SIGNIFICANCE OF THE INTERACTIVE CLINICAL CASES WITH VIRTUAL PATIENTS FOR LEARNING MEDICAL BIOCHEMISTRY

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Abstract. The present paper describes the significance of 13 interactive clinical cases with virtual patients for learning Medical Biochemistry. The cases have been gradually created as part of the Web-based course "Interactive Biochemistry - Sofia" taught in English and Bulgarian language at the Medical University of Sofia. These interactive clinical cases serve as specialized tests to check as a whole creativity, problem-solving skills and decision-making skills. They are useful for illustrating different theoretical topics and creating links within and between Biochemistry topics and different diseases or clinical conditions. With their Web-based form they fit close to the style of perception of the students of today. The cases are free for educational purposes and are available online and on digital versatile disk – DVD. They are dedicated to the following socially important clinical problems: sickle cell anemia, myocardial infarction, poisoning with dinitrocresol, galactosemia, glycogen storage disease type V (McArdle's disease), diabetes mellitus type 1, hypoglycemia, hypercholesterolemia, phenylketonuria, Parkinson's disease, gout, viral hepatitis and IgA myeloma.

Keywords: interactive clinical cases, virtual patients, medical Biochemistry

Introduction

Medical Biochemistry, as a fundamental science, influences all other medical disciplines. In view of this great responsibility, teaching of Medical Biochemistry at the Medical University of Sofia considers the achievements of pedagogy and rapidly developing information and communication technologies (Khan, 2006; Anderson & Elloumi, 2004) as well as the challenges due to the peculiarities of the net generation (Prensky, 2001; Koch et al., 2009) and last but not least the recommendations of the World Federation for Medical Education.[1)]

Medical Biochemistry is the first discipline that has implemented a problem-solving oriented Web-based learning at the Medical University of Sofia for our Bulgarian and English-speaking international students since 2000 and permanently develops, enriches and upgrades both the virtual learning environment

(Trichkova & Kossekova, 2011) and the bilingual Web-based course "Interactive Biochemistry-Sofia" (http://biochemistry.mu-sofia.bg), in particular the section for the interactive clinical cases with virtual patients (ICCVP). The students, graduating as Masters of Medicine in our university are educated for 6 years. In the first three years they study preclinical subjects. Solving clinical cases within Biochemistry teaching in the second year is the beginning of future professional activities.

Aim

To describe the usefulness and significance of ICCVP for illustrating different theoretical topics and creating links between Biochemistry and different clinical conditions/diseases as well as links within and between different related Biochemistry topics.

Methods

The scope and the algorithm for creation and use of the ICCVP have been described (Kossekova & Guner-Akdogan, 2010). The ICCVP are available for the students at the PHP-based virtual university environment (http://biochemistry.mu-sofia.bg) using common Web browsers (e.g., Internet Explorer, Google Chrome or Mozilla Firefox). The same ICCVP, created also as JavaScript-HTML applications, are part of a digital versatile disk – DVD (Kossekova, 2013) prepared using AutoPlay Media Studio (a visual programming and multimedia software).

The scenarios are based on the theory, clinical correlations and cases described and analyzed in prestigious Biochemistry textbooks, journal papers, Web-sources, or information about real patients in the hospitals at the Medical University of Sofia as specified below for each case. In most cases important additions (e.g. molecular mechanisms) or changes were done in pursue of our aim to bridge Biochemistry and clinical practice.

To prepare branched scenarios for the ICCVP qualitative content analysis of the initial data was applied manually and also by using the Ultimate Research Assistant[2)] based on Hoskinson (2005). Thus the important features, molecular mechanisms and treatment of selected diseases were derived in order to develop realistic scenarios for Web-based ICCVP.

