Carbon Dioxide: An Alternative to Iodinated Contrast Media*

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Objectives: To study the use of carbon dioxide as a contrast medium for arteriography.

Methods: Carbon dioxide was used as a contrast medium for intra-arterial digital subtraction lower limb angiography in 12 examinations on 11 patients.

Results: No complication was encountered and no significant changes occurred in the arterial pH, PaCO2 and PaO2. The quality of images as assessed by an independent observer was adequate for the majority of the vessels (77%).

Conclusions: Carbon dioxide is a safe alternative in patients at an increased risk of adverse reaction to iodinated ionic or non-ionic contrast medium and is very cheap.

Introduction

Modern non-ionic low osmolar contrast media are relatively safe and produce good quality angiographic images. However, their use is not entirely free from problems in certain situations. Nephrotoxicity is a well recognized side effect of intravascular contrast. The risk of renal damage is particularly high in patients with diabetes, hypertension, dehydration, multiple myeloma and in the presence of impaired renal function;1 conditions which often co-exist with peripheral vascular disease. The risk of allergic reaction to iodine containing contrast has been estimated to be 4–7% in atopic individuals,2 rising to 38% in those with a previous history of adverse reaction to contrast.3 Rapid injection of contrast can result in pulmonary oedema particularly in patients with poor ventricular function.4 Carbon dioxide has been used successfully in the past as a negative contrast for cystogram,5 arthrogram6 and angiogram.7,8 In the present study CO2 has been evaluated in a prospective controlled study as an angiographic contrast medium during digital subtraction peripheral angiography.

Patients and Methods

Twelve examinations were performed on 11 patients with a median age of 72 years (range 67–82 years). All the patients were being investigated for peripheral vascular disease. Approval was obtained from the University Hospital Ethics Committee and informed consent was obtained from the patients. Angiography was performed with both iopamidol (Niopam, E. Merck Ltd) and Carbon dioxide in 9/12 procedures and CO2 was used alone in three examinations. Of these three procedures two were performed in a patient with a history of severe adverse reaction to iodinated contrast and another patient had refractory cardiac failure. Anterior femoral wall puncture technique was used for the introduction of a 5 F angiographic flush catheter. Iopamidol injections were carried out with the catheter in the abdominal aorta. For CO2 injections the catheter was withdrawn into the external iliac and direct intra-aortic injection was avoided. Medical grade CO2 (BOC Medical gases, Guildford, Surrey U.K.) was drawn into a 60 ml syringe from a laparoscopic insufflator. The syringe was flushed with CO2 a few times to eliminate any air and ipsilateral images were obtained following rapid hand injection of 50 ml of CO2 for each run. The leg was elevated approximately 20° to facilitate the forward flow of CO2 aided by buoyancy. Arterial blood gases were obtained before and within 1 min of completion of the study in 10/12 cases and analysed for pH, PaCO2 and PaO2 on a blood gas analyser.

*Presented at the 8th annual meeting of the European Society for Vascular Surgery, Berlin, Germany (September 1994).

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Paired images obtained with Niopam and CO$_2$ were blindly assessed by MJH (a vascular radiologist from another region) without any knowledge of the nature of the study. He was asked to select the better image in each pair and using it as the standard, grade individual vessels in the other image as adequate or inadequate on the criteria that no important clinical information was missing or misinformation was present. Statistical analysis was performed by using Wilcoxon paired rank signed test for comparing the changes in arterial blood before and after the procedure.

**Results**

1. No complication occurred in any of the procedure.
2. The median volume of CO$_2$ used was 200 ml (range 200–300 ml).
3. There was no significant change in the arterial pH, PaCO$_2$ and PaO$_2$ following CO$_2$ angiography (Figs. 1, 2 and 3).
4. In each pair the image obtained with Niopam was selected as the better image.
5. The quality of images were totally adequate in the Femoral and popliteal regions. Overall 23% of the
images were deemed to be inadequate. Of these 6% were iliac and 17% were tibial images.

(6) Bilateral superficial femoral angioplasties were performed on two separate occasions on one patient who had a history of major adverse reaction to iodinated contrast with good radiological, haemodynamic and clinical result (Fig. 4).

(7) One diagnostic examination was successfully carried out with a 20 G cannula placed in the femoral artery.

Discussion

Carbon dioxide (CO$_2$) has been used as a radiological contrast medium for more than three decades. As an angiographic contrast medium CO$_2$ has been in use since 1968 by Bendib et al. who has reported uncomplicated use of intravenous CO$_2$ in more than 1600 patients for diagnostic study of the right side of the heart. In patients with peripheral vascular disease CO$_2$ was first used intra-arterially as a vasodilator agent by Bartley et al. more than 20 years ago. During subsequent study on therapeutic use of CO$_2$ in patients with peripheral occlusive arterial disease by the same group, it was observed that CO$_2$ delineated the artery by acting as a negative radiological contrast. Since then Hawkins and Herrera have reported safe use of CO$_2$ for angiography in more than 300 patients. However, in Europe the use of CO$_2$ as a contrast medium for peripheral angiography has not been widely reported. Moreover, the quality of images obtained during peripheral digital subtraction arteriography using CO$_2$ and non-ionic iodinated contrast has not been compared in the past.

