Carbon Dioxide
Using Gas in Angiography and PTA

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Assessing $CO_2$ Toxicity

ANIMAL STUDIES

- Renal toxicity
- Hepatic toxicity
- Neuro-toxicity
- Effect on cardiopulmonary circulation
Assessing CO₂ Renal Toxicity
Studies performed on Dogs

**Renal Study**

7 cc/kg of CO₂ were injected into the renal artery in lateral decubitus

- **Radioisotope infusion**, to determine renal function, was done:
  - 24 hours pre-injection
  - Immediately after injection
  - 24 hours after injection

- Immediate Post CO₂ injection - Transient change in blood flow
- 24 hours Post CO₂ injection - Resumed normal flow and function
- SEM showed no changes to endothelial lining, renal parenchyma

**Conclusion:** CO₂ has no renal toxicity

Dr. Hawkins, Univ. of Florida
Assessing CO$_2$ Hepatic Toxicity
Studies performed on Rabbits

Hepatic Study

CO$_2$ was injected into the hepatic artery

• Blood samples to determine ALT (Alanine Transferase)
  • Pre injection (Baseline – Normal)
  • Immediately post – injection (Transient elevation)
  • 7 days post-injection (Return to baseline normal)

• Liver pathology study 7 day post-injection:
  • No significant abnormalities in histopathology

Conclusion: CO$_2$ has no long term hepatic toxicity.
Assessing \( CO_2 \) Cardiopulmonary effect

Studies performed on swine

**Venous Study**

15 \( CO_2 / 5 \) IC, (0.2cc/kg - 6.4cc/kg) IVC

- \( CO_2 \) injected in three different positions:
  - Supine
  - Right decubitus
  - Left decubitus

- Parameters obtained pre-injection and 1, 3, 5, 10 minutes after injection:
  - Pulmonary arterial pressure: *Transient increase*
  - Systemic arterial pressure: *No change*
  - Arterial blood gases (1, 3, 5, 10 min. post inj.): *No change*

- 2 Expired (1IC 3.2cc/kg, 1CO\(_2\) 6.4cc/kg rd)

- **Conclusion:** *Diagnostic doses have no significant effect on cardiopulmonary function.*

Dr. Cho - Univ. of Michigan
Assessing $\text{CO}_2$ Neuro-Toxicity

Studies performed on dogs

**Coronary/Neuro Study**

4-9 injections for a total of 120-300cc per dog

- 9 - injections ascending aorta
- 3 - injections common carotid
- 2 - injections both arteries

Shifrin, et al

**No Change in EEG, ECG, Arterial Blood Gases.**
Assessing $CO_2$ Neuro Toxicity
Experiments performed on rabbits

**Coronary / Neuro Study**

- 27 received 12cc/kg CO2
- 11 received 12cc/kg Renografin 76
- 11 received 12cc/kg Saline

All injections into the left ventricle

Dr. Bettmann Boston Univ

- No damage to Myocardium
- No damage to Blood/Brain barrier
- No differences among study groups
Assessing $CO_2$ Neuro-Toxicity
Experiments performed on albino rats

Intra-carotid injection of CO2 produces:

- Multifocal ischemic infarctions
- Disrupted blood-brain barrier
- Lesions of the endothelial cell membrane

Conclusion: $CO_2$ should not be used for angiographies of cerebral arteries

Coffey, Quisling, Mickle, Hawkins, Ballinger: Radiology 1984 May;151(2):405-10
Assessing CO₂ Toxicity: Human Studies

Retrospective Study

208 procedures / 189 patients (138 males / 70 female, 9 to 86 yrs.)

- CO₂ injected in all 208 procedures
- CO₂ and iodinated contrast 175 procedures
- CO₂ alone 33 procedures.

Results:

- 32 AE with CO₂, 6 with iodinated contrast
- Most common CO₂ AE: GI related (nausea)
- Most common with iodinated AE: Allergic reaction

University of Florida
Assessing $CO_2$ toxicity: Human Studies

**Safety Study**

21 Patients, ages of 50 to 90 years
10 patients $CO_2$ / 11 patients Optiray® 320.

**Safety**: AE’s, ABG levels of $CO_2$, $O_2$, pH, bicarb levels

**Efficacy**: paired images read by investigator

**Results:**

- 1 AE with iodinated contrast, none with $CO_2$
- No significant changes (pH, CO2, O2, or bicarbonate)
- All $CO_2$ films diagnostic, (IC Films - 45% diagnostic-55% excellent)

