Pharmacokinetic 在臨床上的應用

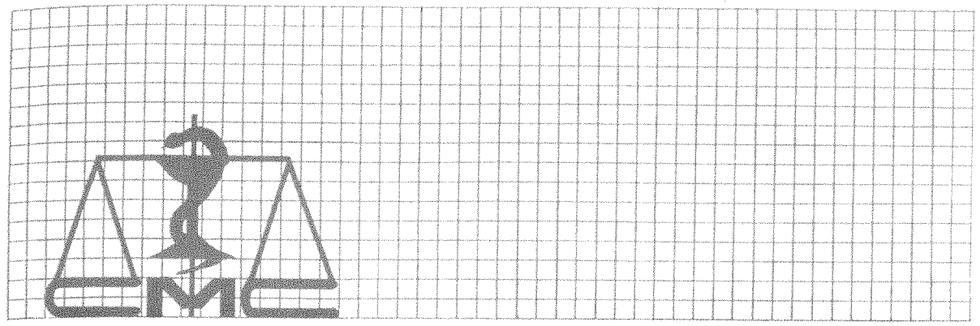
演講者■ 國防醫學院藥學系
藥物動力學
胡幼圃 教授

記 錄■ 傅敏娟

1. Traditional Pharmacy
   - Dispensing(unitdose. TPN)
   - Manufactwring
2. Clinical Pharmacy
   - clinical pharmacokinetic laboratory
   - therapeutics
   - drug information center
   - 提供醫療專業資料
3. drug at absorption site → drug in blood ⇄ (k, k-1) → drug in other fluids of distribution
   - drug in blood —k4→ drug in urine
   - drug in blood —k5→ metabolites
   - drug in blood —k6→ drug in other excretory fluids

∴藥物動力學是以數學方式描述drug 在人體內的 absorption, distribution, metabolism, excretion 速率過程之定量。（研究藥物濃度，因時間的變化情形）

3. Pharmacalogy is divided into 2 parts
   (1) pharmacodynamic



   (2) pharmacokinetic
   pharmacodynamics　　pharmacokinetic 久服後 receptor site reactivity改變為 pharmacodynamics 改變，如：CPZ, MAO-inhibitor

4. 影響 Pharmacokinetics factors.
   (1) effect of gastrointestinal disease
   (2) effect of hepatic disease
   (3) effect of Cardiac disease
   (4) lung and metabolic drug clearance
   (5) plasma, memerane, plasma protein binding effect.
   (6) Chronopharmacology
   (7) Pregnancy
   (8) Pediatric
   (9) Geriatric
   (10) Smoking
   (11) Burn patient
   (12) TDM

以下說明前12.項

① half-eife 變化情形與 dosage 的關係
(eg) liver disease
half-life of antipyrin in normal subject and in patients with a variety of liver disease with normal $t_{\frac{1}{2}}$ = 12 hrs liver function 差者 $t_{\frac{1}{2}}$ = 20-hrs 肝硬化者 $t_{\frac{1}{2}}$ =30-hrs half life 改變dosage

②影響drug 在血中conc 的 factors
ⓐ吃藥時間不同
ⓑ懷孕時 albumin↓，影響酸性 drug 與 albumin binding
ⓒ age 會影響

age↑ → clearance ↓

age↑ → metaboliem, extraction slow

ⓓ smoking與 nonsmoking 比較

③Therapeutic drug Monitoring(TDM)

以 pharmacokinetic principle apply therapeutic drug monitoring 做爲 drug 參考(dosage adjustment)

△ Clinical indications and drugs that TDM should be performed.

（要知有效劑量，在下列情況下考慮ＴDM）

ⓐ欲確定治療方式是否恰當

ⓑ欲尋找有效藥物 conc. range

ⓒ懷疑side effect or toxicity是否爲drug 造成

ⓓ用drug 後缺乏療效， drug 在病人體內的Clearance or absorption 有關

ⓔ懷疑drug 使用過量 or drug 同時使用， drug 間交互作用。

ⓕ病人同時有其他疾病可能影響藥物動力學之參數

ⓖ drug side effect 與疾病非常類似

ⓗ需調整dosage form

△臨床上需ＴDM之特性及監測之主要目的特性

ⓐ有效drug conc range 狹小

ⓑ藥物動力學參數受藥物 conc 影響（非一次動力學）

ⓒ動力學參數受個人差異影響大

ⓓ療效不易評估

ⓔ drug side effect 和所患病的症狀不易區別

ⓕ預防用給藥

5. The appropriate time for sampling

(1) absorption and distribution phases are complete

(2) steady state

(3) trough or peak conc are based on the $t_{1/2}$ of the drug

6. Methodology used in therapeutic drug Monitoring

(1) GC

(2) HPLC

(3) Biossay

(4) EIA

(5) FIA

(6) FPIA

(7) GC-Mass

7. (eg) a patient (70kg) with congestive heat failure digoxin therapeutic plasma conc = 1.5 ng/ml

loading dose = Cpss. Vd

= 1.5 ng/ml (70kg × 7.3 l/kg) = 0.77mg

oral dose = IV dose/F

= 0.77mg/0.62

= 1.24 mg

(eg) Same patient 50 years old male, serum creatinine 1.9mg/dl digoxin maten-ance dose = (clt, $\overline{cpss}$, T)/ F

= 0.31 mg/day

Clcr = (98 - 0.8 (age-20))/SrCr = 74 ml/min

Cltol = 23 ml/min + 0.88 Clcr = 88 ml/min

(eg) same patient with renal disease

Srcr = 5 mg/dl Cclcr = 15 ml/min

Vd changed with uremia

(Vd = 269 + 3.12. Clcr)

loading dose (Vd $\overline{Cpss}$)/ F = 0.762 mg

(orally)

Maintenance dose = (Clt-$\overline{Cpss}$-T)/ F

(orally) = 0.125 mg/day

由血中 conc → clearance (計算)

(eg) 60 years old woman (60kg) with chronic[6] renal failure and a seizure disorder hemodialysis there times a week and takes 300mg/day of phenytoin should her daily dose be increased

Cpss = 7 mg/l (α = 0.25)

Cpss(free) = 0.25 7 mg/l = 1.75 mg/l

therapeutic range (10-20 mg/l)

was evaluated based on α = 0.1

Cpss (total) = 1.75 mg/l ÷ 0.1 = 17.5 mg/l

if seizure disorder is well controlled No adjustment is necessary

8. The benefits derived from TDM were found to be as follows.

(1) decreased mortality

(2) increase deconomic productivity associated with decreased mortality

(3) fever adverse reaction

(4) shorten intensine care unit stay

(5) shorten overall hospital stay

(6) shorten peroid of time to place on oral therapy

(7) (more important) improving the quality

主講者：國防醫學院藥學系
藥物動力學副教授
胡幼圃先生