Advances in Chemotherapy

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Overview of session

• Brief overview of chemotherapy in cancer care: systemic anti-cancer therapy (SACT).
• Advances in chemotherapy.
• Supporting people undergoing chemotherapy.
• Implications for community nurses.
Anti-cancer interventions

Principle modalities

• Surgery
• Radiotherapy
• Cytotoxic chemotherapy
• Hormone therapies
• Biological therapies

one or more may be used in any given case
Specificity of anti-cancer treatment

- Surgery/XRT
- Chemotherapy
- Hormone therapy
- Biological therapy
- Cancer cell
Cytotoxic Chemotherapy: mode of action

Cell-cycle non-specific agents: active throughout the cell cycle;
- Cisplatin/Oxaliplatin
- Adriamycin
- Cyclophosphamide

Prevent cell from going through mitosis;
- Vincristine, Vinblastine
- Paclitaxel, Docetaxel

Prevent development of elements necessary for mitosis;
- Etoposide
- Irinotecan
- Bleomycin

Prevent cells moving out of G1 phase
- steroids

Prevent development of elements necessary for DNA/RNA synthesis;
- Methotrexate
- 5FU
- Gemcitabine
Chemotherapy can be;

- Adjuvant: given in addition to potentially curable treatment.
- Neo-adjuvant: given before potentially curable treatment.
- Primary: no other treatment intended.
- Palliative: non curative intent (although may still be ‘radical’).
Who gets chemotherapy?

- Chemo sensitive tumour
- Post–op “high” risk: tumour size & grade, lymph node status, vascular invasion
- Young/fit inoperable
- Neo-adjuvant eg ovary, breast “de-bulking"
- Relapsed/metastatic/ symptom management
- Clinical trials
Advances in chemotherapy

• Cytotoxic chemotherapy
  – New drugs/new combinations;
    • Chemo-resistant tumours – prior treatment or innate resistance
    • Lower toxicity profile
    • Oral administration
    • More effective
    • Mainly ‘non-curative’ or clinical trials
Drawbacks of chemotherapy

- Non selective: cancer cells AND healthy cells targeted.
- Not all cells exposed at any given time.
- Side effects: cannot predict severity of side effects.
- Cancer cells can be resistant or become resistant.
Targeted therapies

• Targeted cancer therapies are drugs or other substances that block the growth and spread of cancer by interfering with specific molecules ("molecular targets") that are involved in the growth, progression, and spread of cancer. (NCI, 2014).

• Comparison to chemotherapy;
  • Specific target associated with the cancer as opposed to all replicating cells.
  • Designed to interact with target as opposed to cell-killing action.
  • Many are cytostatic rather than cytotoxic (ie stop proliferation rather than kill).

• Main types;
  • Angiogenesis inhibitors
  • Immunotherapies
  • Monoclonal antibodies
  • Vaccines
How do targeted therapies work?

- Faulty/too many receptors on surface
- Faulty/too many messengers in cell
- Special proteins on surface
- Unable to repair faulty DNA
- New blood supply

Find out what makes the cancer cell different then target that.
Biological therapies

Biological therapy involves the use of living organisms, substances derived from living organisms, or laboratory-produced versions of such substances to treat disease (NCI, 2013);

- Cytokine therapies
- Antibody based therapies
- Small molecule therapies
- Cancer vaccines
- Gene therapies
Biological therapies work in two main ways

- Promote or support the body’s existing immune system response

- Use components of the immune system as a basis in order to kill tumour cells (or repress disease growth)
Immune system and cancer

- Protects against invasion
  - Skin, mucous membranes, acid etc
- Surveillance
  - Seek and destroy
- Role in cancer
  - Development
  - Treatment
  - Spread
Biological therapies can be used to:

- Kill cancer cells
- Block processes of cancer growth and spread
- Enhance the body’s ability to repair or replace cells damaged by chemo/XRT
- ↑ susceptibility of cancer cells to destruction by immune system
- Deliver toxic substances into cancer cell
Antibody based therapies: monoclonal antibodies (MAB’s)

- Antibody developed in laboratory to respond to cancer cell antigen (“lock and key”)
- Trigger immune system to then kill cell and/or cell kills itself
- Deliver toxic substance to cell which kills it
Clinical examples (1)

- **Herceptin (Trastuzumab)**
  - Approx 20% breast cancers over-express a protein called HER2
  - HEGF is a growth factor protein which occurs naturally in human body
  - HEGF attaches to receptor (HER2) on breast cancer cell surface
  - Messages sent to breast cancer cells to divide and grow more
  - Herceptin attaches to HER2 receptor instead so that HEGF cannot reach cell
  - Herceptin also attracts immune cells to help destroy cancer cell
Herceptin in Breast Cancer

- Surface antigens
- Killer Leukocyte
- Breast cancer cell
- Monoclonal antibody
- Complement
- Apoptosis
Clinical example (2)

- **Mabthera (Rituximab) in NHL**
  - CD20 is a protein found on surface of all B-cell lymphocytes
  - CD20 also found on surface of NHL malignant B-cell lymphocytes in large quantities
  - Mabthera locks on to and affects both malignant and normal B-cells
  - Body is able to quickly replace damaged normal cells but malignant cells unable to grow
Cytokine therapy