To convert the linear text information to an interactive scenario, the information selected from different sources, was split to small parts. The information is not presented directly at once but gradually, in small portions, step by step. Thus the main features of a given case/disease/condition are used to formulate the following necessary components of the Web-based case: (1) case history; (2) questions related to changing situations, including text, illustrations and schemes; (3) suggested decisions (correct or incorrect with misleading information) for each step as text, formulas or/and schemes; (4) comments to suggested decisions; (5)

data for the inner interrelations between the different steps (screens) determined by the logic of solving the case. Help screens (referent clinical values) and additional information screens to internal and external resources are other necessary components of the case.

Usually 2 to 6 pages linear text from journals or books are converted to about 15 – 20 questions, each one with 5 to 6 proposed decisions and corresponding comments.

The ICCVP contain also data for the weights of the suggested decisions which allows quantitative assessment of the students' decisions. This function is optional. It is more useful for the students in the last years of education. For the second year preclinical students we consider that more important is not the evaluation but bridging the biochemical theory to the clinical practice.

Names were given to personalize the patients as an initial survey has shown that the students feel more engaged and responsible for the patient when they think of him/her as a real person. Collaboration between biochemists and clinicians was useful to create, test and update realistic branched scenarios with different ends (successful or compulsory).

Significance of ICCVP to create links within and between different Biochemistry topics and different clinical conditions/diseases

As creation of such cases is time- and labor-consuming process, only thirteen cases with virtual patients, dedicated to socially important diseases or conditions, have been prepared up to now. Many other clinical correlations are used in the whole Biochemistry course, yet discussed only orally in face-to-face classes but not in the interactive Web-based form as described above.

A case with *sickle cell anemia* (virtual patient "Sandra") illustrates the chapter "Composition, structure and functions of proteins". The scenario is based on the information in (Montgomery et al., 1996a). Proceeding along the diagnostic process, the students have to integrate the theoretical knowledge on the structure and solubility of normal (HbA) and pathological hemoglobin (HbS), tests for HbS, protein separation techniques, molecular diseases, treatment for the disease with different drugs in the past and nowadays with hydroxyurea and other cytotoxic agents which affect maturation of red blood cells and stimulate HbF gene expression in patients.

A case with *myocardial infarction* (virtual patient "Vassil") illustrates the chapter "Enzymes". The scenario is based on the information given in (Montgomery et al., 1996b). Solving the case the students integrate the theoretical knowledge on the structure, isoforms and functions of characteristic intracellular enzymes as creatine kinase, transaminases, lactate dehydrogenase, their appearance and role of their electrophoretic profiles for diagnostics. The therapeutic application of streptokinase and tissue-plasminogen activator (alteplase) for the treatment of myocardial infarction is also included. Role of troponins is given in the additional information.

A case with *poisoning with dinitro-cresol* (virtual patients Stanoy and Ivo) illustrates the chapter "Bioenergetics". The scenario is based on a case described in (Higgins et al., 1994). It helps the students to integrate the knowledge of Biochemistry (dinitro-cresol structure and effect on mitochondrial oxidative phosphorylation in the respiratory chain), Emergency Medicine and Toxicology. The effect of external and natural uncoupling agents, inhibitors of electron transfer and inhibitors of ATP synthesis are compared and more easily understood and learnt.

The chapter "Metabolism of Carbohydrates" is illustrated by three cases. The case with *galactosemia* (virtual patient Rumen) is described in greater details concerning the process of conversion of linear text into a branched scenario (Kossekova & Guner-Akdogan, 2010). It is based on (Dahlquist et al., 1969; Montgomery et al., 1996c). It helps learning of galactose metabolism and differentiating between conditions like galactosemia, phenylketonuria, and jaundice.

A case with the virtual patient Charley is about *glycogen storage disease type V (McArdle's disease)***.** The scenario is written by the late professor Marcel Blanchaer, University of Manitoba, Canada who has been a pioneer in creating computer clinical simulations (Blanchaer, 1984). He has given his permission to use the scenario for preparation of a Web version. Solving this case integrates the theory on anaerobic glycolysis and glycogen catabolism with the specificity of muscle metabolism due to deficiency of glycogen phosphorylase.

