ORIGINAL AUTOMATED DOSING SYSTEM USED IN OPHTHALMOLOGY

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Abstract - The authors propose an original solution of automatic dosing system that can be applied mainly in the treatment of glaucoma. The developed device accurately delivers droplets of less than 10 µl, leading to better use of the ophthalmic liquid, in the meantime being able to electronically monitor, record and store the daily treatment performed by the patient at home.

Keywords: Mechatronic system, dosing of ophthalmic liquids, glaucoma treatment, eye drop device.

1. Introduction

Glaucoma is one of the main causes of irreversible blindness and situates among the disorders that require continuous surveillance and adequate treatment. The condition appears due to the long exposure to high intraocular pressures (IOP), causing the degradation of retinal nerve fibres and characteristic modifications at the level of the papilla of the optical nerve.

Glaucoma has a high social and economic impact, being a major public health issue because grows towards blindness in default of precocious diagnosis and efficient treatment. The affection is usually called "a silent thief of sight" due to the lack of specific symptoms in its first stages of evolution. The term of glaucoma refers to a group of affections whose common feature is a characteristic affectation of the optical nerve (glaucomatous optic neuropathy), associated with modifications of the eye field, the main risk factor being the increased intraocular pressure (IOP). The normal accepted value of the intraocular pressure is of 10-22 mmHg. The illness develops slowly and irreversibly, affecting the eye field, and presents a multifactor etiology. Consensus regarding the factors that produce the alteration of optical nerve fibres was not yet achieved.

Glaucoma can affect any age category, including children, but is more frequent in the case of patients over the age of 40 or of patients that have other cases of glaucoma in their families. Almost 2% of the persons aged over 40 and 5% of the persons aged over 80 suffers from glaucoma.

Glaucoma is a progressive affection that lasts a lifetime. There is no known treatment able to cure it, but a correct treatment allows preserving vision.

Most antiglaucoma medications target the decrease of eye pressure by reducing the amount of aqueous humour or by increasing its draining. They are found mainly as eye drops easy to administer one or more times per day. If the evolution of the affection cannot be stopped only by the use of collyrium, laser and surgery treatment are required.

Because glaucoma can aggravate without warning symptoms, the correct daily administration of the prescribed medication is crucial for the patient. Once prescribed, the antiglaucoma treatment must be strictly observed for a lifetime in order to limit the development of the illness. The early diagnostic, the rigorous treatment and the periodical ophthalmological check are main elements of the glaucoma management.

Recent research proved that many glaucoma patients medicated by eye drops showed good progress during hospitalization and a completely unsatisfactory evolution when individually followed the prescribed treatment. Routine periodical checks denoted the progress of the affection. The cause was found to be the lack of constancy of the medication at home, concerning the schedule of the administration as well as the correct dosage of the drug. The situation is even more alarming in the case of patients that lived in rural areas. Studies also showed that only 50% of the patients renewed their prescription after 6 months and only 30% after another 3 months.

Additionally, the patients tended to increase the drug dosage during the days that preceded the visit to the ophthalmologist, leading to values of IOP that seemed normal, misleading the physician.

It would be thus beneficial if the patients could be endowed with a device that would allow an accurate

dosing and a rhythmic administration of the collyrium required for the glaucoma treatment. The device has to be portable in order to support medication at home, must allow the programming of the treatment prescribed by the physician in terms of scheduling and delivered quantity and must continuously function (24 hours per day) during the period of time between two periodical checks, usually of the order of months.

Another challenge of developing such a device is the fact that, until now, eye treatments with drugs in liquid suspensions are carried out through droplets with specific volumes of 30µl. There are many concerns for achieving dosing systems able to precisely calibrate small volume values, while it was shown that the eye can retain only 10µl of ophthalmic liquid in his conjunctival sac [1]. With an automatic dosing system able to achieve very small drops, even of lower volumes (if the ophthalmologist appreciates them as effective in other forms of treatment), three patients can be treated using the same amount of eye liquid. As a consequence, in relation to the relatively large number of chronically and/or seasonally ill people, significant reductions of costs are achieved in the health area.

These considerations led the authors to develop an original solution of automated dosing system for ophthalmic liquids, able to continuously monitor the treatment prescribed by the physician. The system allows the proper dosing of the collyrium (by the accurate control of the volume of the delivered droplet), the continuous record of the moments of drug administration (day, hour and minute) along a month and the storing of data on a memory card in order to be visualised and analysed by the ophthalmologist during the periodic check of the patient.

