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URINE TEST REAGENT FOR CANCER SCREEN AND MONITORING (URC)

HEALTH TECHNOLOGY ASSESSMENT UNIT

MEDICAL DEVELOPMENT DIVISION

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Prepared by:

Dr Izzuna Mudla bt Mohamed Ghazali
Principal Assistant Director
Health Technology Assessment Unit
Ministry of Health Malaysia
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Reviewed by:
Datin Dr Rugayah bt Bakri
Deputy Director
Health Technology Assessment Unit
Ministry of Health Malaysia
October 2007

EXECUTIVE SUMMARY

Introduction

Cancer can affect any part of the body and lead to high morbidity and mortality. Cancer screening may reduce cancer morbidity and mortality. Various procedures for cancer screening have been introduced. This technology review was carried out to assess the safety, effectiveness and cost-effectiveness of Urine-test reagent for cancer screen and monitoring (URC). It was requested by the Medical Resource Unit, Medical Development Division, Ministry of Health Malaysia.

Technical features

URC react with tumor markers in urine by forming precipitate and change its colour. The color of the precipitate is compared with the standard color plate to determine the results**.**

Conclusion

There were insufficient evidence on the safety, effectiveness and cost-effectiveness of URC.

Recommendation

Further research is needed to determine the safety, effectiveness and cost-effectiveness of URC.

URINE TEST REAGENT FOR CANCER SCREEN AND MONITORING (URC)

1. INTRODUCTION

Cancer is a generic term for a group of over 100 chronic diseases, which can affect any part of the body. A defining feature of cancer is the rapid creation of abnormal cells, which grow beyond their usual boundary and can invade adjoining parts of the body. Cancer is one of the leading causes of death in the world, particularly in developing countries. In 2005, 7.6 million people died of cancer out of 58 million deaths worldwide. Based on projections, cancer deaths will continue to rise with an estimated 9 million people dying from cancer in 2015, and 11.4 million dying in 2030.[1]

In Malaysia, according to the Malaysian Burden of Disease and Injury Study, cancer ranks sixth in the overall burden of disease and is responsible for 6.6% of the total disability adjusted life years (DALYs). Almost 96% of the burden of cancer was contributed by the fatal component of burden of disease.[2] It is estimated that the premature deaths that could have been avoided through screening vary from 3% to 35% depending on variety of assumptions. Screening may also reduce cancer morbidity since treatment for earlier-stage cancers is often less aggressive than that for more advanced-stage cancers.[3]

For each type of cancer, various screening procedures have been introduced. For example, breast cancer screening can be done through clinical breast examination, breast self examination as well as mammography.

Various types of urine test reagent have been developed to detect diseases or conditions. Some are established method such as urine pregnancy test and urine test for glucose and protein, and more are still in development stage.

URC is a urine test reagent developed for cancer screen and monitoring. This technology review was requested by the Medical Resource Unit, Medical Development Division following an application to market the product to government hospitals and community.

2. OBJECTIVES

To determine the safety, effectiveness and cost-effectiveness of URC in cancer screening and monitoring.

3. TECHNICAL FEATURES

URC is the abbreviation of Urine-test Reagent for Cancer Screen and Monitoring. It is a reagent developed by Wuhan Chenkang Science & Technology Co. Ltd. for cancer screening. It measures the in vivo cancer orientation or whether a person has cancer, thus enables early cancer detection, and follows by early diagnosis and early treatment.

According to the manufacturer the development of the product was based on the theory that in pre-cancer or early cancer stage, abnormal multiplication and proliferation of cancer cells lead to abnormal body responses and amino acid metabolism. Amino acids such as tryptophan, tyrosine and other metabolic by products or derivatives like 5-Hydroxyindole Acetic Acid and p-hydroxyphenylypruvic acid etc in urine are found to be much higher in cancer patients than in the normal individual.

