# JOURNAL-BASED LEARNING EXERCISES

Please select your choice of correct answers and complete the exercises online at: **www.ibms.org/cpd/jbl**

## DEADLINE WEDNESDAY 8 JANUARY 2020

### The rivaroxaban-adjusted normalized ratio: use of the prothrombin time to monitor the therapeutic effect of rivaroxaban

Kim B, Jang S, Lee YJ, Park N, Cho YU, Park CJ. *Br J Biomed Sci* 2019; **76** (3): 122–8.
Assessment No: BJBS1019A

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| 01 | Anticoagulants such as warfarin and heparin are widely used to treat venous thromboembolism, and do not require frequent monitoring to ensure correct plasma levels. |
| 02 | Prothrombin time is not a good candidate for a method to measure the plasma concentration of rivaroxaban. |
| 03 | Rivaroxaban is a widely used direct inhibitor of activated factor X (Xa). |
| 04 | The study cohort comprised 337 healthy individuals (157 males, 180 females). |
| 05 | Rivaroxaban (50 mg) was dissolved in 20 mL dimethylsulphoxide (DMSO) to produce a stock solution diluted in phosphate-buffered saline without $Ca^{2+}$ or $Mg^{2+}$ at a final rivaroxaban concentration of 500 mg/mL. |
| 06 | A total of 60 rivaroxaban-spiked plasma samples were analysed. |
| 07 | To evaluate sensitivity variations among different thromboplastins, plots were drawn for the spiked concentration of rivaroxaban and PT of each sample. |
| 08 | Three chromogenic anti-factor Xa assay reagents were used in this study. |
| 09 | Specific rivaroxaban anti-factor Xa activity was measured using two different instruments. |
| 10 | All three thromboplastins tested showed the same sensitivity to rivaroxaban. |
| 11 | The mean (SD) for warfarin-adjusted INR using Neoplastin CI-plus was 1.80 (0.97). |
| 12 | Rivaroxaban-adjusted SI values were different from the current warfarin-adjusted ISI in all tested thromboplastins. |
| 13 | Rivaroxaban-specific NR does not reduce the differences between the PT results from different thromboplastins and coagulometers. |
| 14 | HemoSIL Recombiplastin 2G originates from a human source, so this thromboplastin represents the WHO calibration method. |
| 15 | Studies have shown a poor correlation between the anti-factor Xa assay and mass spectrometric measurement of rivaroxaban in normal plasma samples spiked with known amounts of rivaroxaban. |
| 16 | The authors found that use of a rivaroxaban-adjusted NR did not minimise inter-thromboplastin variability. |
| 17 | Traditional coagulation tests are speedy, widely available and inexpensive, and are suitable for determining plasma DOAC levels. |
| 18 | Spiked samples reflect the potential variations of sensitivity between thromboplastins and between *in vivo* samples with similar levels of rivaroxaban. |
| 19 | Mass spectrometry, the current validated standard, was not used to measure plasma rivaroxaban concentration. |
| 20 | Anti-Xa assay versus NR-rivaroxaban correlation coefficients were 0.97–0.99. |

### Genetic polymorphisms in DNA repair genes and their association with cervical cancer

Abbas M, Srivastava K, Imran M, Banerjee M. *Br J Biomed Sci* 2019; **76** (3): 117–21.
Assessment No: BJBS1019B

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| 01 | Carcinoma of cervix is the third most common cancer among women worldwide, with approximately 530,000 new cases and 275,000 deaths each year. |
| 02 | Epidemiologic studies have shown that most cases of cervical cancer are caused by the human papillomavirus (HPV), mainly HPV-16 and HPV-18. |
| 03 | Among various DNA repair pathways, base excision repair (BER) restores DNA double-strand breaks. |
| 04 | Genetic polymorphisms in DNA repair genes may be associated with repair efficiency of damaged DNA and influence cancer risk. |
| 05 | The Arg188His polymorphism of *XRCC1* plays an important role in pancreatic and colorectal carcinogenesis. |
| 06 | Cervical cancer patients (*n*=230) and healthy age-matched controls (*n*=270) aged between 30 and 70 years were recruited for the study. |
| 07 | Frozen EDTA blood samples were thawed at room temperature and high molecular weight DNA was extracted using a slightly modified salting out method. |
| 08 | The sample size for each SNP was calculated by QUANTO software using major allele frequency and prevalence. |
| 09 | Of the cervical cancer cases, 93.5% were in stages II/III with 6.5% in stages I/IV. |
| 10 | Compared to the GG genotype, adjusted frequencies of GA, AA and GA+AA genotypes were lower in cases compared to controls. |
| 11 | Digested products were visualised on 2% polyacrylamide gel after staining with ethidium bromide. |
| 12 | Cervical cancer is a complex disease where environmental and genetic factors play important roles in pathogenesis. |
| 13 | Women with GA and AA genotypes of *XRCC1*+399A/G showed 2.8–3.4-fold higher risk of cervical cancer. |
| 14 | The raw carriage rates of G (+), G (–) and A (+), A (–) showed significant association with cervical cancer when compared to controls. |
| 15 | Amplification was followed by initial denaturation at 95°C, followed by 35 cycles at 95°C, annealing at 56°C, extension at 72°C, and final extension at 72°C. |
| 16 | The *XRCC3*+18067C/T genetic variant is associated with cervical cancer. |
| 17 | The important molecules of the BER pathway are RAD51, XRCC2 and XRCC3. |
| 18 | In the study population, the frequency of GA and AA genotypes, and the A allele of *XRCC1*+399A/G are significantly lower in cases compared to controls. |
| 19 | Genotypes were determined by polymerase chain reaction-restriction fragment length polymorphism. |
| 20 | The major allele frequency was calculated after genotyping 100 normal individuals for each SNP. |

## REFLECTIVE LEARNING

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| 01 | In certain circumstances, monitoring of plasma rivaroxaban concentration might be needed. Discuss. | 01 | Molecular genetics is set to play an increasing and important role in cytopathology. Discuss. |
| 02 | Explain in detail why this paper by Kim *et al.* represents an advance in biomedical science. | 02 | Explain in detail why this paper by Abbas *et al.* represents an advance in biomedical science. |