Myasthenia Gravis: Analytical Methods for the Determination in Biological Fluids of First-Line Therapeutic Agents Used in the Management of the Disease

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Editorial

Myasthenia Gravis (MG) an autoimmune disease is the prototype of neuromuscular junction disease caused by auto antibodies against the nicotinic Acetylcholine Receptor (AChR) located in the postsynaptic muscle endplate membrane [1,2]. The autoimmune disorder is characterized by weakness and fatigability of the voluntary muscle arising from the distortion and simplification of the postsynaptic muscle membrane and consequent attachment of antibodies and complement to the membrane.

A large number of drugs has been reported to have the potential of inducing myasthenia gravis and they include D-penicillamine, amidoglycoside, fluoroquinolones, tetracyclines, timolol, betaxolol, general anesthetics, chloroquine, sulfonamides, quimidine, barbiturates, gabapentin, phentoyin and calcium channel blockers [3,4].

Myasthenia gravis has been classified on the basis of severity of the diseases into five grades [5]. Such classes include: Grade 0 (asymptomatic), Grade 1 (ocular signs and symptoms); Grade 2 (mild generalized weakness); Grade 3 (moderate generalized weakness, bulbar dysfunction, or both) and Grade 4 (severe generalized weakness, respiratory dysfunction, or both).

The symptoms of myasthenia gravis are specific muscular weakness and fatigability. Ocular symptoms such as ptosis, diplopia, or blurred vision seem to be first manifestation of the disease.

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Ptosis (weakness of levator palpebrae) which may be unilateral, is a common presenting feature. The diagnosis of myasthenia gravis deals with clinical demonstration of fatigability, while the electro diagnostic, pharmacological and serological tests are adjunct to the diagnosis [6]. Infections, initial high dose steroid therapy, or an inadequate treatment can cause myasthenic crisis (exacerbation of myasthenia), a condition that leads to paralysis of respiratory muscles.

Treatment of myasthenia gravis involves use of therapeutic agents (drugs) such as acetylcholinesterase inhibitors, corticosteroids, immunosuppressants, immunomodulating agents and procedures such as plasmapheresis and thymectomy [7]. Initial treatment with drugs usually starts with use of the acetylcholinesterase inhibitor or in combination with corticosteroid. Short-term treatment using immunomodulating agents may be effective in the early stages of treatment or later during an exacerbation. However, for long-term treatment steroid and immunosuppressants are included in the dosage regimen. These first-line drugs namely pyridostigmine bromide (acetylcholinesterase inhibitor), prednisone (corticosteroid), azathioprine (immunosuppressant) are occasionally given in combination with second/or third-line drugs.

In the present paper, analytical methods of choice in the quantification of first-line drugs used to treat myasthenia gravis in biological fluids are considered. Monitoring these drug levels in biological fluids is important to assure appropriate levels are maintained during therapy or treatment.

The bioanalytical methods that have been reported include (i) immunoassay techniques [8,9], electrochemical [10], spectroscopy [11], capillary electrophoresis [12,13] and chromatographic methods.

Despite the availability of a number of analytical methods to determine these first-line drugs in biological fluids, immunoassay methods are rarely used for the analysis due to lack of availability of specific antibodies. Spectroscopic (UV/Vis) methods due to insufficient sensitivity and specificity are not often employed. Capillary electrophoresis (CE) is an attractive alternative to conventional separation techniques such as LC and GC however, its drawbacks in terms of injection modes (hydrodynamic injection or electrokinetic injection), make LC or GC the preferred method of analysis. The advantages of hyphenation of chromatographic methods allow the techniques to enjoy preference amongst analysts. Some reported chromatographic techniques (non-hyphenated or hyphenated) using different conditions for sample preparation, analyte extraction, separation and detection to determine these first-line drugs in biological fluids are presented:

1. Pyridostigmine bromide:
(a) Human Plasma:
(i) non-hyphenated HPLC with UV detector [14-18].
(ii) non-hyphenated GC with nitrogen and phosphorus detector [19]
(iii) hyphenated chromatographic system GC/MS [20,21]
(b) Human Serum:
(i) non-hyphenated HPLC with UV detector [22]
(ii) non-hyphenated GC with electrochemical detector [23]
2. Prednisone:
(a) Human Plasma:
(i) non-hyphenated HPLC with UV detector [24]
(ii) hyphenated chromatographic system LC-MS/MS [25,26].
(b) Whole blood and urine:
(i) non-hyphenated HPLC with UV detector [24]
3. Azathioprine:
(a) Human Plasma:
(i) non-hyphenated HPLC with UV detector [27,28]
(b) Human Serum:
(i) non-hyphenated HPLC with electrochemical detector [10].
(ii) non-hyphenated HPLC with UV detector [29].

These chromatographic methods are not exhaustive however those presented provide evidence that first-line drugs used to treat myasthenia gravis can accurately and precisely be determined in biological fluids.

Conclusion

Numerous chromatographic methods have been developed to determine in biological samples drugs employed in the treatment of myasthenia gravis. Tandem mass spectrometry (MS/MS) and other hyphenated methods with higher sensitivities are they preferred analytical methods of interest. However, because facilities are not available in clinical or hospital laboratories for these very expensive hyphenated methods, therefore sensitive, rapid, accurate, precise and less expensive chromatographic methods (HPLC, GC, CE) are routinely used in clinical settings for monitoring of these drugs in biological fluids.

