric values (Mann-Whitney test). The *P* values of less than 0.05 were considered as statistically significant.

Results

Table summarizes the consumption of digoxin over 4 years (2004–2007); the changes in DDDs per 100 OBD for digoxin during the 4-year period were not statistically significantly different.

The usage of digoxin varied in the different units. Twenty-two departments consumed DU 90% of digoxin during 2007. In 2007, Endocrinology, Pulmonology and Immunology, Cardiology II, Neurosurgical Reanimation and Intensive Therapy, Neurology, Eye Disorders, and Intensive Care Unit of Cardiology consumed 51.05% of total digoxin. The tendencies towards digoxin consumption during the 4-year period are illustrated in Fig. 1. As we can see, the main consumers of this drug remain the same.

In total, there were 58 serum digoxin concentration measurements in 2005, 89 in 2006, and 64 in 2007. The intensity of serum concentration measurements for digoxin is 1/147 DDDs (1 measurement for 147 DDDs) in 2005, 1/89 DDDs in 2006, and 1/107 DDDs in 2007 (Fig. 2). Proportional expressions of concentration findings for digoxin are presented in Fig. 3. There was an increase in normal serum concentration findings of digoxin in 2007.

Discussion

Research was made in Lithuania attempting to evaluate the level of therapeutic drug monitoring. We compared the intensity of serum concentration measurements of digoxin and carbamazepine. There were 57 carbamazepine measurements in 2005, 178 in 2006, and 219 in 2007. The intensity of carbamazepine monitoring was 1/125 DDDs in 2005, 1/47 DDDs in 2006, and 1/36 DDDs in 2007 (9). These

Table. **Defined daily doses per 100 occupied bed days for digoxin over four years**

Year	Mean (SD)	Median	95% CI	*P* value
2004	1.95 (2.57)	1.07	1.21; 2.68	0.591*
2005	1.35 (1.49)	0.88	0.95; 1.79	0.865**
2006	1.97 (3.19)	0.66	1.08; 2.87	0.858***
2007	1.56 (2.1)	1.00	0.96; 2.17	0.602****

**P* value comparing 2004 and 2005. ***P* value comparing 2005 and 2006.
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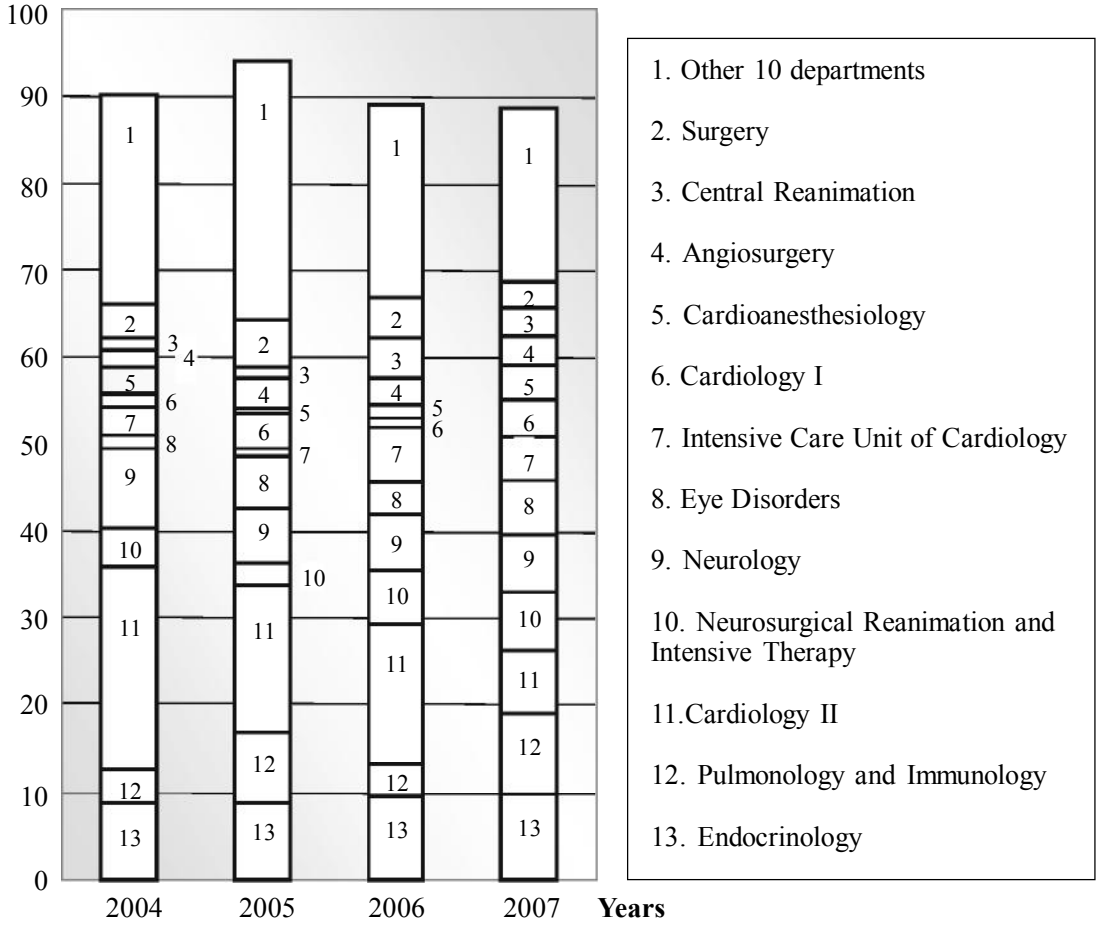