URC will react with the above tumor markers in urine by forming precipitate and change its colour. Therefore, colour change of the reagent implied cancer cells activity even though an individual remains asymptomatic, thus enabling early detection and prevention of cancer.

The manufacturer claimed that URC can be used:-

1. To detect the abnormal metabolism found in cancer development.
2. To detect the early sign of cancer so that early investigation and diagnosis can be made to increase the success rate of treatment and to reduce suffering and medical expenses in treatment.
3. To monitor the effectiveness of cancer treatment. URC can help the physicians in choosing and adjust the therapy and dosage.
4. To monitor and follow up on post-treatment recovery of recovered cancer patients, so that early intervention can be initiated in relapse and recurrence of cancer

URC is composed of nitric acid, sulfuric acid, mercurous nitrate, mercuric sulfate, naphthol and biological abstract. URC also contains a standard board indicator to which the reagent – urine solution is compared.

Method of testing:

Add 3 ml of clean, morning urine specimen into ampoule with 0.5ml of reagent. Shake it well and leave it for 3-5 minutes. Compare the color of precipitate with the standard color plate to determine the result. If the result is negative, there will be no color change or color change of the precipitate to yellow color. If the result is positive, there will be color change of the precipitate to red or brown color. Any color that resembles 5-8 will be considered as positive result.

1. **Main interference factors which can cause false positives:**
    1. Amino acids, hormones, stimulant for the nervous systems, etc.;
    2. Alcohol (for those who have a high sensitivity to alcohol) and other hypersensitivity reactors;
    3. Strenuous exercise, work, lack of oxygen intake, bleeding.
2. **Main interference factors which can cause false negatives:**
    1. Ataractics, acesodyne, antihypertensive drugs;
    2. Nourishing substances and having drank too much water;
    3. Persons with a lack of stress responsiveness due to having a certain type of cancers, such as leukemia or brain cancer, already receiving cancer treatment, or in the late stages of cancer.

4. METHODOLOGY

4.1 SEARCH METHODS

Literature were searched through electronic databases, which included Pubmed, OVID, Proquest, Ebscohost, EBM Reviews for controlled trials, Cochrane database on systematic review, Cochrane Clinical Trial Registry, Science Direct, Springer Link, INAHTA databases and general databases such as Google and Yahoo.
The search strategy used the terms, which are either used singly or in various combinations: "URC" OR "urine-test reagent" OR "urin* metabolites" OR "5-hydroxyindole" OR "p-hydroxyphenylpyruvic acid", cancer OR carcinoma OR carcinoid, effectiveness OR efficacy, safety OR safe OR "adverse effect*" OR "harm* effect*" OR toxicity, "cost effectiveness" OR "cost analysis" OR econom*. There were no limitations in the search.

Literatures were also provided by the distributor URC Global Sdn. Bhd.

4.2 SELECTION OF STUDIES INCLUDED/EXCLUDED

All primary papers, systematic reviews or meta analysis pertaining to safety, effectiveness and cost effectiveness of URC were included in this study.
A critical appraisal of all relevant literature was performed and the evidence level graded according to the Oxford Centre for Evidence-based Medicine Levels of Evidence (May 2001) (Appendix 1).

5. RESULTS AND DISCUSSION

There were no published papers on URC retrieved. Therefore, the results and discussion will be based on the papers provided by the distributor.

5.1 SAFETY

URC was manufactured in People's Republic of China and registered with People's Republic of China, State Food and Drug Administration on 30 April 2004. No registration with US Food and Drug Administration (FDA) or with other countries' compliance agencies obtained. Safety issues in cancer screening procedure includes risks of serious complications that may be immediate or delayed as well as harm due to false-positive result, which may lead to anxiety and unnecessary invasive diagnostic procedure. Another harm, is the false-negative results which may falsely reassure an individual with subsequent clinical signs or symptoms of cancer and thereby actually delay diagnosis and effective treatment.