References

1. Drachman DB (1994) Myasthenia gravis. N Engl J Med 330: 1797-1810.
2. Hill M (2003) The neuromuscular junction disorders. J Neurol Neurosurg Psychiatry 74: 32-37.
3. Drossos AA, Christou L, Galanopoulou V, Tzioufas AG, Tsiakou EK (1993) D-penicillamine induced myasthenia gravis: clinical, serological and genetic findings. Clin Exp Rheumatol 11: 387-391.
4. Bruggemann W, Herath H, Ferbert A (1996) Follow-up and immunologic findings in drug-induced myasthenia Med Klin 91: 268-271.
5. Thaniyavarn M, Abin D, Lindsley CW, Nutt JG (2004) Update on myasthenia gravis. Postgrad Med J 80: 690-700.
6. Johnson RT, Griffioen JH (1993) Current therapy in neurologic disease (4th edn). Morby Yellow Book, St. Louis, USA, 379.
7. Mantegazza R, Bonanno S, Camera G, Antozzi C (2011) Current and emerging therapies for the treatment of myasthenia gravis. Neuropsychiatr Dis Treat 7: 151-160.
8. Meyer HG, Lukey BJ, Gepp RT, Corporuz RP, Lieske CN (1988) A radioimmunoassay for pyridostigmine. J Pharmacol Exp Ther 247: 432-438.
9. Miller RL, Verma P (1989) Radioimmunoassay of pyridostigmine in plasma and tissues. PharmacoI Res 21: 359-368.
10. Morya GL, Sinha Pr, Sharma H, Jhanka KK, Sharma DK (2013). Electrochemical behavior and validated determination of the azathioprine in bulk form and body fluids. Der Pharmacia Sinica 4: 80-94.
11. Ramachandra B, Naidu NV (2017) UV-Visible spectrophotometric determination of azathioprine in pharmaceutical formulations based on oxidative coupling reaction with MBTH. Int J Pharm Chem Anal 4: 117-122.
12. Altira KD, Bestford J (1996). Main component assay of pharmaceuticals by capillary electrophoresis: considerations regarding precision, accuracy, and linearity data. J Cap Elect 3: 13-23.
13. Hadley M, Gilges M, Senior J, Shah A, Camilleri P (2000) Capillary electrophoresis in the pharmaceutical industry: applications in discovery and chemical development. J Chromatogr B 745: 177-188.
14. Marino MT, Schuster BG, Bruecker RP, Lin E, Kaminiski A, et al. (1998) Population pharmacokinetics and pharmacodynamics of pyridostigmine bromide for prophylaxis against nerve agents in humans. J Clin Pharmacol 38: 227-235.
15. Yakatan GJ, Tien JY (1979) Quantitation of pyridostigmine in plasma using high-performance liquid chromatography. J Chromatogr 164: 399-403.
16. Breyer-Pfafl U, Maier U, Brinkmann AM, Schumm F (1985) Pyridostigmine kinetics in healthy subjects and patients with myasthenia gravis. Clin Pharmacol Ther 37: 495-501.
17. Michaels EC (1990) Determination of pyridostigmine plasma concentrations by high-performance liquid chromatography. J Chromatogr 534: 291-294.
18. Cherstniakova S, Garcia G, Strong J, Hellbing N, Bi D, et al. (2003) Simultaneous determination of N,N-dimethyl-M-toluamide and permebrin by GC-MS and pyridostigmine bromide by HPLC in human plasma. Applications to pharmacokinetic studies. Clin Pharmacol Ther 73: 27-32.
19. Chan K, Williams NE, Baty JD, Calve YN (1976) A quantitative gas-liquid chromatographic method for the determination of neostigmine and pyridostigmine in human plasma. J Chromatogr 120: 349-358.
20. Sorensen PS, Flachs H, Friis ML, Hvidberg EF, Paulson OB (1984) Steady state kinetics of pyridostigmine in myasthenia gravis. Neurology 34: 1020-1024.
21. Malcolm SL, Madigan MJ, Taylor NL (1990) Thermospray mass spectrometer as a quantitative specific, sensitive, detector for liquid chromatography. Its application to the analysis of pyridostigmine in human plasma. J Pharm Biomed Anal 8: 771-776.
22. De Ruyster MG, Cronnelly R (1980) Reversed-phase, ion-pair liquid chromatography of quaternary ammonium compounds: determination of pyridostigmine, neostigmine and edrophonium in biological fluids. J Chromatogr 183: 193-201.
23. Davison SC, Hyman N, Prentis RA, Dehghan A, Chan K (1980) The simultaneous monitoring of plasma levels of neostigmine and pyridostigmine in man. Methods Find Exp Clin Pharmacol 2: 77-82.
24. Gai MN, Pinilla E, Paulos C, Chavez J, Puelles V, et al. (2005) Determination of prednisolone and prednisone in plasma, whole blood, urine, and bound-to-plasma proteins by high-performance liquid chromatography. Journal of chromatographic science 43: 201-206.
25. Ionita IA, Fast DM, Akhlaghi F (2009) Development of a sensitive and selective method for the quantitative analysis of cortisol, cortisone, prednisolone and prednisone in human plasma. J Chromatogr B 877: 765-772.
26. Frerichs VA, Tornatore KM (2004) Determination of the glucocorticoids prednisone, prednisolone, dexamethasone, and cortisol in human serum using liquid chromatography coupled to tandem mass spectrometry. J Chromatogr B 802: 329-338.
27. El-Yazigi A, Wahab FA (1992) Expeditious liquid chromatographic analysis of azathioprine in plasma by use of silica solid phase extraction. Therapeutic Drug Monitoring 4: 312-316.
28. Maddocks JL (1979) Assay of azathioprine, 6-mercaptopurine and a novel thiourea metabolite in human plasma. Brit J Clin Pharmacol 8: 273-278.
29. Birnheck T, Meyer H, Wellhoner HH (1996) HPLC assay for the measurement of azathioprine in human serum sample. J.Chromatogr B Biomed Anal 2: 287-294.
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