Fig. 1. **Digoxin consumption during 2004–2007**

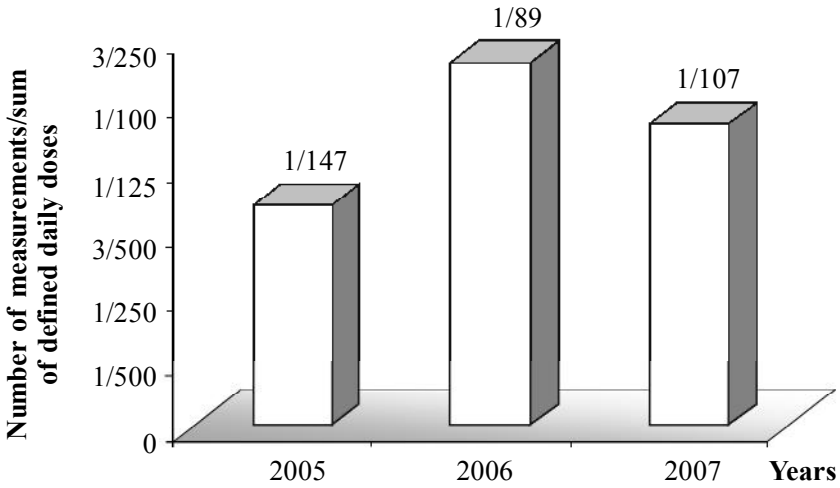

Fig. 2. **Intensity of serum concentration monitoring for digoxin**

results show that the level of therapeutic monitoring of digoxin is lower than carbamazepine. Similar study was carried out in a tertiary hospital for gentamicin and vancomycin. The intensity of serum concentration measurements of these two drugs in 2006 was 1/84 DDDs for vancomycin and 1/1516 DDDs for gentamicin, and it is lower than for digoxin (1/89 DDDs) (10). Digoxin is monitored better than gentamicin, but worse than carbamazepine.

We found no similar studies on the consumption of digoxin using DDD methodology over the world. One study on monitoring of digoxin was made in the Higher Medical Institute, Plovdiv, Bulgaria. They also tried to evaluate the level of serum concentrations mo-

