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Effect of ketofol on persistent pain in patients with cancer that has spread to the bone

Submission date	Recruitment status	[ ] Prospectively registered
08/11/2013	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
21/11/2013	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
13/06/2014	Cancer	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Intractable (unmanageable) cancer pain is a serious health problem when the cancer spreads to the bone. There are options for relieving cancer pain. Conventional painkillers are usually used according to the principles of the World Health Organization. Cancer patients generally develop tolerance to systemic opioids. As conventional pain relief methods do not always relieve intractable cancer pain, researchers are investigating drugs such as ketamine to increase the effectiveness and to decrease their side effects. Ketamine has been recommended to effectively relieve pain patients with chronic pain. Ketamine can also be used as an painkiller for cancer pain. Some studies suggest that another drug, propofol, has pain relief properties, and it has been used as an adjuvant painkiller. We put forward that giving ketamine plus propofol, known as ketofol, may be effective in patients with intractable cancer pain.

Who can participate?
Patients who had intractable cancer pain caused by the cancer spreading to the bone can participate in this study.

What does the study involve?
The patients were randomly allocated to two groups. The control group received a placebo (dummy) fat emulsion and the ketofol group received ketamine plus propofol into their vein. We recorded age, body measurements, heart rate, blood pressure and pain. These measurements were done at the start of the study and at various intervals for 48 hours.

What are the possible benefits and risks of participating?
Patients in the ketofol group may experience a reduction in pain. The side effects include nausea, vomiting, hallucination, double vision, dreaming and nightmares.

Where is the study run from?
The study is run from Ankara Numune Training and Research Hospital, Ankara, Turkey.

When is study starting and how long is it expected to run for?
The study started in December 2009 and is expected to run for 3 months.

Who is funding the study?
Devrek-Dent Private Health Care Limited Company, Turkey.

Who is the main contact?
Dr Derya Gokcinar
dgokcinar@yahoo.com

Contact information

Type(s)
Scientific

Contact name
Dr Derya Gokcinar

Contact details
Yildirim Beyazit Mahallesi, Derman Caddesi, No.17 Kazan, Ankara, Turkey
Ankara
Türkiye
06980
+905052283639
dgokcinar@yahoo.com

Additional identifiers

Protocol serial number
B100IEG0110001

Study information

Scientific Title
The analgesic effect of ketofol on intractable pain in cancer patients with bone metastasis

Study objectives
It was hypothesised that Ketofol infusion relieved pain and decreased the supplemental analgesic requirement in patients with intractable cancer pain with bone metastasis. The null hypothesis was that there was no any analgesic effect of ketofol on intractable pain in cancer patients with bone metastasis.

On 13/06/2014 the following changes were made to the trial record:
1. The anticipated start date was changed from 03/12/2012 to 01/12/2009
2. The anticipated end date was changed from 03/07/2013 to 28/02/2010
3. The target number of participants was changed from 85 to 80

Ethics approval required
Old ethics approval format

Ethics approval(s)
Ethics committee of the Turkish Ministry of Health, Ref: B100IEG0110001

Study design
Prospective double-blind randomized controlled trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Intractable pain in cancer patients with bone metastasis

Interventions
Based on the dosage of ketamine, propofol and ketofol for the sedation and/or analgesia in the previous studies, we conducted a preliminary study on 20 cancer patients with intractable pain to determine the effective analgesic ketofol dose without performing sedation. We found that the dosage of ketofol including ketamine 5μgkg per min and propofol 5μgkg per min could maintain Ramsey Sedation Score at 2 and the VAS pain score < 4 cm in more than 50% of the subjects.
All patients for analgesia was initially provided via titrating morphine in increments of 3 mg every 5 min until the VAS pain score was < 4 cm. Patients were also given access to a PCA device set to deliver 1mg boluses of IV morphine, with a lockout period of 5 min and no background infusion or limits. The PCA regimen was continued for 48 h. The patients were randomly divided into 2 groups. The control group (n = 36) received intravenous 10% fat emulsion (Intralipid® 10%, Fresenius-kabi Turkey Inc., Istanbul, Turkey) 5μgkg per min over 48 h and the ketofol group (n = 36) received Racemic ketamine (Ketalar®, Pfizer Warner Lambert Turkey Inc., Istanbul, Turkey) 5μgkg per min plus propofol (Propofol 1% Fresenius®, Fresenius-kabi Turkey Inc., Istanbul, Turkey) 5μgkg per min over 48 h. Propofol (150 mg) and ketamine (150 mg) were diluted with 0.9% sodium chloride (150 mL); the concentration of both ketamine and propofol was 1 mgml per min.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Ketofol

Primary outcome(s)
1. VAS scores were recorded at baseline (after first morphine titration), 1 h, 3 h, 6 h, 12 h, 24 h and 48 h
2. Cumulative morphine consumption (CMC) was recorded at 1 h, 3 h, 6 h, 12 h, 24 h and 48 h after the start of the drugs infusion

Key secondary outcome(s))
1. Age, gender, weight, height, underlying disease, length of stay in hospital (LOS) measured at baseline
2. Vital status at hospital was evaluated at one month
3. Simplified acute physiology score III (SAPS III) points, and SAPS III predicted mortality (%) were

recorded at baseline
4. Heart rate (HR) and mean arterial pressure (MAP) were recorded by an independent investigator at baseline, 5 min, 15 min, 30 min, 1 h, 3 h, 6 h, 12 h, 24 h and 48 h
5. Side effects including nausea, vomiting, hallucination, double vision, dreaming and nightmares were recorded at 48 hours

Completion date
28/02/2010

Eligibility

Key inclusion criteria
1. Intractable cancer pain caused by bone metastasis
2. Age 18 years or over
3. Recent use of the fentanyl patch
4. Duration of pain being 4 weeks or longer
5. Visual analog scale (VAS) pain intensity score during the previous week ≥ 5 cm (on a scale of 0-10 cm)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
We excluded the patients with a confirmed or suspected allergy to intravenous fat emulsion, propofol or ketamine

Date of first enrolment
01/12/2009

Date of final enrolment
28/02/2010

Locations

Countries of recruitment
Türkiye

Study participating centre
Yildirim Beyazit Mahallesi, Derman Caddesi, No.17 Kazan, Ankara, Turkey
Ankara
Türkiye
06980

Sponsor information

Organisation
Devrek-Dent Private Health Care Limited Company (Turkey)

Funder(s)

Funder type
Industry

Funder Name
Devrek-Dent Private Health Care Limited Company (Turkey)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration