Antimicrobial Stewardship
CRP POCT to guide Antibiotic Prescribing decisions for RTI's

Theresa Lowry-Lehnen RGN, BSc (Hons), MSc, PGCE (QTS), H.Dip.Ed, M.Ed, PhD

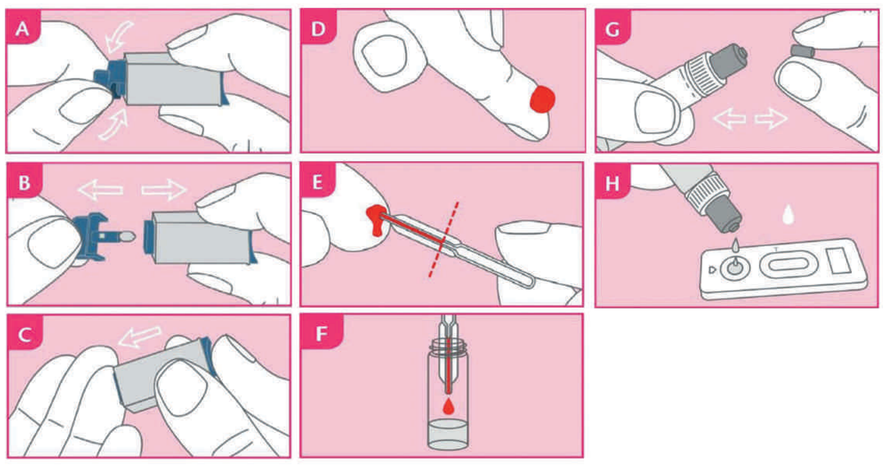
Nurse Practitioner, Tyndall Clinic Carlow

Background

- Antimicrobial resistance is a significant threat to public health, and widely associated with the excessive and inappropriate consumption of antibiotics.
- In February 2018, the Health Information and Quality Authority (HIQA) commenced work on a health technology assessment (HTA) in relation to C-reactive protein point-of-care testing (CRP POCT).
- The aim of the HTA was to establish the clinical and economic impact of providing CRP POCT to inform antibiotic prescribing for patients presenting with symptoms of acute respiratory tract infections (RTIs) in primary care.
- The objective of CRP POCT is to assist the clinician rule out serious bacterial infection, thereby supporting a decision not to prescribe an antibiotic for those who are unlikely to benefit from treatment.
- This small scale study was carried out based on the HIQA HTA, using CRP semi-quantitive (CE marked) testing kits to identify the effectiveness of CRP POCT as a guide to inform antibiotic prescribing decisions for acute RTIs in a well-defined population aged 18-35 yrs, in a primary care setting.
- An estimated 2.4 million prescriptions are issued for respiratory tract infections in Ireland each year. This number could fall to 1.2 million if GPs used CRP POCT and were provided with supports to facilitate conversations with their patients about appropriate antibiotic prescribing.
- Although CRP levels do not allow differentiation between bacterial or viral origin of an infection, they are proxy for the disease severity. Clinical trials have demonstrated that the use of CRP POCT in primary care settings to inform antibiotic prescribing for acute respiratory tract infections leads to a significant reduction in antibiotic prescribing without compromising patient safety.

Methods

- 36 CRP semi-quantitive testing kits (CE marked) were used to carry out the CRP point of care testing. A CRP POCT reader device was unavailable for use in this study.
- To assess the reliability and validity of the CRP POCT semi- quantitive tests used, one third (12) of the subjects in the study consented to a CRP venous blood sample being taken and sent to the lab for analysis and comparison with the test kit results.
- CRP POCT (semi-quantitive) (36 /107) was carried out after history and clinical examination and only when diagnostic uncertainty remained regarding viral or bacterial RTI's.
- C-reactive protein testing to guide URTI antibiotic prescribing in this study followed the manufacturers guidelines.
- To ensure that the semi-quantitive CRP testing kits were being used consistently, a protocol, a flow chart and a simple audit sheet was developed.



Guidelines:

- Do not routinely offer antibiotic therapy if CRP is < 40 mg / L.
- Consider back-up antibiotic prescription if CRP 40–100 mg/ L.
- Offer antibiotic therapy if the CRP is > 100 mg / L.

CRP POCT

- C-Reactive Protein (CRP) is an acute phase protein produced in response to infection or tissue inflammation. CRP is a non specific marker which is mainly produced by the liver and used to diagnose bacterial infectious disease and inflammatory disorders.
- CRP is a very sensitive and fast appearing indicator which can be helpful for deciding if antibiotic treatment is appropriate. Raised concentrations of CRP often occur in bacterial infections, while typically only minor elevations are observed in viral infections.
- With the semi-quantitive CRP tests used in this study interpretation of the result is determined by the intensity of colour of the three lines that appear in the device.
- In healthy patients, CRP concentration is lower than 8mg/L while the concentration level can be higher than 100mg/L in case of severe infection or during inflammatory process. Intermediate levels, within 8 and 100mg/L, are concomitant with more or less mildly viral or bacterial infections that can be easily overcome by appropriate treatment ordered by the clinician.
- The objective of CRP POCT is to assist the clinician rule out serious bacterial infection, thereby supporting a decision not to prescribe antibiotics for those unlikely to benefit from treatment.

CRP POCT Considerations and Debate

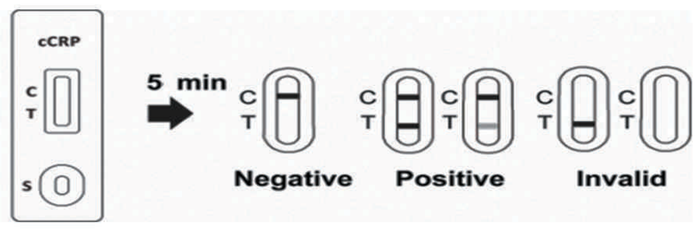
- Debate on CRP POCT and effect on antibiotic prescribing is ongoing. The ability of CRP POCT to aid diagnosis of serious bacterial RTIs remains unclear. CRP POCT can produce false positive or false negative results.
- Medications such as lipid-lowering agents, ACE inhibitors, ARBs, anti-diabetic agents, anti-inflammatory, anti-platelet agents, and beta-adrenoreceptor antagonists are known to lower CRP levels.
- International data suggest that primary care accounts for 80% to 90% of all antibiotic prescribing, with RTIs accounting for approximately 60% of prescriptions for antibiotics issued in that setting.
- In a Eurobarometer survey 44% of Irish respondents reported using at least one antibiotic in 2016 and 39% of respondents in 2017 reported that they were prescribed an antibiotic in the previous 12 months.
- Over 18 European countries have CRP POCT technology available for use in primary care settings.

CRP Screen self testing kit

Antimicrobial Stewardship

CRP POCT

- Provides support for clinicians to facilitate conversations with their patients about appropriate antibiotic prescribing.
- Supports antibiotic prescribing decision & leads to a significant reduction in antibiotic prescribing without compromising patient safety.
- Increases patient satisfaction and understanding of when antibiotics are required or not necessary



Results and Analysis

Primary Care Antimicrobial Consumption Results Ireland (HPSC 2018)

Antimicrobials	2011	2012	2013	2014	2015	2016	2017	2018
Penicillin	12.3	12.5	13.5	13.4	15.3	14.0	13.0	13.2
Macrolides & related drugs	4.2	4.2	4.7	4.5	4.2	4.4	4.2	4.0
Tetracycline	2.8	2.9	3.0	2.7	2.6	2.5	2.8	2.6
Cephalosporin and other beta-lactam drugs	1.2	1.2	1.6	1.1	1.2	1.2	1.1	1.1
Quinolones	0.9	0.9	0.9	0.9	0.9	0.9	0.8	0.8
Sulfonamides & Trimethoprim	1.2	1.2	1.0	1.0	1.0	1.1	1.1	1.0
Other antibiotics	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.1
Total Consumption	22.7	22.9	24.8	23.8	25.3	24.1	23.1	22.9

Total outpatient antimicrobial use in Ireland for recent years by major antimicrobial class, expressed in DDD per 1000 inhabitants per day (HPSC 2018)