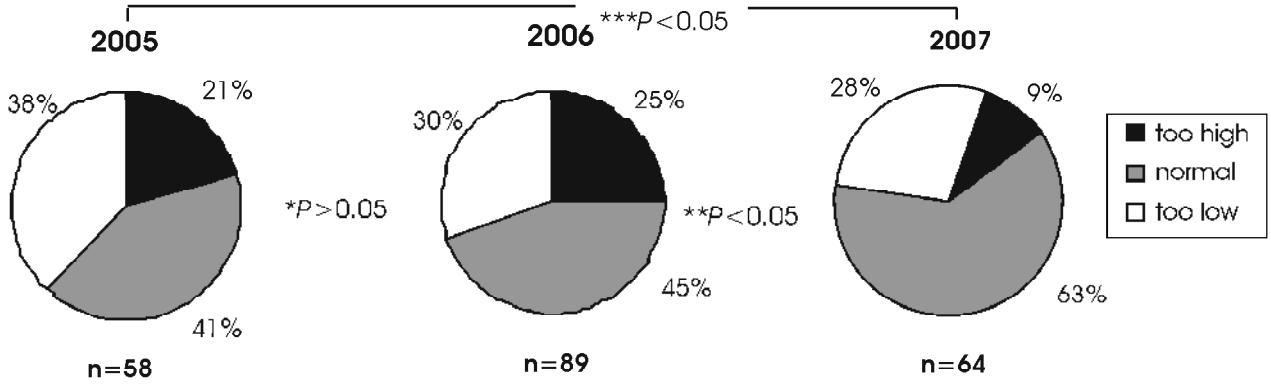

Fig. 3. **Serum digoxin concentration measurements in 2005–2007**
Normal digoxin concentration: **P* value comparing 2005 and 2006.
***P* value comparing 2006 and 2007. ****P* value comparing 2005 and 2007.

nitoring for digoxin. Their results show that the prescribed dose provided serum digoxin levels within, above, and below the targeted therapeutic range for 50.2%, 38.4%, and 11.4% of the patients, respectively (11).

Therapeutic monitoring is an important part of rational drug use. The level of rational drug use is not very well known in Lithuania, but a few studies showed that improper and irrational use of drugs, especially antibiotics, is a big problem in hospitals (12–15). Patients' incompliance is a common problem in Lithuania as well (16). Few studies on the usage of different pharmacotherapeutic group drugs in Lithuania were conducted (17–20). However, no research about digoxin consumption and monitoring had been performed in our country before.

Our study shows that in Lithuania monitoring is insufficient, and the number of serum concentration measurements is too small; moreover, about half of all findings show too high or too low concentration. These results reveal high need for intensifying digoxin concentration measurements starting from main consumers, covering the major part of consumption (Units of Endocrinology, Pulmonology and Immunology, Cardiology II, Neurosurgical Reanimation and Intensive Therapy, Neurology, Eye Disorders I, Intensive Care Unit of Cardiology).

Conclusions

Of the 63 departments, 22 cover the main part of digoxin consumption per year (90%). The changes in digoxin consumption were not statistically significantly different in 2004–2007. There was a tendency towards an increase in serum digoxin concentration measurements during the 3-year period. Digoxin concentration outside therapeutic ranges was established in about half of all cases in 2005–2006, but there was an increase in normal serum concentration findings in 2007.

Digoksino vartojimo poreikio įvertinimas tretinio lygio ligoninėje

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Raktažodžiai: racionalumas, apibrėžtoji dienos dozė, vaisto vartojimo įvertinimas, digoksinas.

Santrauka. *Tyrimo tikslas.* Surinkti duomenis apie digoksino suvartojimą, įvertinti šio vaisto vartojimo pokyčius 2004–2007 m. ir nustatyti daugiausia digoksino vartojančius tretinio lygio ligoninės skyrius. Įvertinti digoksino serumo koncentracijos matavimų intensyvumą 2005–2007 m.

Tyrimo medžiaga ir metodai. Studija atlikta tretinio lygio ligoninėje, turinčioje 63 skyrius bei 2600 lovų. Digoksino suvartojimas 2004–2007 metais išreikštas apibrėžtųjų dienos dozių skaičiumi 100 lovadienių. Įvertinti visi 2005–2007 m. atlikti digoksino koncentracijos tyrimai.

Rezultatai. Daugiausia digoksino vartojantys skyriai 2007 m. buvo: Endokrinologijos, Pulmonologijos-alergologijos, II kardiologijos, Neurochirurgijos reanimacijos ir intensyviosios terapijos, Neurologijos, I akių ligų, Kardiologijos intensyviosios terapijos. Šie skyriai suvartojo 51,05 proc. viso per metus suvartoto digoksino kiekio. 2005 m. atlikti 58 digoksino koncentracijos tyrimai, 2006 m. – 89, 2007 m. – 64. Gydymo stebėsenos intensyvumas 2005 m. buvo 1/147 (1 tyrimas 147 apibrėžtosioms dienos dozėms), 2006 m. – 1/89, 2007 – 1/107.

Išvados. 22 skyriai iš 63 yra pagrindiniai digoksino vartotojai. Digoksino suvartojimo pokyčiai 2004–2007 m. buvo statistiškai nereikšmingi. Trejų metų laikotarpiu pastebėta digoksino koncentracijos matavimų intensyvėjimo tendencija. Digoksino koncentracijos nukrypimai nuo normos nustatyti apie pusę visų atvejų, bet 2007 m. užfiksuotas normalios koncentracijos padidėjimas.

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