The important risk factors related to contrast
medium induced renal damage are pre-existing renal insufficiency, diabetes mellitus with the risk becoming more significant in patients with diabetic nephropathy. In a prospective study of non diabetic patients with impaired renal function undergoing intravenous urography (IVU) the incidence of acute renal failure has been reported to be as high as 62%. Patients undergoing IVU are more likely to have impaired renal function than those undergoing arteriography but the volume of contrast used for peripheral angiography is nearly three to four times greater than the volume used for IVU and there is some suggestion that the nephrotoxicity may be dose related. CO$_2$ could therefore be used as an alternative for arteriography in patients with impaired renal function, diabetic nephropathy and multiple myeloma who are at an increased risk of contrast induced renal damage. The iodine load following injection of 100 ml of triiodinated non ionic contrast medium could be 3–4 g. This could produce hyperthyroidism in euthyroid

![Image of angiography](image)

Fig. 5. (a) Ipsilateral digital subtraction angiography with intra-arterial CO$_2$ injection. (b) Paired image obtained with Niopam 300 (Merck Ltd.).
individuals with autonomous thyroid nodules\textsuperscript{13} and 
\textsuperscript{10} CO\textsubscript{2} again offers a safe alternative in such patients.

In patients with impaired ventricular function, injection of osmolar contrast medium can lead to 
pulmonary oedema particularly when the volume 
injected exceeds 200 ml.\textsuperscript{4} CO\textsubscript{2} does not add to the 
circulatory fluid load and could again be useful in 
such patients.

One other advantage of CO\textsubscript{2} is its low viscosity 
which is almost 400 times less than the conventional 
mono acid monomeric salt contrast medium.\textsuperscript{10} This 
means that angiography can be performed via rela-
tively fine catheters and small puncture in the femoral 
artery. In the present study we were able to perform 
the procedure with a 20 G cannula (Viggo, Spect-
tramed) instead of the standard 4 or 5 F catheter.

Because there is some evidence from animal studies 
that CO\textsubscript{2} may be neurotoxic,\textsuperscript{14} we avoided direct 
aortic injection to avoid any adverse effect on the 
spinal cord. The visualisation of the proximal iliac was 
therefore dependent upon reflux of the CO\textsubscript{2} and could 
account for the 6% of the inadequate images being in 
the iliac region (Fig. 5a). It seems likely that antegrade 
filling of the iliac artery from aortic injection would 
overcome this problem. Of the inadequate images 17% 
were in the tibial region. In some studies fragmenta-
tion of the column of CO\textsubscript{2} was seen in the tibial vessel 
(Fig. 5a). It appears to be related to slow transit in 
patients with poor ventricular function. However, the 
visualisation of tibial vessels was not a consistent 
problem and good images were also obtained (Fig. 
6).

Cost is an important consideration. A cylinder of 
CO\textsubscript{2} containing 450 l of medical grade CO\textsubscript{2} costs less 
than 100 ml of non-ionic contrast. In other words, the 
contrast cost of angiography with non-ionic contrast is 
1000 fold greater than CO\textsubscript{2}. However, the overall cost 
benefit may not be a significant one if CO\textsubscript{2} is used only 
selectively in a relatively small number of patients at 
an increased risk of adverse reaction to iodinated 
intravascular contrast.

In the present study no complication was encoun-
tered and no significant changes were observed in the 
arterial pH and gases. This is somewhat expected 
since the volume of CO\textsubscript{2} used for each study was close 
to the amount excreted by the body each minute at 
rest. CO\textsubscript{2} injection not only enabled diagnostic angiog-
raphy but angioplasty was also performed in a patient 
with bilateral SFA stenosis who had a major adverse 
reaction to iodinated contrast in the past. Duplex scan 
guided angioplasty which requires two operators is 
another technique that can enable angioplasty without 
the use of intravascular contrast.\textsuperscript{13} With further 
experience it may provide another safe alternative for 
localised studies and angioplasty.

In summary, CO\textsubscript{2} is safe and effective as a contrast 
medium during peripheral angiography with digital 
subtraction imaging. It could be used as an alternative 
in patients with history of adverse reaction to iodin-
nated contrast and those individuals who are at an 
increased risk of renal damage and pulmonary 
 oedema from the conventional intravascular 
contrast.
Contrast Media

References

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Accepted 28 December 1994