• Cytokines are proteins released by one cell to interact with receptors on another

• Involved in regulation of immune system response (fever, inflammation, antibody production, white cell development)

• Supportive cytokine therapy;
  – G-CSF
  – Erythropoietin
    – Produce new cells

• Cytokine cancer therapy;
  – Interferon (MM, renal, lymphoma, leukaemia)
  – Interleukin (MM, renal)
    – Stimulate/support immune function
Angiogenesis inhibitors

- Block the growth of new blood vessels to tumour
- Tumour deprived of oxygen and nutrients needed for growth
  - Bevacizumab (Avastin): advanced disease (bowel, lung)
  - Thalidomide: myeloma
Small molecule kinase inhibitors

- Tiny chemicals selected for their ability to bind and block a particular protein. May have multiple targets.
- Small enough to enter the cell. May cross BBB.
- May be oral preparation.
- Drug companies have huge libraries of chemicals that can block kinases – therefore drug development is quick and costs are relatively low.
- Not yet in widespread use: mostly advanced disease and clinical trials.
  - Afatinib (Giotrif)/Erlotinib (Tarceva) (NSCLC)
  - Lapatinib (Tyverb) (breast)
Cancer vaccines

• Stimulate the immune system to recognise and destroy cancer cells
• Use small amount of altered/weakened form of disease
• Target both cancer cell antigens and also antigens produced by cancer causing viruses
Clinical example

- Cervical cancer vaccine
  - HPV virus gets into normal cell DNA (viral DNA into host DNA) causing mutation
  - Cells stop responding to normal signalling controls
  - Uncontrolled cell growth leads to more mutations and cancer
  - Vaccine stops binding between viral and normal DNA
  - Could be both preventative and therapeutic
Gene therapy

• Early stage of development
• Patient-specific therapy/personalised medicine
• involves putting genetic material (DNA) into cells so that cells produce certain proteins which can then;
  • Kill cell
  • Make cell more sensitive to chemo/radiation
  • Strengthen immune system response
  • Replace faulty part of gene
  • Make cells resistant to side effects of treatment
Gene therapy: the future of anti-cancer treatment?

• Specimen of tumour obtained during surgery/blood sample
• Analysis in laboratory to identify faulty genes or tumour antigen
• Faulty gene corrected and replaced back into the body or
• Antibody to antigen developed and then injected into patient or tumour
Challenges in biological therapy

- Not all cells in tumour will express antigen in required amount or on cell surface
- Normal cells may express the antigen
- Uptake by tumour cells variable
- Multiple strains of viruses exist (>100 HPV) many of which will not respond to one vaccine

- Very expensive
- Much remains unknown about actions of biological agents
- Potential/actual side effects do occur despite treatment targeting cancer cells
- Long term effects of therapies
- Natural course of disease changing
Supporting patients undergoing chemotherapy: acute oncology assessment and triage

- National Confidential Enquiry into Patient Outcome and Death (NCEPOD) report of 2008 “For better, for worse?”;
  - Poor care in oncology patients, especially those receiving SACT (both curative and palliative)
  - Only 35% of patients received ‘good’ care
  - Approximately one third of patients’ deaths may have been caused or hastened by treatment.
- In Scotland, CAG/Scottish Government Health Directorate made this a national priority.
- Every acute hospital should have an acute oncology service to co-ordinate care and management of acutely unwell oncology patients.
West of Scotland initiative

• AOAU:
  – Day case area for urgent assessment/monitoring
  – 8am – 8pm Mon – Fri
  – Last admission 6pm
  – Current patients/within 6 weeks of completion
  – Oncology NPs with medical back up
24 hour Cancer Treatment Helpline

• Available to all Beatson WoSCC oncology patients on or within 6 weeks of treatment.
• ONPs from AOAY 8am – 8pm Mon – Fri
• Unit nurses 8am – 8pm weekends
• 8pm – 8am cover by National Cancer Treatment Helpline (diverted to NHS24)
Advice for patients: contact if:

- Shivering or flu-like symptoms
- Temperature greater than 37.5°C
- Gum/nose bleeds or unusual bruising
- Mouth ulcers that prevent eating and drinking
- Persistent nausea/vomiting/diarrhoea/constipation
- Leg weakness/difficulty walking
- Worsening or sudden breathlessness
- Sudden increased or uncontrolled pain
- Any other concerning symptoms associated with treatment
Assessment tool

- Prompt the practitioner with appropriate questions to ask in order to gain information from the patient
- Prioritise the level of urgency indicated by the presenting symptoms and will aid in identifying potential emergency situations
- Cancer Treatment Helpline
Assessment tool

• RED any toxicities graded here take priority and action should follow immediately.

• Two or more AMBER toxicities should be escalated to red action.

• Amber one toxicity in amber should be followed up within 24 hours. The caller should be instructed to call back if they continue to have concerns or their condition deteriorates.

• Green callers should be instructed to call back if they continue to have problems or their condition deteriorates.
Following assessment;

- Attend local A&E/AOAU
- Advice and follow up call within 24 hours
- Call back if condition deteriorates
- Advice
- Call back if condition deteriorates
Implications for community nurses

- Training and education
- Patient/family education
- Patient support: emotional, physical, psychosocial and financial
- Where to access information
Thank you