The case with the virtual patient Petya is about *hypoglycemia*. It is based on the information in (Montgomery et al., 1996d). The case allows understanding and facilitates learning of important items of carbohydrate metabolism, such as imbalance of glucose production, imbalance of glucose utilization, and also appropriate treatment of the patient. The case accentuates on the most serious side effect of exogenous insulin administration, resulting in severe hypoglycemia. Successful solving of this complicated case also requires knowledge on signal transduction, hormonal regulation, multiple effects of insulin on carbohydrate metabolism, structure of preproinsulin, proinsulin, insulin, and endogenous C peptide.

The chapter "Diabetes mellitus" is illustrated by a case with *diabetic coma* (virtual patient Rossitsa). The case is based on the information in (Murray, 1996a). The case helps to achieve a thorough understanding and facilitates learning of diabetic ketoacidosis, a severe complication of diabetes mellitus type 1 associated with high glucagon-insulin ratio which stimulates ketogenesis in liver and reduces the peripheral utilization of glucose and ketone bodies. Questions about diabetes type 1 as autoimmune disease are included. Besides external symptoms and hyperglycemia due to insulin deficiency, the case focuses on the changes in the carbohydrate, lipid, amino acid metabolism and on the changes which occur in the metabolism of water, K^+ and in the acid-base balance. The case also

includes the most emergency measures to treat the coma and correct the severe metabolic disorders.

The chapter "Metabolism of Lipids" is illustrated by a case with *familial hypercholesterolemia* (virtual patient Vassil 2). The case is based on the information in (Lieberman & Marks, 2009). The case is useful for training of medical students since the frequency of atherosclerosis, myocardial infarction and brain attacks is very high in Bulgaria. Good knowledge of lipid metabolism and mechanisms of atherogenesis are important for prophylaxis and treatment. Together with the main characteristics of familial hypercholesterolemia, the case introduces useful information about plasma lipoproteins, their classification, chemical and physical properties, role of lipoproteins, assembly of lipoproteins and their interactions, enzymes involved in lipoprotein metabolism, lipoprotein metabolism in the artery wall, lipoprotein down-regulated and scavenger receptors, mechanisms of atherogenesis due to a deficiency of LDL-receptors or mutation in apolipoprotein B.

The chapter "Metabolism of amino acids" is illustrated by two cases.

The case with *Parkinson's disease* (virtual patient Dimiter) is based on the information in **(**Murray, 1996b). Initial questions accentuate on the dopamine deficiency as the major pathobiochemical symptom and on the causes for neurons degeneration in substantia nigra and other brain areas. Knowledge of the synthesis and degradation of dopamine is the necessary base to understand the mechanisms of neuroprotection and delaying the disease progression via treatment with anticholinergic agents or dopamine precursors (L-DOPA) in combination of inhibitors of the peripheral DOPA decarboxylase. The case also allows the students to understand and learn about the action of monoamine oxidase and catechol-O-methyl transferase inhibitors, dopamine agonists, and drugs increasing dopamine concentration in the synapses or inhibiting back uptake of dopamine. The harmful action of reserpine and neuroleptics is also considered.

The case with *phenylketonuria* (virtual patient Marina) is dedicated on the most common enzymopathy in the amino acid metabolism, leading to mental retardation. The case is based on data from the Maternity Home Hospital at our university. Solving of the case integrates knowledge on metabolism of phenylalanine and tyrosine with the causes (mutations in the gene encoding phenylalanine hydroxylase), symptoms (accumulation of phenylalanine and its degradation to toxic products, lack of tyrosine and its important derivatives), treatment of classical phenylketonuria and variants. Questions about the lack of the cofactor tetrahydrobiopterin resulting from defects in genes encoding enzymes required to synthesize or reduce the coenzyme dihydrobiopterin are also included. The case points out why phenylketonuria meets the requirements for mass screening of newborn babies.