Boston University and Dartmouth

**Conclusion**: $CO_2$ is at least as Safe as Iodinated Contrast Medium.
Assessing $CO_2$ toxicity: Human Studies

**Canadian Trial**

IND Study - 2 Clinical sites
- 20 patients per site, 40 patients total
- Patients received both iodinated contrast and $CO_2$
- Paired images compared for efficacy
- Blood gases, adverse events, vital signs used for safety analysis

**Results:**
- AE’s in 51% of study group
- Most common AE-injection site reaction (32%)

- Safe & Effective - Peripheral Angiographic Evaluation
- Diagnostic Utility Comparable to OPTIRAY® 320
Review of Clinical experience with \( \text{CO}_2 \)

*Relevant studies*

- Renal transplant arteriography in children 1997 V Kriss et al (Lexinton KY)
- Upper arm venography to insert CV lines 1995 S Hahn et al (Seoul Korea)
- Congenital renal A-V malformation 1993 T Miyanaga et al (Japan)
- Embolization and AV shunts in liver Ca 1994 Y Teshima et al (Japan)
CO₂
Specific Advantages

- Non Allergenic
- *20 times* more soluble than O₂ in blood
- Non Toxic
- *400 times* less viscous than iodinated contrast
- Allows Low Pressure Injections
- Buoyant for Anterior Vessel Filling
- Radiolucent
Setup A: hand injection

Setup:
- Digital Subtraction Angiography
- CO$_2$ canister N48-99.998
- Laparoscopic insufflators
- Bacterial filter
- 20 ml. Syringes
- Three way stop-cock
- One-way anti-reflux connector

Advantages:
- Perfect timing
- Complete injection control
- May arrest injection at any moment
- Inexpensive

Dis-advantages:
- High radiation exposure for the Operator
- Open system
- Possible air contamination
Setup B: *automatic injection*

**Setup:**
- Digital Subtraction Angiography
- Automatic self-priming CO\(_2\) Injector
- Bacterial filter
- 50 or 100 ml. Syringes
- Two three-way stop-cock
- No anti-reflux connector

**Advantages:**
- Lower radiation exposure
- Closed system
- Self-priming
- No air contamination

**Disadvantages:**
- Timing imprecise
- Limited injection control
- Slightly higher cost due to kit
Retrospective study

- Informed consent specific for CO₂ injection
- 1999 – 2007 - 8-year period
- Single operator

- 654 procedures
  - 245 arteriographies
    - 64 CO₂ only
    - 181 CO₂ and Iopamiro
  - 409 PTA
    - 185 CO₂ only
    - 224 CO₂ and Iopamiro
119 episodes of Pain or discomfort in 7290 injections
- 75 out of the first 180 injections in 12 procedures (42%)
- 44 out of the subsequent 7110 injections in 642 procedures (0.6%)

15 complete failures (>50 ml of iodinated contrast used) (2.3%)
- Uncooperative patient
- Excessive bowel motility and air content
- Unclear visualization of details

157 partial failures (<50 ml of iodinated contrast used) (24%)
- Good visualization of only a part of the arterial tree
- Need for iodine contrast integration in part of the exam

482 complete success (No iodinated contrast used) (73.7%)
- Only Carbon Dioxide used to complete the exam
- Satisfactory visualization and guidance
Additional complications

- Mild intestinal discomfort (4%)
- Delayed CO$_2$ reabsorption in 2 cases (0.3%)
- Missed renal artery in 2 cases
- Missed popliteal aneurysm in 1 case
- No allergic reaction
- No fluid overload
- No patient death
CO$_2$ versus CO$_2$ + iodine contrast

- 122 patients retrospective study

  - Pre-angio creatinine level (p=0.46)
    - 2.8 ± 1.4 mg/dl in CO$_2$ only group
    - 3.0 ± 1.4 mg/dl in CO$_2$+iodine group

  - Post-angio creatinine increase (p=0.27)
    - +0.17 ± 0.87 mg/dl in CO$_2$ only group
    - +0.03 ± 0.98 mg/dl in CO$_2$ + iodine group

Dowling J Endovasc Ther 10(2):312-6 2003
$\text{CO}_2 + \text{small amount of iodinated contrast}$

versus

Iodinated contrast alone

82 patients

prospective randomized study of Renal angiography and PTRA

The amount of iodinated contrast was significantly related to an increase in serum creatinine 2-days post-procedure ($p=0.011$)

The larger the amount of iodinated contrast, the higher the risk of renal failure

Liss, Berqvist, Olsson, Nilsson: J Vasc Interv Rad;16(1): 57-65 2005
<table>
<thead>
<tr>
<th>Procedure</th>
<th>Pre op</th>
<th>3 days Post</th>
<th>significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Complete failure</td>
<td>1.8 ± 0.4</td>
<td>2.9 ± 0.9</td>
<td>p &lt; 0.05</td>
</tr>
<tr>
<td>Partial failure</td>
<td>1.9 ± 0.6</td>
<td>2.0 ± 0.8</td>
<td>ns</td>
</tr>
<tr>
<td>Complete success</td>
<td>1.7 ± 0.8</td>
<td>1.8 ± 0.4</td>
<td>ns</td>
</tr>
</tbody>
</table>
Is CO$_2$ adequate for readability?