All the studies provided by the manufacturer did not compared URC with gold standard in diagnosis of cancer.[4,5,6,7,8,9] All the cancer subjects in the studies were diagnosed cases but the method of diagnosis were not standardized.

Since the screening method only uses urine, risks of serious complications did not aroused. However other form of harm should be taken into account in assessing this screening and monitoring tool.

5.2 EFFICACY/EFFECTIVENESS

As a screening tool, URC should be sensitive enough to detect cancer at early stage where intervention may improve the outcome of the patient. There was no evidence retrieved to show that this tool is capable to do that. Based on the available evidence, the sensitivity of URC to detect confirmed cancer cases, ranged from 59.8% to 61.0%. [4,6,7 Level 4] Only one study showed that the sensitivity was more than 80% (81.8%).[5 Level 4]

As for monitoring tools, the available evidence only showed that there were significant difference in the positive rate of URC before and after treatment but there were no evidence retrieved to show that the results correlate with clinical regression of the cancer.[5,9 Level 4]

The evidence also showed that there were various factors that could interfered the results of URC which may lead to false positive or false negative results.[8 Level 4]

Further longitudinal and more specific research should be carried out to assess the effectiveness of URC.

5.3 COST-EFFECTIVENESS

There was no evidence retrieved on the cost-effectiveness of URC. However, the cost per test is RM88.00.

6. CONCLUSION

There were insufficient evidence regarding the safety, effectiveness and cost-effectiveness of URC.

7. RECOMMENDATION

From the results of the above review, URC, as now, cannot be recommended until more clinical research is available to support its safety and effectiveness.

8. REFERENCES

1 . World Health Organisation. Cancer. World health Organisation (website). Retrieved on 17 October 2007 from http://www.who.int/cancer/en/

2 . Ahmad Faudzi Y, Amal Nasir M, Gurpreet K et al. Malaysian Burden of Disease and Injury Study. Health Prioritization: Burden of Disease Approach. Division of Burden Of Disease, Institute for Public Health, National Institutes of Health, Ministry of Health Malaysia, 2004.

3. National cancer Institute. Cancer Screening Overview (PDQ®) health Professional version. Last modified 3 February 2007Retrieved on 16 October 2007 from http://www.cancer.gov/cancertopics/pdq/screening/overview/healthprofessional/allpages

4. Cancer Hospital Clinical Laboratory, Cancer Hospital Chinese Academy of medical Sciences. Urine test reagent for cancer screen and monitoring clinical research and application, and its popularization. In: Urine-test reagent for cancer screen and monitoring project. Wuhan Chenkang Technology Company Limited, pg 9-13.

5. Beijing Cancer Hospital. Clinical report on probation of urine-test Reagent for cancer Screen and monitoring Test Reagent. In: Urine-test reagent for cancer screen and monitoring project. Wuhan Chenkang Technology Company Limited, pg 14-16.

6. Zhang F. Verified report on clinical application of medical appliance by experts in Hebei Province. Hebei Medicine Inspection Bureau Character (97651), number (0047), 1997. In: Urine-test reagent for cancer screen and monitoring project. Wuhan Chenkang Technology Company Limited, pg17-22

7. Yankun A, Xinqiang J. Clinical application of urine-test reagent for cancer screen and monitoring. In: Urine-test reagent for cancer screen and monitoring project. Wuhan Chenkang Technology Company Limited, pg 26-31.

8. Niu F, Chen Z, Li M et al. Report on urine reagent for cancer screen and monitoring application in general inspection of gynecopathy at Wuhan iron & Steel Group Co., Ltd. In: Urine-test reagent for cancer screen and monitoring project. Wuhan Chenkang Technology Company Limited, pg 32-36.

9. Cao Y. Primary exploration on curative effect of early cancer screening and monitoring of TSGF & urine-test reagent cancer screening and monitoring. In: Urine-test reagent for cancer screen and monitoring project. Wuhan Chenkang Technology Company Limited, pg 43-47.