2. Construction Of The Automatic Dosing System

Different solutions of dispensers operating with pumps and valves, pistons, with different actuating systems, in peristaltic system, piezoelectric transducers or electrolysis principle, are known in the scientific literature [2-7].

The state of the art in the field of dispensing systems highlighted that the dosage principle of very small volumes of eye liquid of the order of 10µl or less relied on the precise axial movement of a piston in a cylindrical body (like a syringe where drive is manual). Accordingly, a system of automatic adjustment of the position with micrometric precision, small stroke in a field of 10 ... 40mm and displacement driving forces in the 10 ... 20N, produced by an electric drive power of battery type and autonomy for at least a month was designed. The resulted mechanical-electronic equipment has all the features of a mechatronic product and fully achieves all the functions mentioned above.

The solutions adopted by the authors propose a normalized syringe dispenser, endowed with a driving system of movement of the piston using a screw-nut mechanism with a rotating nut where the rotation of the screw is prevented. The rotation of the nut is obtained from a DC micro motor coupled with a planetary gearbox. The solution also features an incremental rotary encoder. Between gearbox output and nut rotation, a toothed belt drive is provided, which allows a lateral arrangement of moto-reducer group and thus a reduced axial size of the device. The total transmission ratio, of high value, allows the use of a micro motor with reduced torque and gauge. Considering the rotary encoder, a dosing resolution of less than 1µl is achieved. The drive of the dispenser is provided with (end-stop) stroke limiters, adjustable, which enables both the protection of the system, as well as the possibility of automatic filling with ophthalmic liquid.

A longitudinal section through the axis of the drive motor and the axis of the screw, which generates the translation movement, is shown in Figure 1. A cross-section (A-A section) through the screw for rotation preventing is also represented. A three-dimensional view of the device is given in Figure 2.

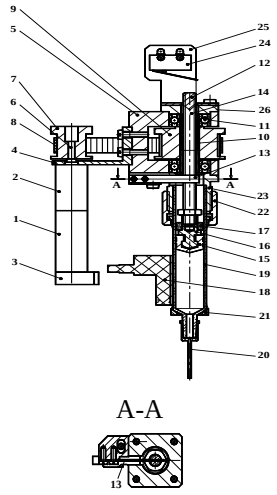

Figure 1: The principal section of the automatic dosing system

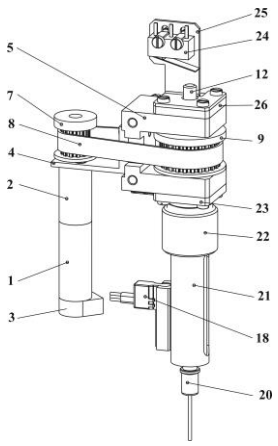

Figure 2**:** *A three-dimensional view of the device*

The automatic dosing system is made up of the micro motor 1 coupled to the reduction gear 2 and the rotation encoder 3. The reduction gear is fixed through the bracket 4 at the body 5 of the device. On the gearbox output shaft 6 is mounted the toothed belt wheel 7, which, by means of belt 8, puts in motion the toothed belt wheel 9 mounted on the shaft 10, supported on bearings 11. In its inner part, the shaft 10 is threaded in correspondence with the thread of screw 12. The screw is prevented from rotating by a lamella 13 introduced in a groove 14 from the screw 12. The axial movement of the screw is taken up by the piston 15 mounted on the mandrel 16, which is fixed on the screw. On mandrel is mounted the annular permanent magnet 17, which carries an electrical signal to the inductive transducer 18 when the piston arrives at the lower end of its stroke. The piston moves within the syringe barrel 19, at which is fixed the hypodermic needle 20 through which is delivered the dose of eye liquid.

The body of the syringe 19 is detachable from the body 5 of the device through the tube 21, the nut 22 and the bottom cover 23 of the device. Microswitch 24 for delivering the electrical signal at the upper end of the stroke of screw is fixed to the body 5 of the device by the bracket 25 and the top cover 26. Volume programming of ophthalmic liquid dose is performed by programming the number of pulses obtained from the rotary encoder 3.

Figure 3 presents the 3D model of the innovative automatic dosing system for ophthalmic liquids. The prototype of the automatic dosing system developed by the authors is shown in Figure 4.