- 50 cases - Retrospective study PTA-PTRA
  - 88% CO2 only
  - 12% additional iodinated contrast needed


- 100 cases – Retrospective study EVAR
  - CO2 versus Iodinated
    - Longer operating time
    - Longer fluoroscopy
    - Higher radiation exposure
    - Similar procedural success
    - No change in creatinine levels
    - 81% additional iodinated contrast needed

  *Chao, Major, Weaver et al. :J Vascular Surgery 45(3);451-60 2007*
CO$_2$ in renal transplant evaluation

- 17 patients retrospective study

- CO$_2$ compared to iodinated contrast as Gold standard
  - No false positive
  - Positive predictive value = 100%

Lorsch et al.: CO$_2$ angio in transplant Rontegnpraxis 55(1) 26-32 2003
CO$_2$ (Stacking) Software

Un-Stacked

Stacked

Courtesy of ANGIODYNAMICS®
Comparing Accuracy

**Fluid Iodine contrast**

Fluid-Angio shows good results of stenting
The stent structure is not visible due to contrast opacity

**Gaseous CO\textsubscript{2} Contrast**

Gas-Angio shows protruding plaque through the stent
The stent structure is made visible by the negative effect of the gas-contrast

Interventional Profundoplasty
Iodine contrast
Superficial Femoral artery stenosis

Nitinol stent insertion
Arteriography with CO₂
Leg elevation by means of a radiotransparent table may sometimes improve gas delivery to the distal vessels.
Iliac artery angiogram

Iodine

CO₂
CO₂ Hand Delivery Set
Syringe injection: 90% of CO2 is injected in the last 0.5 sec during a 4 sec. injection
Visualization of distal vessels in the leg in a young girl with borderline renal failure due to nephrotic syndrome
Selective left renal gas arteriogram
Selective Right renal artery gas arteriogram
Checking right renal stent insertion with a gas aortogram
Leg and foot arteriograms
Comparing iodinated fluid contrast versus CO₂ gas contrast
Distal Peroneal artery
Lateral and medial plantar arteries
Comparing Fluid and Gas contrast

Carbon Dioxide, visualizes a longer segment of patent tibialis posterior.
This is an useful indication for a surgeon when performing a bypass showing more suitable space to accommodate and perform the distal anastomosis.
A long term control with CO2 because of the radiolucency of the gas lets one see both the flow inside the vessel and the structure of the stent.
CO₂JECT Injector

- CO₂ tank: 1,000,000 ml gas
- Autonomy: 2000 injections
- Cost in Italy: ........ Euro
- No explosive Delivery
- Computerized adjustment to catheter length and lumen
- ECG gated
- Double capability: Iodinated & CO₂ injection head
- Complete monitoring system
CO$_2$ Arteriography

Why?

- Avoid allergic reactions to contrast
- Avoid renal toxicity
- Avoid fluid overload
- Reduce costs
- Utilize thinner catheters
- Visualize stents
- Oncological embolization
CO$_2$ Arteriography

*When?*

- Borderline renal failure
- Chronic renal failure on dialysis
- Renal transplant vascular evaluation
- Previous reactions to contrast
- Evaluation of stent function and status
- Evaluation of Gastro-Intestinal bleeding
- Evaluation of Arterio-Venous fistulas
CO₂ Arteriography

How?

- N48-99.998% CO₂
- Disposable canister
- Bacterial Filter
- Hand Injection
- Laparoscopy set
- Safety bag

- CO₂-Jet (Angiodynamics)
CO₂ Arteriography
*When Not?*

- Neurovascular Studies
- Uncooperative patients
- Poor quality equipment
- Most studies above the diaphragm
- Untrained eye
- Learning Curve
An Integrated Approach

Carbon Dioxide
- Borderline Renal failure
- Terminal Renal Failure
- Allergic Reactions
- Load Reduction

Iodinated Contrast
- Supradiaphragmatic Angio
- Coronary angiography
- Neurovascular Studies
- Uncooperative Patients
- Posterior Located Vessels

Peripheral Angiography
- PTA
- Endoprosthesis
Conclusion

Angiography with gas (Carbon Dioxide) eliminates:

– allergic reactions
– fluid overload
– renal toxicity