The chapter "Metabolism of nucleotides" is illustrated by a case with *gout* **(**virtual patient Emil). The case is based on the description and analysis of Montgomery et al. (1996e). It facilitates learning of purine nucleotides metabolism and bridges

this metabolism with allosteric modulation. The case helps to understand the causes for hereditary gout disorders (mutations in genes encoding X-linked phosphorybosyl pyrophophate (PRPP) synthetase, glutamine PRPP amidotransferase, guanine-hypoxanthine phosphoribosyl-transferase) and other enzyme defects leading to gout (glucose 6-phosphatase and aldolase B deficiencies). The mechanism of allopurinol, a structural analogue of hypoxanthine, is presented in details as a competitive inhibitor of xanthine oxidase.

The chapter "Metabolism of porphyrins" is illustrated by a case with *viral hepatitis* (virtual patient Kiril). The case is based on description and analysis of Montgomery et al. (1996f) and Cohn & Roth (1996). The case introduces and checks up all necessary data about different types of porphyrins, hemoglobin breakdown and metabolism of bile pigments, in particular formation and catabolism of bilirubin, differences between indirect and direct bilirubin and enterohepatal circulation of bile pigments. The case also introduces the role of the two important intracellular enzymes aspartate aminotransaminase and alanine aminotransferase and the measurements of the concentration of bile pigments for making differential diagnosis of different types of jaundices.

The chapter "Metabolism of Synthesis of DNA" is illustrated by a case with *IgA myeloma* (virtual patient Todor): cf.[3)] It creates links between the structure and functions of different immunoglobulins, polyclonal and monoclonal gammopathies and the use of modern methods, such electrophoresis of proteins and radial immunodiffusion for diagnosing IgA myeloma. It requires knowledge on DNA synthesis and drugs used to inhibit tumor DNA replication.

Discussion

Educational value of the ICCVP

Problem-solving case approach is an efficient and powerful method for teaching clinical concepts. The Web-based ICCVP have made this approach still more effective and useful. It allows students to test their knowledge and prepares them for the clinical practice. The cases with virtual patients are simplified to the level of second year medical students. The students acquire experience to proceed along the diagnostic process and differentiate among important and misleading information.

Whether each part of the information will be chosen by the students depends on their choice/knowledge/intelligence. This will determine the different exits from the ICCVP: normal successful end (complete solving of the problem), or partial solving of the problem with complications for the patient, or fatal end. Compulsory exits can occur: if the student ignores some of the data; if he/she cannot make the initial diagnosis in spite of the laboratory tests and consultations with specialists; if he/she is not aware of the molecular mechanism of the disease.

ICCVP are specialized tests, which evaluate a higher level of knowledge, creative abilities and professional skills than theoretical tests. Solving a clinical case, the

students can choose from suggested decisions, or make their own decisions. They can reach the correct pathway and solve the case even making mistakes because each chosen decision is commented. The possibility for interrelations between any two screens (steps) allows a variety of outcomes. Thus the students acquire new information. Incorporation of this new information into students' existing framework of knowledge is referred to as a process of consolidation, leading to bigger students' confidence and abilities to communicate and collaborate (Wood, 2004).

Assessment of the ICCVP

Detailed survey on the students' attitude to ICCVP was done (Kossekova, 2003). Correspondent and regular Medical University students' attitude to the ICCVP was definitely positive. The annual oral and written inquiries confirm this positive assessment and stimulate the further creation of ICCVP.

Conclusion

In unison with the significant changes that are taking place in medical education all over the world to fit the World Global standards for higher quality, the clinical cases with virtual patients facilitate integration of basic and clinical sciences and shift of emphasis from passive to active learning. Bridging Biochemistry and Medicine is exciting and useful for students. Solving the cases gives the students an opportunity to learn from their mistakes in a non-clinical environment in order to avoid these mistakes in real life situations.

The authors are open to proposals, suggestions and critical notes.

NOTES

1. http://wfme.org/standards/bme/78-new-version-2012-quality-improvement-in-basic-medical-education-english/file
2. http://www.ultimate-research-assistant.com
3. http://emedicine.medscape.com/article/204369-overview

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