CRP POCT Semi-Quantitive Study Results and Analysis

Duration of study Population (RTI's)	12 weeks 107 patients presented with acute RTI symptoms.
Defined Population	18-35 year age group
CRP POCT Semi-quantitive Tests	71 patients were diagnosed and treated appropriately based on clinical history and examination. 36 semi-quantitive CRP POCT tests were carried out when diagnostic uncertainty remained.
Pre-test Decisions	Results based on pre-test decision. (36 Patients) • 19 (52.8%) would have received an antibiotic prescription. • 8 (22.2%) would have been given a backup prescription. • 9 (25%) would not have received an antibiotic prescription.
Post-test Decisions	Results of post CRP semi-quantitive testing. (36 Patients) • 10 (27.8%) patients received an antibiotic prescription. • 7 (19.4%) received a backup prescription. • 19 (52.8%) received no antibiotic prescription.
Results	25% less antibiotics prescribed following semi-quantitive tests. Outcomes followed up at 7 & 14 days.
Backup Prescriptions	2 of 7 (29%) of the post-test backup prescription were used.
Reliability / Validity	1/3 (12) of the subjects tested consented to a CRP venous blood sample being sent to the lab for analysis and comparison. Accuracy of CRP POCT semi-quantitive tests was high = 93%

Result Interpretation

Read the results after 5 minutes

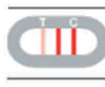
The results are interpreted depending on the intensity of the 3 lines that could appear in the device window.

CRP level lower than 8 mg/L

Only two lines (No line under the mark T (Test)) appear.
This result means that there is neither infection nor inflammation.

CRP level in the range of 8 to 40 mg/L

Three lines appear in the window but the intensity of the 3 lines are more or less equal. This result indicates that a viral or bacterial infection could be developing.

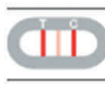


CRP level over 100 mg/L

Three lines appear in the window but the intensity of the lines under T and C marks are stronger than the intensity of the middle line. In case of very high CRP concentration, the middle line may disappear. This result indicates a bacterial / severe bacterial infection.

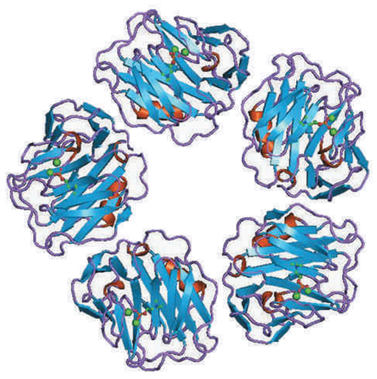
Non valid result

If no line appear under the mark C (Control), it is not possible to interpret the test, which must be considered as non-valid even if a line is visible under T (Test) mark and/or the middle line appears. In this case, it is recommended to repeat the test with a new C-REACTIVE PROTEIN Test.



Discussion and Conclusion

- This study demonstrates that CRP POCT is a useful tool to optimise antimicrobial prescribing in primary care. The study confirms that the use of POCT for CRP can reduce the rate of antibiotic prescription for acute RTIs. Studies show < 40% of patients use backup prescriptions which reducers antibiotic consuption. CRP testing in RTI patients can support antibiotic prescribing decisions, increase patient understanding, reduce over prescribing rates and promote antimicrobial stewardship.
- Cost of the study: Since each test cost around €11.50, purchase of a CRP POCT reader would be more cost effective.
- Practical concern: Within the context of a standard 10 minute consultation an average of 5 additional minutes are required to complete CRP POCT and explain the test results to the patient. This could have a substantial impact on clinicians workload, patient flow and work practices. It is estimated that approximately one quarter of consultations in primary care are for RTI's and that approximately 34% of these would be associated with clinical uncertainty. The introduction of CRP POCT could add 5 minutes to approximately 8% of all consultations.
- Sources of error: Can include collection procedure; sample quality; competence of the sample taker, poor device maintenance and transcription errors relating to the test result. Sources of error can be moderated through regular training and the use of robust standardised operating procedures, however they cannot be eliminated.
- The accuracy between the reference test and the POCT was found to be good with the semi-quantitive devices used in this study, but also shown to decrease after the optimal 5 minutes. Semi-quantitive devices narrow CRP threshold choices available for clinical guidance on higher CRP cut-points. The semi-quantitative tests used in this study were effective, however a CRP POCT reader would be a more reliable, cost effective and accurate device for long term use.



C-Reactive Protien Structure

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