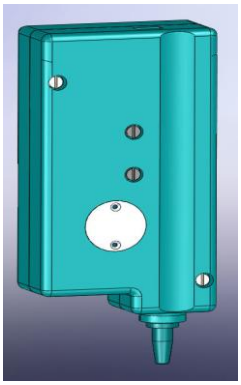

Figure 3: 3D model of the developed solution

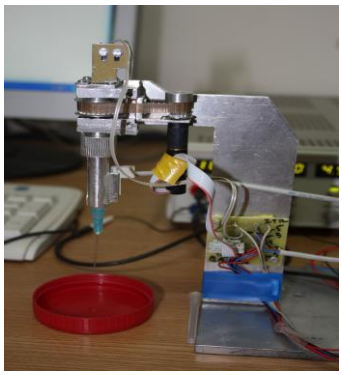

Figure 4: The prototype of the automatic dosing system

Experimental tests confirmed the feasibility of the original design solutions [8]. The droplet dosing function, the most important in the functioning of the device, was performed with very good results.

Main features of the automatic dosing system for ophthalmic liquids

The main features of the innovative automatic dosing system developed by the authors are:

- type of liquid to be dosed: hydrous solutions, including ophthalmic liquids;
- total volume of liquid: 2ml (2000µl);
- shape of the liquid to be dosed: drop;
- range of volumes of dosed droplets: 1 ... 20µl;
- maximum frequency of dosage: 3 dosages/min;
- volume of standard droplet: 10µl;
- number of dosed droplets: 200 (corresponding to a medical treatment of 31 days);
- dimensioning and calibration of the droplet: by programming the number of angular pulses received from the incremental rotation sensor;
- time required for generation of a drop: 0.5s;
- pause between two successive dosages: 2s;
- dosage control: by manual pressing the START button during 1s;
- supply: two 1.5V batteries (mounted in the dosing device);
- autonomy of functioning: 1 month;
- duration of monitoring: 1 month;
- acoustic warning of the scheduled drug administration;
- duration between two successive moments of drug administration: programmable between 1h and 12h;
- monitoring of the drug administration by visualisation and analysis of the records stored by the electronic micro system.

3. Conclusions and further research

The controlled dosing of 10 µl drops (the quantity that can be retained by the human eye) leads to the ability to treat three times more patients with the same amount of drug.

A market study regarding the automated dosing system developed by the authors shows that the costs involved by its manufacturing can be amortized in 22-24 months, the amortization period varying in function of the price of the antiglaucoma medication prescribed by the physician.

The design of the autonomous dosing system allows the ease of its use, being suitable for patients with any level of education.

Further researches aim to obtain droplet volumes of less than 10 µl. Improvement of the device construction in order to reduce positioning errors and clearances in the areas where displacements are generated and transmitted is also considered.

4. Acknowledgements

This work was supported by the National Agency for Scientific Research under the grant 71022 –

"Automated dosage system, with continuous monitoring, storage and computerized display of information for the verification of optimal implementation of prescribed eye treatments".

5. References

[1] W.L. Zielinski and T.R. Sullivan, "Ophthalmic Drug Therapy – Challenges and Advances in Front-of-the-eye Delivery," Mystic Pharmaceuticals Inc., Special Report, 2007.
[2] E. Rauh, "Hose pump for the exact dosing of small quantities of liquids," U.S. Patent 5693020 A, 1997.
[3] U. Kipfer, "Device for administering a liquid solution of an active substance," U.S. Patent 20040176720 A1, 2004.
[4] R.F. Papen, R.E. Pelc, N.S. Chibucos and W. Meyer, "System for dispensing microvolume quantities of liquids," U.S. Patent 5927547 A, 1999.
[5] V. Van Toi and P.A. Grounauer, "Portable Device for Programmable, Automatic, or On-Demand Delivery of Artificial Tears," in Advances in Experimental Medicine and Biology, vol. 438, 1998, pp. 1027-1032.
[6] J.F. Collins, Jr., R.B. Chinnock, J. Melanson and J. Howard, "Ophthalmic drug delivery system," U.S. Patent 7883031 B2, 2011.
[7] S. Saati et al., "Mini Drug Pump for Ophthalmic Use," in Trans Am Ophthalmol Soc., vol. 107, 2009, pp. 60–70.
[8] T.C. Apostolescu et al., "Design and Testing of an Automatic Dosing System for Ophthalmic Liquids", Proceedings of the International Conference on electronics, Computers and Artificial Intelligence ECAI 2015, vol.7, no.3, 2015, pp. 85-90.