proteins such as HIF-1 or using hypoxia to obtain tumour specific gene expression for gene therapy.

Tyrosine Kinase inhibitors as Radiation Sensitizers

The discovery of highly selective and potent compounds called the 4-anilinoquinazolines has led to the development of small molecule tyrosine kinase inhibitors as potential anti cancer agents. These agents inhibit essential cellular pathways in growth factor expression and can be administered as an oral formulation. Some of these agents, such as ZD 1839 and OSI-774, tend to bind in vitro only to the epidermal growth factor receptor tyrosine kinase while others, such as C1-1033, bind to multiple members of the ErbB family. The first clinical compounds that were developed such as ZD 1839 were reversible inhibitors. Recently developed irreversible compounds may be found to be more effective at producing long-term suppression.

These molecules have the ability to block cell growth, decrease the clonogenic potential of cells after chronic exposure, down regulate specific genes important for neoplastic potential and to sensitize cells to the lethal effects of ionizing radiation. In vitro studies have shown that combining multifraction radiation exposures (15Gy) with chronic administration of CI-1033, (an irreversible inhibitor of Erb B Kinases) can decrease the number of clonogens in a population of breast cancer cells by nearly a factor of 100 compared to that achieved with radiation alone[10]. Preliminary in vivo studies have shown that the combination of fractionated radiation and CI-1033 can produce a significant growth delay beyond that which occurs from either treatment alone. This occurs even when the cells have only moderate (i.e. clinically relevant) over expression of EGFR. Histopathologic evaluationof tumours treated with radiation and CI-1033 show central tumour and vascular necrosis, suggesting that the combination effect may depend on anti-angiogenic or other cytokine mediated factors.

Conclusion

The advances in molecular biology and the insight into the mechanisms of neoplastic transformation, progression and its response to radiation therapy is just beginning. A new frontier is being opened up, the vast vista of this knowledge is still in infancy and the next few years will help us unravel these mysteries.

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Literature Review

Compiled by Dr. P.D. Gulati

Efficacy of tamsulosin in the medical management of juxtavesical ureteral stones. Dellabella M, Milanese G, Muzzonigro G. J. Urol 2003Dec;170(6Pt1):2202-5.

The authors evaluated the efficacy of the alpha-adrenergic antagonist tamsulosin for conservative expulsive therapy in patients with ureteral colic due to juxtavesical stones. A total of 60 consecutive symptomatic patients with stones located in the juxtavesical tract of the ureter were randomly divided into group 1-30 who received oral floroglucine-trimetossibenzene 3 times daily and group 2-30 who received 0.4mg tamsulosin daily. The 2 groups received 30mg deflazacort daily for 10 days plus cotrimoxazole 2 times daily for 8 days and 75mg diclofenac injected intramuscularly on demand. Ultrasound followup and medical visits were performed weekly for 4 weeks. Stones passage rate and time, analgesic use, hospitalization and endoscopical intervention were evaluated. Statistical analysis was performed using the student test. The stone expulsion rate was 70% for group 1 and 100% for group 2. Mean stone size was 5.8 and 6.7mm, respectively (p=0.001). Mean expulsion time was 111.1 hours for group 1 and 65.7 hours for group 2 (p=0.020). The mean number of diclofenac injections was 2.83 for group 1 and 0.13 for group 2 (p<0.0001). Ten group 1 patients were hospitalized, of whom 9 underwent ureteroscopy, compared with none in group 2 (p<0.001, respectively). Tamsulosin used as a spasmolytic drug during renal colic due to juxtavesical calculi increased the stone expulsion rate and decreased expulsion time, the need for hospitalization and endoscopic procedures, and provided particularly good control of colic pain.

Association of Small Dense LDL with Coronary Artery Disease and Diabetes in Urban Asian Indians: Chennai Urban Rural Epidemiology Study.V Mohan, R Deepa, K Velmurugan, K Gokulakrishnan. JAPI 2005;53:95-99.

Earlier studies in Europeans have identified small dense LDL to be associated with coronary artery disease and diabetes. In this study we assessed the associated of small dense LDL with diabetes and CAD in Asian Indians. Study subjects were selected from the Chennai Urban Rural Epidemiology Study (CURES), a population based study on representative sample of Chennai City in Sourthern India. Group 1:non-diabetic subjects (n=30); Group 2: diabetic subjects without CAD (n=30); Group 3: diabetic subjects with CAD (n=30). LDL subfractions were estimated using LipoPrint LDL system. LDL subfractions 3 and above, defined as small dense LDL was summed up to determine the overall small LDL. 75th percentile of the overall small dense LDL in non-diabetic subjects was used as a cut-off for defining elevated levels of small dense LDL.

The mean age of the study subjects was not significantly different among groups. Overall small dense LDL was significantly higher in diabetic subjects with CAD (16.7 $\pm$ 11.1mg/dl, p<0.05) and without CAD (11.1$\pm$8.0mg/dl, p<0.05) compared to non-diabetic subjects without CAD (7.2$\pm$6.8mg/dl). Small dense LDL showed a positive coirrelation with fasting plasma glucose (r=0.252, p=0.023), HbA1c (r=0.281, p=0.012), total cholesterol (r=0.443, p<0.001), riglycerides (r=0.685, p<0.001), LDL (r=0.342, p=0.002), total cholesterol/HDL ratio (r=0.660, p=<0.001) and triglycerides/HDL ratio (r=0.728, p<0.001) and a negative correlation with HDL cholesterol (r=-0.341, p=0.002) and QUICKI values (r=-0.260, p=0.019). ROC curves constructed to predict elevated small dense LDL (9.0mg/dl) revealed that triglycerides/HDL ratio and total cholesterol/HDL ratio had higher AUC values compared to other parameters. A triglycerides/HDL ratio of 3.0 had the optimum sensitivity (80.0%) and specificity (78.0%) for detecting elevated small dense LDL.

This data suggests that in Asian Indians, small dense LDL is associated with both diabetes and CAD and that a triglycerides/HDL ratio (3.0 could serve a surrogate marker of small dense LDL.